

**Microcurrent therapy in the
management of chronic tennis
elbow**

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Abstract

Microcurrent therapy (MCT) involves the application of sub-sensory electric current and can promote tissue repair, possibly by mimicking endogenous electrical cues for healing. It has been used successfully to treat recalcitrant bone fractures and skin ulcers, but its effects on other forms of tissue have received little attention. This study aimed to investigate the potential of MCT to promote healing and alleviate symptoms in a selected soft connective tissue disorder.

A systematic review of human studies involving MCT for soft connective tissue damage was conducted. A survey of 93 musculoskeletal physiotherapists was used to help select a common, recalcitrant disorder to treat with microcurrent in a clinical trial. Novel sonographic scales to quantify tendon structural abnormality and tissue healing were developed, and their measurement properties evaluated along with several clinical and patient-rated outcome measures. Two preliminary clinical trials, involving 62 people with the selected disorder – chronic tennis elbow - were conducted, comparing four different types of microcurrent applied daily for 3 weeks.

The review found fair quality evidence that certain forms of MCT can relieve symptoms, and low quality evidence that they can promote healing, in several soft connective tissue disorders, including those affecting tendons. Optimal treatment parameters are unknown. In the survey, clinicians identified frozen shoulder, plantar fasciitis and tennis elbow as particularly problematic, and tennis elbow was selected for treatment in the trials. The sonographic scales of hyperaemia had fair-to-good inter-rater and test-retest reliability. Minimum Detectable Change values are calculated for the sonographic scales and for pain-free grip strength measurements.

The trials suggest that monophasic microcurrent of peak amplitude 50 μA applied for 35 hours was most effective in symptom alleviation, with a 93% treatment success rate three months after treatment. By final assessment, pain-free grip strength increased by 31% (95%CI:5,57%), pain measured on a multiple-item questionnaire reduced by 27% (95%CI:16,38%) and patient-rated functional disability by 26% (95%CI:14,28%). MCT with a current amplitude of 500 μA was significantly less effective, and varying the waveform appeared less important in determining outcomes. Differences between groups were non-significant on several measures, though there was a risk of type II error in the tests used. No significant differences between any groups were seen in sonographic assessments, although consistent patterns in bloodflow change suggested that MCT may modulate hyperaemia levels. Higher baseline hyperaemia was associated with sustained falls in hyperaemia levels after treatment, and with improved clinical outcome. MCT's analgesic effect does not rely on sensory stimulation, and further investigation of its influence on tendinous blood flow and vascularity, or on the local biochemical milieu, may help elucidate its mechanism of action. On the basis of this investigation, a fully-powered controlled clinical trial is justified. A protocol, combining MCT with an exercise programme, is proposed.

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Terms & Abbreviations

AC	Alternating current
ANCOVA	Analysis of covariance
ANOVA	Analysis of variance
CI	Confidence interval
CR	Current regulated
DC	Direct current
DOMS	Delayed-onset muscle soreness
ESWT	Extracorporeal shockwave therapy
GCS	Global change score
HVPC	High Voltage Pulsed Current
ICC	Intraclass Correlation Coefficient
MCSD	Minimum clinically significant difference
MCT	Microcurrent treatment
MDC	Minimum detectable change
MGS	Maximum grip strength
MRI	Magnetic resonance imaging
NRS	Numerical rating scale
NSAID	Non-steroidal anti-inflammatory
p.d.	Potential difference
PD	Power Doppler
PFGS	Pain-free grip strength
PPT	Pressure pain threshold
PRTEE	Patient-rated Tennis Elbow Evaluation
PSFS	Patient-specific Functional Scale
RCT	Randomised control trial
SD	Standard deviation
SGP	strain-generated potential
TENS	Transcutaneous electrical nerve stimulation
ULTT	Upper limb tension test
VAS	Visual analogue scale
μA	Microampere (10 ⁻⁶ amps)

Chapter 1

Introduction

Electricity plays an essential role in life. Many physiological processes in living organisms involve the flow of charge and the maintenance of potential differences across cell walls and tissue boundaries. Bioelectricity is the name given to these endogenous currents and voltages, which have been found to modulate growth, adaptation and repair in a variety of species, including humans. The role of bioelectricity in tissue growth and repair has been recognised and - to some extent - elucidated over the last century. This has provided a rationale for the application of externally generated currents to the body, particularly where natural healing is dysfunctional. Microcurrent therapy (MCT) is one example of this. Its defining feature is that in size (and sometimes in other characteristics) it resembles the internally generated currents that are thought to be one of the drivers of tissue healing.

MCT – under a variety of names and specifications – has been employed clinically for some decades, and has proved effective when used to promote repair in damaged skin and bone tissue. Numerous studies have suggested that healing in non-uniting fractures, spinal fusions, venous ulcers and skin grafts can be enhanced by MCT. Clinically-oriented research to date has focussed primarily on these applications. Much less attention has been paid to its potential with soft connective tissues such as ligaments, tendons and fascia. This is an area ripe for research since slow or dysfunctional healing in these tissues is seen in a range of connective tissue disorders, such as repetitive strain injuries, that are painful and debilitating and respond poorly to existing conservative treatments.

Current understanding of MCT is deficient in several regards, theoretical and empirical. Although several models have been proposed to explain its action, none has gained general acceptance, and so the modality lacks a firm theoretical foundation. Also, systematic reviews of electrotherapeutic applications tend not to distinguish MCT from other modalities, so its particular character and effects are rarely considered separately. In consequence, there is much uncertainty about whether some forms of microcurrent are more potent than others. Until these issues are addressed, there is scant justification for clinicians to employ MCT in their practice.

This context provided the rationale for the present investigation. Its central thesis is that:

microcurrent therapy can promote healing and resolution of symptoms following soft connective tissue damage.

The investigation addressed this thesis through two activities: (i) a review of existing evidence regarding the use of microcurrent to promote tissue healing, and (ii) an experimental evaluation of microcurrent's capacity to promote healing and resolve symptoms in a selected soft connective tissue disorder. These activities involved several studies, each with its own aims, but linked together in sequence to provide a response to the thesis. Three themes guided the work as a whole:

- A. MCT as a distinct therapeutic entity.** Many forms of electrotherapy bring about physiological change but their effects and mechanisms of action may differ radically. The study focus was kept exclusively on MCT to determine if it has a particular therapeutic value.
- B. Tissue healing and symptomatic relief.** Microcurrent appears to have particular value in promoting tissue healing, thereby addressing the causes as well as the symptoms of a disorder. Its effects both at the tissue level and on clinical manifestations such as pain and function were therefore considered.
- C. Clinical significance.** Although there is a continuing need for development of the basic science behind MCT, the primary focus of this investigation is its clinical potential.

The structure and process of the work undertaken is illustrated in Figure 1.1. Chapter 2 introduces the concept of "the body electric", the science of bioelectricity that supplies part of the rationale for the use of MCT. It provides an overview of experimental work on the role of endogenous electricity in normal physiology and in the healing process, and the ways in which applied electricity can influence the physiology of healing. Chapter 3 comprises two literature reviews focussing on the therapeutic application of microcurrent. The first is a narrative review of the broad literature concerning the influence of microcurrent on cells and tissues in laboratory studies, and on different forms of tissue damage in animal and human studies. The

second is a systematic review of human clinical trials of MCT applied particularly to soft connective tissues. To maximise relevant data from a relatively small empirical database, all forms of experimental design were included, and the quality and strength of the evidence were evaluated in each case. This comprehensive review approach is uncommon and an evaluation tool was specifically developed for the purpose. Together, these reviews assess the evidence regarding the therapeutic value of microcurrent. They conclude that, although there is strong evidence in favour of MCT for a variety of bone and skin lesions, studies involving other forms of tissue are less common, provide a lower standard of evidence, and leave important questions unanswered. These include the optimum treatment parameters, whether these vary between tissue type and form of damage, and whether MCT brings about tissue change as well as symptom alleviation in all applications.

The rest of the investigation was devoted to generating and analysing original experimental data on the clinical potential of MCT, and the remaining chapters describe this work. A clinical trial was planned, but several preliminary issues had to be addressed before it was undertaken. These were (1) what population and disorder is most likely to benefit from MCT, (2) how should treatment effectiveness be measured, and (3) what form of MCT should be used? A number of studies were conducted to address these questions. Chapter 4 focuses on the first of them – choosing a population and a disorder. It draws on evidence from various sources. To maintain a clinical focus, a survey of practising physiotherapists was used to investigate which common and disabling soft tissue disorders they rated as particularly recalcitrant to treatment, and hence in need of new treatment options. The literature concerned with the top three disorders identified by the survey was then consulted to obtain additional information on prevalence, impact and the effectiveness of existing treatment strategies. The feasibility of using each of these disorders in the planned trial was also considered. As a result, chronic tennis elbow was selected as the disorder to be treated in the trial.

Experimental design issues are considered in Chapter 5. These include the generation of an operational definition of tennis elbow, the choice of a trial methodology and the selection of appropriate outcome measures. The tennis elbow trial literature was consulted for these purposes. A provisional set of outcome variables and measurement instruments was identified on the basis of their capacity to address tissue healing, their clinical relevance, and their measurement properties. Various proprietary devices are available to deliver MCT, and these were evaluated for suitability. This included

laboratory testing, and resulted in three devices being judged suitable for use in the trial.

Chapter 6 is concerned with the experimental evaluation of several of the outcome measures identified in the previous chapter. The reliable use of three measurement processes - sonography, dynamometry and algometry - was deemed particularly dependent on the operator, and so training was undertaken and experience gained to improve the investigator's skills using them. Sonographic scales to quantify tissue abnormality and blood flow were developed during this work. This was followed by studies to evaluate their reliability with both healthy individuals and those with tennis elbow. A choice of measures for inclusion in the trial protocol was made on the basis of this work.

Equipped with the accumulated evidence, the investigation proceeded to trial MCT with chronic tennis elbow, and this work is described in the next two chapters. Because the existing literature leaves considerable uncertainty about the most appropriate treatment parameters, it was decided that the trial should focus on this question by comparing different forms of MCT. Chapter 7 begins by drawing up a full protocol for this purpose, drawing upon the findings of previous chapters. A trial comparing the effects of two different microcurrent intensities is then described. This involved 31 participants allocated to two treatment groups, receiving treatment for 3 weeks and followed up for three months after treatment. It provides limited evidence that MCT has an effect on blood flow levels within the tendon, and can improve clinical outcomes; it also concludes that one form of MCT, with lower current intensity, is more effective than the other. A second trial, using a similar protocol and sample size to compare two other forms of MCT, is described in Chapter 8. It provides additional support for the contention that MCT can influence processes involved in tissue healing, and can alleviate symptoms. It also suggests that waveform may not be critical to the effectiveness of the treatment. A pooled analysis of data from the two trials finds that the forms of treatment evaluated are safe, suitable for patient-controlled home-based use, and may promote good patient adherence to the protocol. Also that there is some evidence that MCT may regulate blood flow in damaged tendons, and that baseline blood flow levels are predictive of treatment success. However, changes over time and differences between group averages on some variables were small, and the studies were underpowered to detect statistically significant differences in some cases. These studies provide evidence suggesting that a full clinical trial of MCT with particular

parameters, used for the treatment of chronic tennis elbow, is warranted, and sample sizes for the trial are calculated.

In the final chapter, the implications of the investigation are discussed in terms of two of the broad investigative themes: MCT as a distinct therapy, and its capacity to influence both tissue healing and clinical outcomes. The original contributions of the various studies making up the investigation are identified, and their limitations are discussed. The implications of the work for the research and clinical communities are considered, and a protocol for a full randomised controlled trial is proposed.

The balance of material in this report reflects a particular concern with methodological issues. This was a response to a growing awareness that attention to methodological rigour is essential both to provide a credible response to the thesis and to enhance the investigator's development as a researcher. Thus, the chapters concerned with experimental design issues and with the development and reliability-testing of outcome measures are seen as key to the overall process of the investigation, not merely as ancillary to the clinical trials they preceded. For the same reason, considerable regard is given to methodological issues in discussing the findings, contributions and limitations of this investigation.

Note: a superscript-based system of referencing is used in this report to aid its legibility. In the references section, citations are listed in the order in which they appear in the text. A bibliography section – with papers listed by topic and author – has also been provided, indicating those publications the investigator regards as key sources for this work.

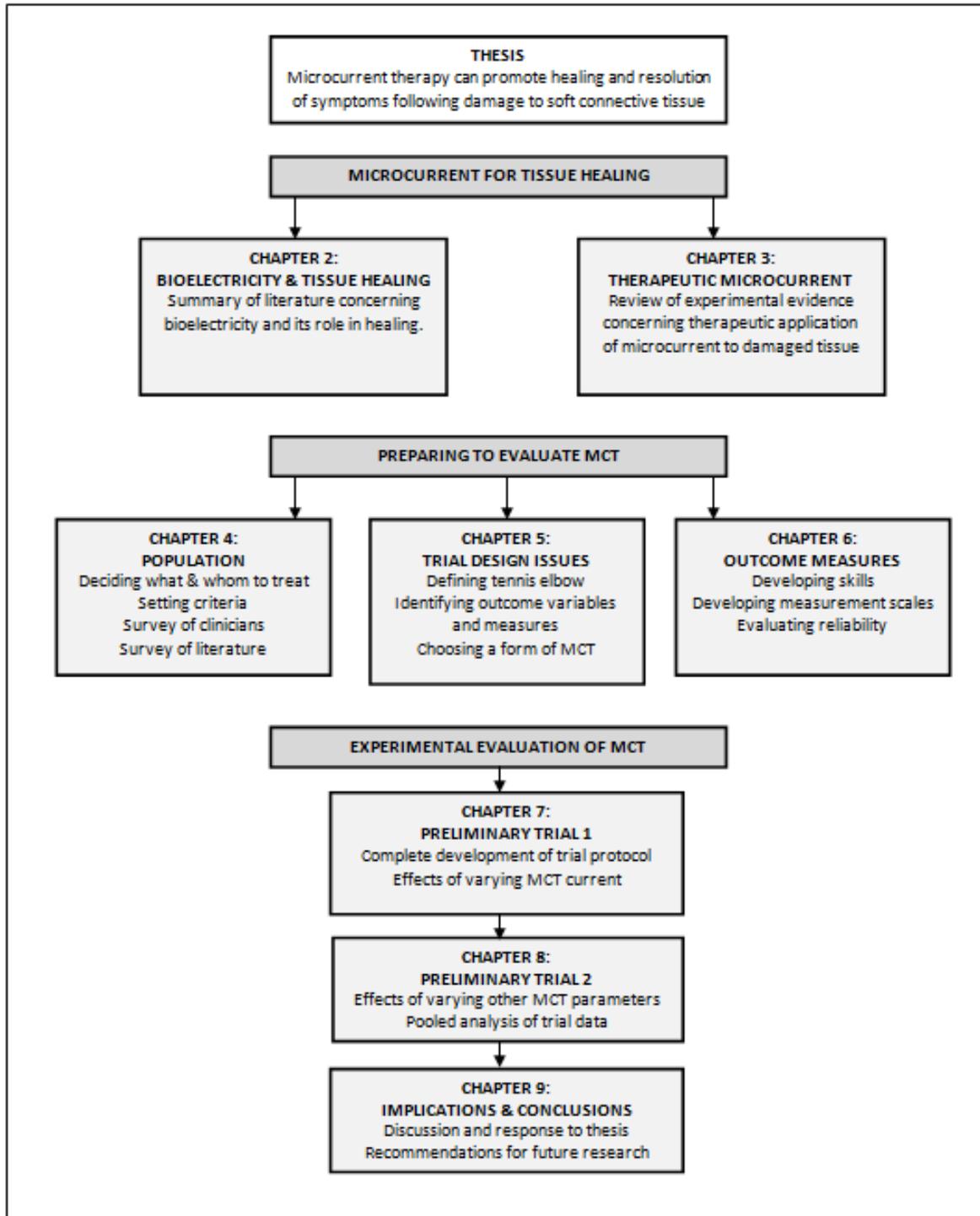


Figure 1.1: Outline of investigation structure and process

Chapter 2

Bioelectricity and tissue healing

"Life is a set of electromagnetic events performed in an aqueous medium"¹

2.1 INTRODUCTION

The application of electricity to reduce symptoms of tissue damage and aid tissue healing long predates any understanding of how it might bring about these effects. Shocks delivered by electric fish were being recommended to treat gout pain more than 2000 years ago², and electric current was applied to assist bone healing in the early 19th century³. An appreciation of how electricity might be involved only began to emerge in the last century and much is still unknown about its mechanisms of action. It is not unusual for the implementation of a therapy to precede an understanding of how it works: there is still debate about the mechanisms of action of therapeutic exercises, manual techniques and drug therapies commonly used in the management of musculoskeletal disorders⁴⁻⁶. Adequate and robust clinical trial evidence in favour of a treatment, rather than a comprehensive understanding of the biology underpinning it, is the essential precondition for its use. Nevertheless, some scientific rationale for the therapeutic application of electricity is desirable, particularly because of the quackery that characterised much of it in the 19th and early 20th centuries⁴. This has contributed to a healthy scepticism of novel electrotherapies that lingers to this day⁵. An appreciation of the effects of electricity within the body may also inform decisions about which tissues and types of damage may respond to which forms of electrical treatment, and so aid formulation of clinical trial protocols and treatment guidelines.

Microcurrent therapy (MCT) is the application of a particular form of electricity for therapeutic effect. It has been prescribed for a wide variety of disorders, from depression and fibromyalgia to skin ulcers and non-uniting bone fractures. This chapter aims to provide a physiological account that might justify the application of microcurrent specifically to promote tissue healing. It begins with a brief account of the science of bioelectricity. Broader reviews of the subject are available^{4, 6-10}, and the intention here is

to provide an overview of those aspects that are particularly pertinent to tissue healing. Evidence for a link between endogenous currents and tissue changes is presented. The possibility that bioelectricity may drive some aspects of tissue healing is then considered, drawing upon studies of the effects on cells and tissues of applying electric fields and currents similar to those generated within the body. This provides a biological rationale for the therapeutic application of microcurrent to stimulate healing, which may be appropriate if endogenous processes have become dysfunctional.

2.2 BIOELECTRICITY

Like non-organic substances, body tissue possesses passive electrical properties such as resistance and capacitance. These stem from the presence of ions and electrically polarised molecules in the tissue. Ions, such as potassium (K^+) and hydrogen carbonate (HCO_3^-) are atoms or molecules that have lost or gained electrons when they are dissolved in body fluids. Polar molecules, such as water and lipids, are electrically neutral but their electron configurations give different charges to different parts of their structures. The behaviour of these charged particles determines the electrical properties of tissue. Because of the complex composition and physiology of many body components, these properties are neither constant nor simple to predict. For instance, the conductivity of blood depends on the number density of red blood cells within it, and on its flow rate¹¹; skeletal muscle conducts electricity seven times more easily parallel to its fibres than across them¹²; and the capacitance of the skin changes on sweating¹³.

Living tissues may also demonstrate active electrical behaviour. In fact, all cells in the body expend a significant proportion of their energy generating electric fields across their membranes^{7, 14}. These are maintained by channels that continuously transport ions through the membrane against their concentration gradients¹⁵. This results in a steady potential difference (p.d.) of about 70 – 100 mV between the cell cytoplasm and the extracellular environment. The magnitude of the p.d. varies according to the cell type, though the cell interior is always negative with respect to the exterior*. In this sense cells

* By convention, a reference point (in this case the extra-cellular space) is ascribed electrical neutrality (0 V), so the term “potential” (inside the cell) rather than “potential difference” (between cell interior and exterior) is often used in the literature. The term

act as miniature batteries, converting chemical energy generated by their mitochondria into stored electrical energy. When conducting paths are available, these cellular p.d.s can drive currents in the microamp (μA) range across their membranes or through the tissue containing them⁷.

The combined electrical activity of cells results in potential differences being established across a variety of tissue layers within the body^{7, 14, 16-20}. The gross electrical character of intact human skin was first mapped by Foulds and Barker. In 1983 they reported a study in which the potential difference between the dermis and the skin surface was measured at various points on the bodies of 17 human subjects¹⁸. It varied considerably with position on the body surface, from about -15 mV on the thigh to -58 mV on the palm, with a body average of -26 mV (the stratum corneum being negative with respect to the underlying dermis). These potentials are generated by cell-mediated transport of sodium and potassium ions through the epidermis²¹. As elsewhere in the body, channels pump these ions to maintain higher concentrations of potassium and lower concentrations of sodium within the cells. In the epidermis there are additional channels on the apical (outward-facing) surfaces of the cell membranes that draw sodium ions into the cell, and on the basolateral surfaces that push potassium ions out in these directions. This results in continuous transport of these positive ions to deeper levels of the epidermis, making them positive with respect to the surface - hence the observed transcutaneous potential. The excess ions leach back towards the surface along the narrow gaps between cells, and so energy is required by the cells to maintain the potential. The sodium ions that are drawn into the apical cell surfaces are thought to originate from sweat secreted by nearby glands, because the transcutaneous potential is lower in areas of skin that do not possess these glands²². The key role of sodium transport in the generation of the transcutaneous p.d. is demonstrated by application of amiloride - a sodium channel blocker - to the skin, which results in the abolition of the transcutaneous potential²².

Potential differences have also been recorded along and across the cortices of animal bones. Friedenberg and colleagues measured p.d.s of less than 10 mV along the periosteum and the stripped cortical surface of live rabbit tibiae.¹⁷ Borgens recorded currents of density 0.5 - 12 $\mu\text{A}/\text{cm}^2$ entering the surfaces of intact mouse metatarsal explants (whole bone samples recently excised and kept alive in vitro). This suggests that

“voltage” is used synonymously. They all indicate the same thing: the electrical energy stored when charges accumulate or are separated.

a p.d. is maintained between bone interior and exterior. By selective removal of different ions from the bathing medium, Borgens concluded that transport of the chlorine ions (Cl^-) was primarily responsible for establishing this p.d., since the current was significantly reduced in its absence, although transport of sodium and other ions was also thought to contribute. Trumbore and colleagues¹⁹, working with embryonic chick skull bones, concluded that a steady voltage of 4 mV is maintained across the periosteum and suggested that this is established by the active transport of sodium ions into the bone interior. However, Borgens questioned the methodology of this study and claimed that the endosteum or cortex itself was the battery generating the p.d. Becker suggested that neural activity was responsible for the p.d.²³ but Friedenbergs and colleagues found that surface potentials varied little following severance of the nerve supplying the area, but dropped significantly when bone cell death was induced chemically¹⁴. This appeared to confirm its cellular origin. Later experimental work by others²⁴ suggested that osteocytes, far from being quiescent cells in bone tissue, are intimately involved in the ion transport that results in this voltage.

Steady endogenous potential differences have been measured in numerous other tissues, including muscle, corneas, kidney tubules, intestinal and respiratory tracts, and blood vessel walls^{7, 20, 25-27}. The p.d.s exist across tissue boundaries, but in bone and skin they are also present between points along the surface. Normally, tissue resistance prevents ion flows under the influence of these p.d.s but, when a conducting path is available, they give rise to currents of density 1 – 60 $\mu\text{A}/\text{cm}^2$.

Transient and regularly varying bioelectric phenomena also occur, particularly when tissues are subject to mechanical stress. Such behaviour was first observed in bone: in 1953 Yasuda reported that applying a bending stress to an ex-vivo rabbit tibia changed the potential along the cortical surface²⁸. The area under maximum compression became negative with respect to the unstressed epiphysis, whilst the area under tension became positive. Basset and Becker confirmed this observation, and also found that the size of the generated p.d. was dependent upon the rate and magnitude of bony deformation²⁹. Such strain-generated potentials (SGPs) went on to be observed in muscle, skin, blood vessel walls, tendons and other collagen-based tissues³⁰⁻³². In bone, potentials of about 40 mV are generated across each centimetre of tissue^{32(p67)}, and these produce transient currents of up to 30 μA ³². In tendons, SGPs caused by stretching the structure can drive currents of density 1 – 10 $\mu\text{A}/\text{cm}^2$ along their length³³. As in bone, these potentials and their resultant currents increase with loading frequency³⁴. Tonic activity in muscles has been found to generate varying biocurrents of frequency 5 – 20 Hz in the bones to which they are

attached; walking produces variations of $< 10 \text{ Hz}$ ³⁵ (cited in 36). Hence endogenous fields and currents can occur as brief or low frequency repeated pulses in response to applied stresses.

Initially these potentials were thought to be a result of the piezoelectric effect, in which mechanical deformation of crystalline structures within the extra-cellular matrix resulted in the generation of a p.d. However, subsequent experimental and theoretical work showed that brief movements of tissue fluid following the deformation were responsible^{33, 37}. The p.d.s set up by this process are known as streaming potentials³⁸. By a similar mechanism, the flow of blood through vessels generates a p.d. between the bloodstream and the vessel wall, measured as 5 – 10 mV in a live rabbit aorta³⁹.

2.3 THE ROLE OF BIOELECTRICITY

Bioelectricity is observed in every living cell and tissue that has been studied – it appears integral to the physiology of most basic life processes. Yet endogenous p.d.s and currents might be mere epiphenomena – by-products of ion transport mechanisms that are required for normal metabolism. However, there is evidence to suggest that they can modulate – or even drive – processes of change within living organisms. Avian and amphibian experiments have confirmed the existence of endogenous electric fields of typical strength 1 – 200 mV/mm and currents of density up to $105 \mu\text{A}/\text{cm}^2$ in the embryos of these developing animals⁸. Artificial perturbation of these fields and currents causes mal-development of the organism, suggesting that they influence normal morphogenesis⁸.

The SGPs measured in many tissues may play a part in adaptation. When Yasuda observed SGPs in bone, he speculated that the separation of oppositely charged ions within bone might drive the adaptive formation and resorption of tissue²⁸. Osteogenesis occurs naturally in areas of bone compression, as an adaptive response to applied stresses, and his study demonstrated that these areas become negatively charged during loading. He applied a $1 \mu\text{A}$ current to a rabbit femur via implanted electrodes, and observed osteogenesis at both electrodes, but more at the (negatively charged) cathode, confirming that such a current could indeed promote bone growth. This provides circumstantial evidence of an association between bone biocurrent and osteogenesis, but does not prove causality. It has since been demonstrated that osteocytes can respond directly to mechanical forces without the necessity of an electric current⁴⁰, and this would provide an

alternative model of the adaptive driver. Friedenberg and colleagues found that areas of bone growth (that occur during development or repair) are electronegative even in the absence of applied forces¹⁷. So, if bioelectricity has a role in osteogenesis, SGPs cannot be the only mechanism; steady state p.d.s may also be involved. Patterns of potential on unstressed growing bone surfaces map onto areas with different bone growth rates, suggesting an association between the two⁴¹.

More comprehensive accounts of such studies are available, and they conclude that bioelectricity plays a significant role in growth and adaptation^{6-8, 40, 42, 43}. Its significance in tissue repair is particularly pertinent to this investigation, and this is now considered in greater detail.

2.4 BIOCURRENTS AND TISSUE REPAIR

In the mid-19th century, Dubois-Reymond detected an electric current of about 1 μA in a small cut in his finger⁴⁴. In 1910, Herlitzka confirmed the existence of this current and found that it diminished as the wound healed. He proposed that this current might initiate the cell division necessary for wound healing⁴⁴. Cunliffe-Barnes later measured a changing voltage between a healing skin abrasion and intact skin elsewhere on the human body, and suggested that it could be used as a measure of healing rate⁴⁵. These papers have been seminal in the development of an electrophysiological account of healing. The term “current of injury” was used in the 1920s to depict the flow of ions generated by damage to plant tissue⁴⁶, and it has been adopted to describe similar phenomena observed in other living organisms, including humans⁴⁷⁻⁴⁹. Changes in tissue potentials, the establishment of currents of injury, and the reduction in those currents as healing progresses have been observed in many tissue types, including bone, skin, nerves and tendons^{16, 33, 43, 50-55}. Currents of injury also occur when individual cells membranes are punctured and then diminish as repair progresses⁵⁶.

Evidence that these bioelectric phenomena may be at least partly responsible for driving healing is derived from studies in which blocking biocurrent interferes with healing. If a skin wound is allowed to dry out its conductivity falls and the current of injury drops towards zero. Concomitantly the healing process slows or halts⁵⁰. Manipulation of endogenous wound potentials by pharmacological modulation of membrane channels has been found to slow or accelerate multiple aspects of healing after rat corneal damage⁵⁷. In

this study, the channel blockers were selected for their different mechanisms of action and inertness in the biochemistry of healing. However, alternative interpretations are possible: many biochemical reactions require an aqueous medium and so wound-drying may interfere with this; blocking membrane channels is also likely to interfere with normal cell metabolism. More compelling evidence is provided by studies showing that application of a p.d. in opposition to the current of injury can slow, abolish or even reverse healing in epithelial tissue^{24, 58}. In one study, for example, newts were given small skin wounds and fields were applied either to enhance the current of injury or reduce it to zero⁵⁹. Wounds with zero currents still healed, but more slowly than those with enhanced currents. Such studies appear to demonstrate that the current itself is a prerequisite for normal healing.

2.4.1 Mechanisms by which bioelectricity may promote healing

Tissue response to damage is complex and involves the actions of, and interactions between, multiple components, including biochemicals, cells, the extracellular matrix and the environment⁶⁰⁻⁶². If bioelectricity affects healing, it may do so by influencing one or more of these components. The mechanisms by which it may do so have been investigated through cellular and tissue studies, and an account of these follows. First, a brief description of the process of healing is provided. This varies between tissue types and depends on the nature and extent of the damage, but several features are common. An initial insult precipitates an inflammatory response, initiated by the release of chemicals from damaged cells. These activate several biochemical cascades that draw in a variety of local and distant cells, particularly macrophages, which attack any foreign organisms present and ingest necrotic tissue and debris. These cells have a long life span and mediate much of the repair process that follows through their release of a variety of chemicals. Inflammation also involves changes to the local vasculature, including release of many biochemicals, and dilation and enhanced permeability to allow cells in the bloodstream to enter the damaged tissue.

Both inflammation and the repair processes that follow it involve the migration, proliferation and increased activity of a variety of cells. Not only macrophages, but also cells that can synthesise new tissue. These include endothelial cells in the blood vessel walls and cells specific to the tissue that has been damaged: osteoblasts in bone, keratinocytes in the epidermis, and fibroblasts in tendons, ligaments and other collagen-

based tissues. The reproduction and activities of these cells is dependent on a range of complex biochemicals, such as growth factors, and simple ions, such as calcium (Ca^{2+}), that act as messengers to up-regulate or down-regulate cellular activity. A complex interplay between these components results in neovascularisation of the damaged tissue and – in the case of connective tissue - synthesis of the extracellular matrix that gives the new tissue structural integrity. This initially weak and immature material is gradually strengthened by replacement with stronger components bound more firmly in place. Remodelling into a mature and more organised form occurs over subsequent weeks and months, guided in large part by the external forces acting upon the tissue.

Electric fields and currents similar to those occurring naturally in damaged tissue are capable of modulating many of these components of healing. They can increase proliferation and protein synthesis by the constituent cells of skin, tendons, cartilage and bone^{54, 63-72}. Applied fields can increase expression of growth factors that promote osteogenesis and collagen synthesis^{72, 73}. Microcurrent boosts the number of organelles responsible for these activities, and can substantially increase concentrations of ATP, the cellular currency of energy^{36, 74}. Ion channels in cell membranes may migrate under the influence of an applied field, resulting in cytoskeletal modifications, including creation of membrane projections that cause cell movement^{36, 75}. Cells may also change shape and align themselves with an applied field³⁶.

Directed movement of cells within an electric field – known as galvanotaxis – has been observed with many cell types. These include macrophages and a variety of cells involved in new tissue formation, such as keratinocytes, corneal cells, vascular endothelial cells, osteoblasts, osteoclasts, chondrocytes, neurones and fibroblasts^{36, 54, 75-77}. The speed of migration is dependent on the strength of the applied field³⁶, and different cell types have been found to move in opposite directions within a field; reversing the field direction reverses their migration^{36, 78}. The direction of macrophage migration may vary according to the stage of healing⁷⁹.

At the tissue level, unidirectional fields and direct currents (DC) in the microamp range can promote vascular permeability⁷⁹ angiogenesis⁸⁰ and neural sprouting^{53, 81} as well as formation and maturation of new skin, bone, cartilage and soft tissue formation^{67, 82-87}. The alignment of newly-formed collagen in healing ligaments and osteons in bones is parallel to the applied current^{54, 88}.

Thus, the currents that are established immediately after damage and decline as healing progresses are capable of driving multiple components throughout the whole process of healing. This is a key concept in the electrophysiology of tissue repair. It provides grounds for arguing that bioelectricity is integral to the process, and may be as important as biochemistry in its co-ordination. Other forms of bioelectricity may be involved in specific stages. For instance, streaming potentials set up by blood flow within vessels can assist clotting when the vessel walls are breached⁸⁹, and promote angiogenesis in the early stages of tissue synthesis⁸⁰. SGPs in connective tissue could provide the impetus for differential tissue formation and adaptation to everyday stresses that occur later, during the remodelling phase.

The applied fields and currents in many of these studies are similar to those generated naturally within tissue. Applying currents at other levels can have deleterious effects. In one study, current above 1000 μA reduced ATP levels and protein synthesis in rat skin cells⁷⁴; in others, current densities or frequencies above certain levels reduced cell proliferation or caused cell death^{64, 90, 91}. However, studies have produced apparently conflicting findings. In one, the effects of various microcurrent parameters on bovine fibroblasts in a collagen matrix were investigated⁷⁰. Stimulation with currents above 1 $\mu\text{A}/\text{cm}^2$ reduced collagen synthesis by cells in the matrix by 30% compared to unstimulated control samples. The effect was most marked at 1 Hz, less at 10 Hz and absent at frequencies above 100Hz. Bone resorption has been observed with applied currents of 30 – 50 μA ³⁸. These parameters are similar to those occurring endogenously during normal healing but are producing different effects.

In fact, healing can be promoted using applied fields and currents with a variety of parameters, including high voltage pulses and high frequency waveforms, that have not been observed in living tissue^{36, 75, 92}. One reviewer concluded that almost any form of electrical stimulation can result in osteogenesis³⁸. A number of explanations may help reconcile these findings: (i) the effects of currents on cells are likely to depend on their environment and on the stage of repair, so applying the same parameters in different contexts may produce very different outcomes; (ii) healing processes may be the product of a dynamic synergy between bioelectricity and biochemistry⁷⁵ for which in-vitro models provide a poor analogue; and (iii) applying artificially-generated currents – whether similar to endogenous ones or not – may activate physiological pathways quite different from those that occur naturally after tissue damage.

2.5 CONCLUSIONS

Empirical evidence has established that cells within living organisms, including humans, generate electricity, producing steady and varying voltages in tissues throughout the body. These drive currents of injury whenever tissue is damaged. Endogenous voltages and currents are capable of driving multiple components of the healing process. It may be that the current of injury is a homeostatic trigger⁹³ that initiates a physiological response once normal metabolism has been unbalanced by tissue injury. Certainly, several reviews have concluded that bioelectricity is essential to healing^{6, 21, 94}. This evidence is circumstantial, however, and not always consistent. The association between bioelectricity and healing may not be causal. Whilst bioelectricity can influence healing, it may not necessarily do so. If it does, it may not be the only - or even the main - driver. Nevertheless, the data are consistent with bioelectric involvement in the process, and so provide a biological rationale for the application of currents with similar parameters. If these can activate or promote endogenous healing, particularly when the natural process has become dysfunctional, they surely merit further consideration. This is the focus of the next chapter.

Chapter 3

Microcurrent therapy

*'After the limb was electrized ...
the man was able to walk and left the hospital cured.'*^{95 (p204)}

3.1 INTRODUCTION

The previous chapter argued that the behaviour of living tissue can be described in terms of bioelectricity as well as biochemistry. An appreciation of the role of chemical interactions in physiology has underpinned the development of many pharmaceutical interventions. In the same way, a more complete understanding of electrophysiology may result in the emergence of new electrotherapeutic technologies. The evidence cited in the previous chapter suggests that the application of microcurrent can influence healing; it is also consistent with at least some forms of microcurrent achieving this by mimicking the biocurrents that are generated during tissue damage and repair. Hence, microcurrent therapy may be regarded as a distinct form of electrotherapy with particular mechanisms of action. However, reviews sometimes fail to make this distinction, and draw generic conclusions about electrical stimulation based on evidence from trials using quite different modalities^{96,97}. These may differ not only in their influence on physiology but also in their therapeutic value for a particular disorder. Separate evaluation of each modality is more likely to produce valid conclusions about their individual effects and effectiveness. A review of experimental studies focusing specifically on the effects of microcurrent is therefore desirable, but none has been published to date. Hence, one was conducted as part of this investigation.

The literature contains much evidence relating specifically to the action of microcurrent, involving cell cultures, tissue samples, live animals and humans, and relates to a variety of tissue types. Caution must be exercised in interpreting the data from such a broad-based literature. Ex-vivo tissue samples and in-vivo animal tissue lesions provide imperfect analogues for human pathology, and do not necessarily predict human response to treatment. Also, the majority of published human clinical trials involve bone and skin, muscle

and nerve, which differ significantly in structure, pathological features and repair processes from soft connective tissues, such as tendons, ligaments and fascia. These have a collagen-based matrix manufactured by phenotypes of the fibroblast cell, and they heal by laying down poorly organised scar rather than regeneration of identical tissue⁹⁸. Whilst findings from these studies may enhance confidence in the potential of MCT generally, a separate analysis of human clinical trials of the modality specifically applied to damaged soft connective tissues is required.

The purpose of this chapter is to review the literature relevant to MCT. It begins by constructing a working definition of microcurrent therapy, which is used to define the scope of the work that follows. A narrative review follows, addressing in-vitro and animal studies relating to all tissue types, and then human clinical trials that do not involve connective tissues. Clinical trial evidence relating specifically to the soft connective tissues is then addressed through a systematic review, in which the breadth and quality of existing data is more fully appraised. The chapter ends with conclusions about the strength of available evidence regarding microcurrent therapy, and identification of issues that require further research. These are used to inform the experimental work that forms the rest of this investigation.

3.2 DEFINING MICROCURRENT THERAPY

Microcurrent therapy is one of a number of terms used in the literature to describe electrical stimulation that involves delivery of very small currents. These include microcurrent electrical therapy⁹⁹, microcurrent stimulation⁵, low intensity direct current¹⁰⁰, low-voltage microamperage stimulation¹⁰¹, micro-amperage neural stimulation¹⁰², microampere transcutaneous electric nerve stimulation¹⁰³, electroionotherapy¹⁰⁴ and horizontal therapy¹⁰⁵. In some cases, a generic term such as direct current¹⁰⁶ or bioelectric stimulation¹⁰⁷ is used. The common feature of these forms of therapy is the application of electric current in the microampere range, delivered to the tissue via contact electrodes. They may differ in several other respects, particularly in the waveform of the current: it may be constant and unidirectional (also known as direct current, or DC), monophasic (varying in magnitude but unidirectional) or biphasic (varying in magnitude and direction); if varying, the waveform may be sinusoidal (known as alternating current, or AC), rectangular or another shape, and of fixed or modulated frequency and amplitude; it may also be pulsed. Clearly, this can produce an almost limitless variety of parameter combinations.

The physiological rationale used in this investigation for the application of microcurrent is its similarity to the endogenous currents seen during tissue healing. These natural currents are constant or slowly varying, so many of the therapies described in the literature do not mimic bioelectricity, despite claims or implicit assumptions that they do so^{82, 85, 108}. In some cases, it may be that the current is pulsed or reversed to reduce the accumulation of potentially harmful electrolytes at the electrode/tissue interface⁸²; in others, current modulation may be intended to activate neurones in the area, although this is unlikely at currents of less than 100 μA ¹⁰⁹. In any case, the waveforms used in studies are seldom justified, and comparisons of their effectiveness are rare. It may be that variables such as frequency, pulse rates and wave shapes have no bearing on the healing effect. They might influence other clinically significant outcomes, however, such as side effects and pain levels. A narrow definition of microcurrent therapy, based entirely on its similarity to endogenous electricity, would exclude consideration of many clinical studies that use sub-milliamp currents but vary them “unnaturally”. If the size of the applied current is the most important factor in its effectiveness as a promoter of healing, this exclusion is unwarranted. Indeed, including such studies in the analysis may help elucidate the issue of parameter dependence. Therefore, for the purposes of this investigation, microcurrent therapy is defined as

therapeutic application of electric current of intensity in the microamp range.

While this definition is simple and identifies the primary characteristic of MCT, it is not entirely satisfactory. There are modalities that have been applied to promote tissue healing and which may produce currents in the microamp range, such as High Voltage Pulsed Current¹¹⁰ (HVPC) and Radio-frequency Stimulation¹¹¹. However, their parameters are typically expressed in terms of voltage applied or energy delivered rather than current produced. In the case of radio-frequency stimulation, the induced current is very difficult to measure but likely to be above the microamp range³². Typically, HVPC generates very brief pulses of current that constitute less than 2% of the waveform - for the rest of the time, the current is zero^{112 (Ch 5)}. Hence, even if these pulses have microamp amplitudes, it was judged inappropriate to class HVPC as a form of MCT. These modalities are excluded from the discussion that follows.

The definition says nothing about the electric field produced in the tissue by the modality. This might be interpreted as inferring that electric currents rather than fields modulate the healing process. In fact, the two are intimately related since, during healing, fields drive currents and ion movements set up fields. However, current intensity rather than field strength are mostly commonly reported in clinical studies and so this variable is adopted

pragmatically for the definition. In fact, it may be that current density (current per unit surface area, usually measured in $\mu\text{A}/\text{cm}^2$) is more significant than current intensity in determining the bioeffects of microcurrent. This possibility is considered later. However, unless the electrodes delivering the current are in direct contact with the target tissue, neither the intensity nor the density of current at the site of damage is known. So once again, current intensity is the pragmatic choice for the definition, although if the electrode dimensions are known, current density at its interface with tissue can be calculated.

3.3 TISSUE AND ANIMAL STUDIES

This section considers evidence gathered from experiments in which microcurrent is applied to in-vitro tissue samples and live animals. Such studies can facilitate control of conditions whilst providing an approximation of normal anatomy and metabolism in the tissue. Live animal studies can provide analogues for some forms of human tissue damage, such as bone fractures and surgically-induced wounds, but are less capable of simulating some of the common soft tissue pathologies such as repetitive strain injuries and natural ruptures^{113, 114}.

3.3.1 Bone

The capacity of MCT to promote bone healing has been explored in many mammalian studies from the 1960s onward. Typically, these compared real MCT and sham-MCT, the latter comprising identical apparatus and electrode placement but no current delivery. Surgical osteotomies have been used to model fractures and spinal fusion surgery, and radiological evidence of osteogenesis, callus formation and union have been used as indicators of healing. Resistance to bending stress has also been measured. Studies have consistently shown that direct or pulsed monophasic currents of amplitude 10 – 20 μA , delivered via a wire cathode of 1 – 2 cm length placed into the lesion and an anode sited nearby, applied for several hours each day for several weeks, accelerates bone healing compared to controls groups^{72, 87, 115, 116}. Current intensities well below these values have no effect and those well above it cause resorption or osteonecrosis^{84, 117, 118}. One study compared the effects of various combinations of current intensity, frequency and waveform on healing of surgically-induced osteotomies in rabbit skulls¹¹⁹. Intensities between 3 and 1400 μA , and DC, square waves or sinusoidal AC of 1 or 60 Hz were used. The investigators concluded that current intensity (or density) was the

key parameter and that varying the waveform, frequency and pulse rates did not materially influence healing.

There have been suggestions that electrolytic products at the electrode interface or movement of the implanted electrode, rather than the microcurrent itself, may drive osteogenesis^{120, 121}. However, the current intensity-dependence of osteogenesis suggests that electrode movement cannot be solely responsible for healing. Reviews considering MCT (amongst other electrotherapies) for animal bone healing have concluded that there is convincing evidence that it can accelerate healing after osteotomies and fusion surgery in mammals when appropriate parameters are employed^{72, 87, 122}. The studies reviewed have all involved fresh lesions; the effects of MCT on dysfunctional healing - for example in non-uniting fractures - have not been explored in animals, possibly because of the difficulty in creating animal models¹²³.

3.3.2 Skin

Since 1968, when Assimacopoulos used microcurrent to treat surgical scars on rabbit ears¹²⁴, many studies have investigated the effects of MCT on animal skin wound healing. Lesions caused by incision, scalding or burns, and skin grafting have been treated with DC and pulsed monophasic current, applied via a conductive dressing applied to the wound and another adherent electrode sited nearby¹²⁵⁻¹³¹. Wound closure times, exudate levels, tissue strength, bacterial load, levels of cellular proliferation and neovascularity have all been used as indicators of the healing process^{82, 93}. Compared to bone, a wider range of microcurrent parameters have proved efficacious. Current intensities between 1 μA and several hundred μA promote healing more effectively than sham MCT used with control groups. Electrode surface areas appear to vary substantially between studies, however, and effective current densities probably fall in a narrower range. Some authors suggest that initial cathodal stimulation followed by polarity reversal a few days later may improve effectiveness^{132, 133}, but others do not support this contention^{129, 134}. Some controlled trials have failed to show benefit using MCT within the suggested therapeutic window for current intensity. In one case this might have been due to the lack of an applied dressing and the formation of a scab whose high resistance may have reduced the current reaching the wound⁶⁷. The authors of the other study¹²⁸ suggest several possible factors that could have accounted for the ineffectiveness of the treatment, but their findings demonstrate that the evidence for MCT is not consistent. Nevertheless, more comprehensive reviews of controlled animal studies have concluded that

MCT can promote healing in surgically induced wounds^{82, 135}. There is also limited evidence using a rabbit model that it may be effective with ischaemic wounds¹³⁶.

3.3.3 Other tissues

There is some animal study evidence to suggest that very low intensity currents may promote healing following peripheral nerve damage. In one study⁸¹, artificial crush injuries were created in sciatic nerves of rats, and electrodes implanted either side of the injury delivered a nominal 1 μ A direct current continuously for three weeks. Functional performance of the limb served by the nerve improved more rapidly in those given MCT compared to sham-MCT controls, and at 3 weeks there was significantly greater nerve fibre density and neovessel formation in the stimulated nerves than in controls. Several other *in vivo* studies have also confirmed that DC microcurrent can stimulate regeneration after peripheral nerve injury in rats^{137, 138}. A review of early studies concluded that DC current intensities of approximately 1.4 μ A were most effective in promoting regeneration without adverse effects¹³⁹.

MCT has also been observed to promote healing in damaged cartilaginous tissue. DC of amplitude 2 μ A and pulsed at 100 Hz, started 48 hours after surgery and applied continuously over four days, increased chondrocyte proliferation compared to controls in surgically damaged rabbit femoral condyles¹⁴⁰. Normal growth of cartilage in young rabbit hips has also been enhanced by continuous application of 8 μ A DC for 3 – 5 weeks⁸⁶.

3.3.4 Soft connective tissues

A number of studies have examined the effects of MCT on soft connective tissues, particularly tendons. In one, explants of transected and repaired rabbit flexor tendons were given either 7 μ A DC or sham MCT for 42 days, via electrodes sutured onto the tendon with the cathode in the lesion and the anode about 4 cm away¹⁴¹. Histology revealed evidence of repair in all explants, but the stimulated samples had substantially more collagen fibres visible by day 7. Fibres bridged the lesion in the epitenon of stimulated samples, but in none of the tendon bodies. The authors speculated that healing was inhibited in the immediate vicinity of the cathode, since collagen deposition occurred some distance from it and there was evidence of necrosis immediately adjacent to it at 42 days.

Parameter-dependence has been investigated in several studies. Application to cultured equine tenocytes of monophasic current pulsed at 150 Hz and with several intensities between 50 and 1500 μA , demonstrated increased cell proliferation and protein synthesis in all cases but maximal at 100 μA ⁶⁴. Apoptosis was observed in all samples but increased with number of treatments and current intensity. Microcurrent stimulation of tissue growth was examined using explants of flexor digitorum tendons from chickens, exposed to pulsed monophasic current or sham treatment⁶⁹. Fibroblast proliferation was greater in the MCT group, with the maximal effect using a 1 Hz, 1 ms pulse duration waveform, and with current densities of 0.4 – 0.8 $\mu\text{A}/\text{cm}^2$. Above 24 $\mu\text{A}/\text{cm}^2$ difference became negligible. Collagen synthesis maximised at 0.7 $\mu\text{A}/\text{cm}^2$ and fell above 10 $\mu\text{A}/\text{cm}^2$. Applying current along the explant caused increased proliferation and synthesis, but perpendicular current produced no detectable effect. So the direction of charge flow appeared a significant determinant of treatment effect. In another study⁶⁵, explants of rabbit flexor tendons and their synovial sheaths were exposed to constant DC of 0.5, 1 and 6 μA , applied longitudinally for one or two weeks. Investigation of the cut surfaces revealed evidence of cell proliferation and collagen deposition in both treated and control samples, with adhesions forming in the epitendon-sheath as a result. Cells in the stimulated explants showed increased numbers of organelles. Above 1 μA there was evidence of tissue degeneration and cell death; at 0.5 μA proliferation continued in the tendon substance but was significantly reduced in the sheath. The latter observation is particularly significant because it suggests that microcurrent selectively inhibited proliferation that would lead to counterproductive adhesion formation during sheathed-tendon healing. In other words, the therapy did not merely promote particular elements of the healing cascade, but facilitated a broader process of adaptive healing. This remarkable finding has not been replicated by other groups.

In-vivo animal studies have also been conducted. Norrie surgically injured forelimb superficial flexor tendons bilaterally in six ponies, and for up to 6 weeks treated one side with current generated by a bimetallic strip via a platinum cathode implanted at the injury site and a silver anode 3 cm distal¹⁴². Tendons segments were removed at 4, 5 and 6 weeks post-injury and subject to visual and microscopic inspection. No significant differences were observed between treated and control tendons, although the current was not monitored and was thought to be less than 1 μA , so it may have been below the therapeutic window.

In a later study, Stanish and colleagues surgically divided right patellar tendons of nine dogs¹⁴³. The legs were then either immobilised in plaster casts (group 1), dressed with compression bandaging for 48 hours and were then free to move (group 2), or given constant 20 μA DC delivered to the tendon using a cathode wire wrapped around it, with the anode

implanted subcutaneously (group 3). After six weeks the dogs were killed and tendons with their bone attachments removed bilaterally, the contralateral tendon as a control. The mean breaking strengths as percentages of the contralateral limb for the groups were 47%, 50% and 92% respectively. Later work by numerous groups using rats, rabbits and dogs suggested that monophasic or unbalanced† biphasic microcurrent in the amplitude range 10 - 100 μ A, applied via wire electrodes placed in or near surgically induced lesions, resulted in greater breaking strengths in treated tendons compared to sham treated controls^{85, 144-146}. Total treatment times were of the order of hours, spread over several weeks; frequencies were usually less than 100 Hz, but in the kHz range in some cases. The use of breaking strength as an outcome measure is problematic because it could be a product of tissue hardening caused by chemical reactions near the electrode, rather than of cell-mediated tissue healing. One study also used histological examination and found that more collagen was laid down in treated tendons in later weeks of treatment, with a significantly higher proportion of type I (mature) collagen deposited, compared to control tendons¹⁴⁶.

The effects of MCT on damaged ligaments and joint capsules have also been investigated. Sham or real microcurrent was applied to bilaterally divided and sutured medial collateral rat ligaments in two studies^{147, 148}, using either DC or low frequency AC waveforms. Both suggested that treatment increased stiffness and breaking strength, but histological examination was not conducted. Rat knee joint contracture, caused by temporary suturing in flexion, was treated by DC or 1 Hz AC and compared with sham MCT controls in two studies^{149, 150}. After 2 or 3 weeks treatment, range of movement in the treatment groups were significantly better than in controls, and mechanical testing in one study suggested that this was due to decreased stiffness of the supporting ligaments¹⁵⁰. The authors speculated that the treatment may have promoted tissue adaptation that would normally result from mechanical stimulation.

3.3.5 Clinical significance

Many of these studies were controlled with sham-MCT. In most of the connective tissue studies, contralateral lesions provided well-matched control groups. These features enable a cause-effect relationship to be established between treatment and outcome. However,

† Biphasic currents involve periodic reversals in charge flow direction. With unbalanced currents, the flows are not equal in magnitude so there is a net current in one direction. The term "asymmetrical" is also employed: this signifies a biphasic current whose negative and positive phases have different waveforms, and which may or may not be balanced.

evidence is limited by a number of shortcomings. Histological analysis of treated soft connective tissue has been surprisingly rare, and so information about the effects of MCT on tissue anatomy and physiology is scant. Radiology has been used to confirm healing in bone; visual inspection and surface measurement has provided evidence of healing in skin wounds; but outcomes directly related to tissue healing have rarely been measured in soft connective tissue animal studies. The use of an untreated contralateral limb as a control is also potentially problematic, since damage to one limb may produce compensatory changes in the other, resulting in structural and histological changes that would not have occurred otherwise. Hence, the control limb may be affected by conditions of the study.

In most cases, tissue damage was caused surgically and treatment applied in the acute and sub-acute stage of healing. Animal models of chronic lesions resulting from disease, hypoxia, degeneration, cumulative microtrauma and dysfunctional healing are in the early stages of development^{114, 151-153}, and little data on the effects of MCT on such lesions is available from animal studies. Long term outcomes for the soft connective tissues have not been measured, even though the latter stages of healing may continue for many months. Thus, the potential effects of MCT on the remodeling process remains unexplored in animal studies.

Parameter-dependence remains a contentious issue. Whilst there is consensus that current intensities within the microamp range can promote healing in a variety of tissues, the effective values appear to be significantly lower in bone and tendons than in skin. This discrepancy diminishes (but is still present) if current density is considered, since the implanted wire electrodes used with bone and tendon lesions are usually of much smaller surface area than the conductive dressings applied to skin wounds. Where electrodes are applied to the body surface, the current reaching the damaged tissue is, in any case, virtually impossible to measure or calculate for deeper lesions. Such is the heterogeneity of treatment protocols, it is also impossible confidently to draw conclusions about the influence of waveform. However, the majority of reviewed studies demonstrating the effectiveness of microcurrent use DC, monophasic or unbalanced biphasic currents with frequencies less than 100 Hz. Arguments have been proposed for the use of total charge or energy delivered as key parameters^{84, 154} but these have not gained currency. Similar total charge or energy delivery could be achieved more quickly than MCT by using greater current intensities but, as has been seen, these may lead to cell death and tissue damage. Therefore these parameters must be subsidiary to current intensity in determining effects.

Thus, the evidence from tissue and animal trials, whilst strongly suggestive of therapeutic potential, can only provide measured support for its investigation in human trials, and broad guidelines for which parameters should be employed.

3.4 HUMAN STUDIES

In this section, human trials involving bone, skin, muscle and nerve are considered. Trials specific to the soft connective tissues, which may respond differently to MCT, are dealt with by a systematic review later.

3.4.1 Bone

In 1812 the surgeon John Birch – who ran an electrotherapy department in a London hospital – used percutaneous electrodes to pass electric current through a 13-month old non-uniting tibial fracture[‡]. After 6 weeks of treatment the bone was deemed healed¹⁵⁵. Although the size of the current was not reported, this may be the first record of MCT for healing human bone. Other clinicians of the time recorded similar successes³, but the treatment then fell into disuse until the late-20th century. In 1971 case report appeared of a malleolar fracture, non-united for more than a year, but treated successfully with 10 μ A DC via a cathode placed in the fracture site¹⁵⁶. Since then, many trials have been reported, though few have employed separate control groups⁸⁷. Patients have been assumed to be their own controls since spontaneous healing is rare in the cases typically treated, with no radiographic or clinical evidence of healing for at least 3 months. In a typical study, 57 lower and upper limb non-unions were treated with 10 – 20 μ A, delivered to the site by 2 – 4 cathodes for 12 weeks, followed by 12 weeks further immobilisation¹⁵⁷. The authors found that the lower intensity current was inadequate to promote osteogenesis in larger diameter bones and conducted a subgroup analysis of the 46 cases receiving “adequate current”. Of these, 39 (85%) achieved solid bony union. Side effects of such treatment are reported as rare, although in some cases they are serious: in one multicentre study with 178 non-unions, there were 21 cases of skin

[‡] An observer described the case: ‘One of these patients, whom I often visited during his illness, entered St. Thomas’ Hospital in the month of January, 1812, with an unconsolidated fracture of the tibia below the middle of thirteen months’ standing. The leg below the fracture could be easily moved in any direction and without exciting much pain. Shocks of electric fluid were daily passed through the space between the ends of the bones, both in the direction of the length of the limb and that of its thickness. The man, being somewhat weak, used bark and porter at the same time. After the limb was electrized, the ordinary apparatus for fractures of the leg was applied. At the expiration of two weeks the limb had evidently become less flexible in the situation of the fracture; and after a continuance of the same treatment for six weeks, the man was able to walk and left the hospital cured.’⁹⁵

irritation, probably caused by mechanical friction between the wire insert and overlying cast, 7 cases of irritation under the surface-mounted anode and three of cathode dislodgement¹⁵⁸. Occasional cases of severe irritation under the surface anode, or of implant wound infection, have been reported¹⁵⁷. A 10-year follow-up study traced 38 of 81 cases treated with microcurrent and found continued union, normal remodelling and no adverse effects in any of them¹⁵⁹.

In a study involving a mixed caseload of 61 non-unions following fractures, congenital pseudarthroses, osteotomies and leg-lengthening procedures, DC current pulsed at 20 Hz with a pulse amplitude of 20 – 25 μA and duration of 30 ms, was applied via a cathode wrapped around or threaded through the fracture site and with the anode implanted in the medulla¹⁶⁰. Treatment times varied according to case until union or failed union was observed radiographically, and were between 2 and 12 months. The overall success rate was 87%, although adjunctive treatments and patient characteristics varied considerably. An experienced research group concluded that constant DC always produced superior outcomes to pulsing with non-unions, but presented no data in support of this claim¹⁵⁷. An example of the equipment and effects used in one study is provided in Figure 3.1.

The lack of more recent studies may reflect the greater popularity of less invasive electrotherapeutic modalities¹⁶¹, although MCT gives superior results in selected cases. A comparison with capacitative and inductive coupling (which generate high frequency electric or electromagnetic fields in the tissue) after bone graft treatment of tibial non-unions found that microcurrent was more effective with high risk cases such as those with atrophic non-unions or previous graft failure¹⁶². Where there were no identified risk factors, none of the electrotherapies was superior to graft alone. MCT produces superior outcomes in selected cases of lumbar spinal fusions, and continues to be the adjunctive electrotherapy of choice for this application. Direct current, typically of 20 μA applied by a single or multiple cathodes to the fusion site for 5-6 months, has been evaluated in several controlled trials¹⁶³⁻¹⁶⁵. Typically, patients receiving MCT in addition to standard treatment had successful fusion rates of 81 – 96%, compared to 54 – 81% for those on standard treatment alone, as assessed by radiographic and clinical criteria. Results for methodologically sound controlled trials consistently indicate statistically significant outcomes in favour of DC MCT compared with control groups¹⁶⁶. It is particularly effective when used in high risk cases such as those with previous failed fusions, multiple level surgery, smokers and those with co-morbidities such as diabetes and obesity^{72, 96, 167}. An economic evaluation of the therapy as an adjunct in spinal fusion surgery¹⁶⁸ also found that it provided significant cost savings and shorter in-patient stays.

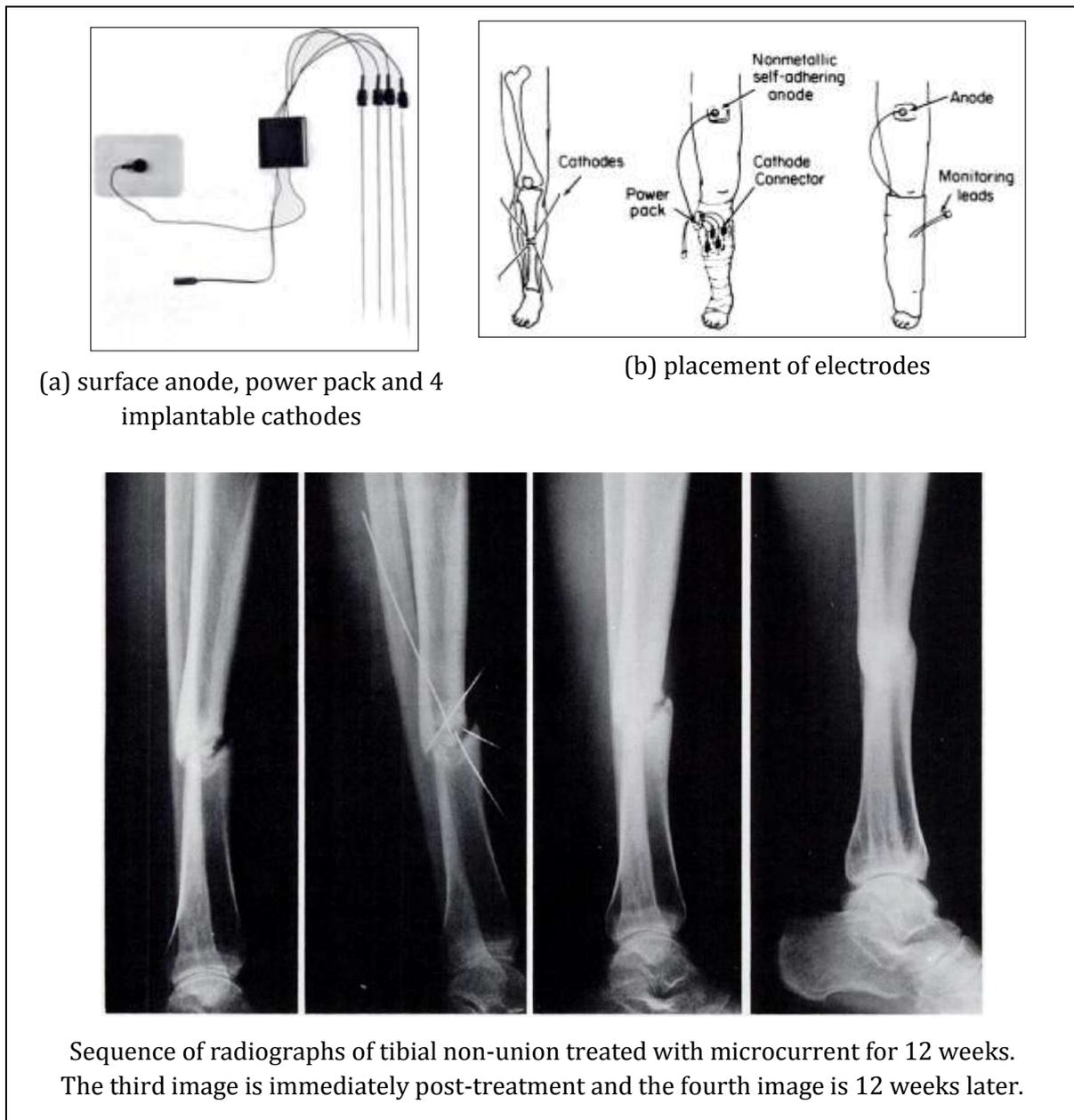


Figure 3.1: Microcurrent treatment of non-uniting fractures¹⁵⁸

Despite encouraging results of some animal studies, few human studies have investigated the potential of MCT for accelerating healing after normal fractures. Two, using 20 – 40 μA DC, found in favour of the modality^{169, 170}. However, although these trials were controlled, randomisation or matching of participants was not attempted, and they are poorly described. Reviews rarely focus specifically on this application, but at least one has concluded that fresh fractures do not respond to DC microcurrent¹⁷¹.

Systematic reviews of trials have concluded that the best evidence for promotion of bone healing by application of small electric currents is in cases of non-uniting lower limb

fractures, osteotomies and spinal fusions^{87, 96, 166, 172-178}. Stimulation on non-unions is reported to be particularly effective when other forms of therapy have not helped repair⁸⁷. However, meta-analyses have been weakened by pooling data from trials using heterogeneous groups and treatment parameters, and even different forms of electrotherapy^{166, 174}. Many studies are criticised as poorly conducted or reported, and for drawing conclusions based on statistical rather than clinical significance³⁸.

3.4.2 Skin

Several authors have erroneously identified the seventeenth century use of charged gold leaf for resolution of smallpox lesions as the first example of electrotherapy for skin healing^{82, 111, 179}. In fact there is no mention of electric charge in the cited source¹⁸⁰ §. Charged gold leaf was used successfully in the 1960s to assist healing in surgical vascular wounds and cutaneous ulcers^{181, 182}, but charging was considered an aid to adherence of the leaf rather than an agent of healing in itself. Nevertheless, reviews of more recent studies have consistently concluded that electrical stimulation, including MCT, can successfully promote healing in various types of skin wounds, particularly ulcers^{82, 183, 184}.

The first modern account of MCT for skin wounds described the treatment of recalcitrant leg ulcers in three patients¹⁸⁵: an 18-year old man with a history of diabetic leg ulcers, and two elderly people with venous ulcers. Previous conservative treatment had been unsuccessful. All were treated initially with antibiotics and then by direct current between 50 and 100 μA , delivered continuously via mesh electrodes. The cathode was soaked in saline and placed on a moist dressing on the wound, and the anode was affixed to the thigh or abdominal wall. One wound healed in seven days, and the others within 6 weeks. Histological assessment of tissue taken from one of the healed diabetic wounds 18 months later indicated well-healed dense connective tissue. No side effects of treatment were reported.

Evidence from trials with larger samples and control groups accumulated in subsequent years. Outcomes observed included exudate production, bacterial load, neovascularisation, rates of re-epithelialisation, time to wound closure, and pain. Typically, successful treatments used DC of 100 – 800 μA applied directly to a non-healing wound via a conductive dressing, applied for several hours daily for several weeks, sometimes months^{100, 186-188}. A trial using

[§] In an early example of a n=1 controlled trial, the English royal physician Kenelm Digby reported that, having applied gold leaf to the face of a young woman scarred by smallpox, “half her face where the Gold lay was clear from any Pocks at all, and [the] other half, where they laid no Gold, was deform’d with Scars” (Shuttleton, D.E., *Smallpox and the Literary Imagination: 1660-1820*. 2007, Cambridge: Cambridge University Press, p117).

300 μA amplitude monophasic current pulsed at 128 Hz, applied to chronic venous ulcers for several months, showed no benefit of real over sham MCT, however¹⁸⁹. Some studies have suggested that swapping the polarity of the electrodes periodically can improve outcomes, but the evidence is inconsistent^{82, 186}, and the rationale unclear.



Figure 3.2: An adherent wound dressing with a built in microcurrent generator¹⁹⁰

MCT has also been found more effective than conventional treatment in promoting skin graft healing following thermal injury¹⁹¹; and case series and controlled trials have suggested that low frequency (<1 Hz) 600 μA biphasic microcurrent is capable of stimulating healing in recalcitrant pressure ulcers^{192, 193}. Reviews of electrical stimulation for skin wound healing have consistently concluded that the weight of evidence is in its favour when it is used as adjunctive treatment with other conservative management strategies^{82, 135, 166, 179, 183, 194-196}. Where MCT studies are considered alone, the range of protocols employed means that optimum parameters cannot yet be identified. Both continuous and pulsed, monophasic and biphasic, anodal and cathodal stimulation appear capable of promoting healing, although the low methodological or reporting quality of many studies leaves them open to bias and reduces confidence in their findings^{171, 179, 196}. Reviews are usually unable to draw firm conclusions about which parameters are most effective^{183, 195}. Those supported by a majority of studies are current intensity (in the hundreds of microamps)¹⁹⁷, treatment time (typically several weeks, for hours rather than minutes each day)^{5, 112} and application directly to the wound bed. This is typically via normal dressings with mesh electrodes attached and a separate power supply, but several more recent pilot studies have used a dressing with an in-built circuit and power supply¹⁸⁴ – see Figure 3.2 for an example. Monophasic or unbalanced currents are more common in the studies indicating MCT effectiveness^{82, 197, 198}, although steady DC is rarely used in practice^{82, 171}.

3.4.3 Other tissues

Trials of MCT for delayed-onset muscle soreness (DOMS), due to microtrauma in muscle tissue following intense exercise, generally do not support its use for this application^{101, 199-203}. Treatment times are much shorter than in the bone and skin studies, and pain intensity is the most common outcome measure. One study evaluated a skin-mounted charged dielectric pad, providing an average 20 μ A over 96 hours²⁰². Serum creatine kinase (CK) levels, which elevate following muscle damage, were found to be lower in DOMS-induced muscles after MCT than in an untreated control group. The authors speculated that the therapy might have a prophylactic effect, reducing the degradative biochemical process that lead to microstructural damage in DOMS. A small number of trials provide very limited evidence that MCT may be of benefit in other disorders where tissue damage is a factor, such as osteoarthritis^{204, 205} and macular degeneration²⁰⁶⁻²⁰⁸. None of these studies used any measure of tissue healing, however, and those concerned with macular degeneration had low methodological or reporting quality. It is rather surprising that the promising results of studies using MCT to promote nerve regeneration in animals appear not to have been followed up with clinical trials with humans.

3.4.5 Parameter dependence

Reviews of trials have consistently concluded that there is insufficient data available to be confident about which parameters combinations are optimal. Comparisons studies using different combinations have rarely been attempted with human subjects. However, a few such studies have been conducted in vitro or with live animals, and those cited earlier suggest that the size of the current and the total duration of treatment are key. This is consistent with the suggestion that total charge or energy delivered determines treatment success because these quantities are functions of current and time. The influence of waveform, polarity, and frequency of variation or pulsing is much less apparent. Indeed, if MCT's effectiveness is dependent on its similarity to bioelectricity, the application of complex or high frequency waveforms would not be justified. Mimicking endogenous currents of injury would also require the applied current to reduce as healing progresses, but no studies attempting this could be found.

Most clinical trials describe the current delivered in terms of intensity rather than density, although the latter measure may be the more significant. For a current of known intensity at the skin surface, the intensity (and density) at the site of the lesion will depend on the dimensions of the lesion and the electrodes, the distance between the lesion and the

electrodes, and the electrical characteristics of the intervening tissue. Modelling the effects of these factors for deep lesions is problematic but, where studies use electrodes in direct contact with the lesion and state electrode dimensions, it is possible to calculate approximate current density values. These are given for some exemplar studies in Table 3.1.

Table 3.1: Effective current densities calculated from data generated in human trials of MCT

Tissue - lesion	Current density at electrode ($\mu\text{A}/\text{cm}^2$)
Bone – non-union ¹⁶²	15 – 25
Bone – pseudarthrosis ^{209, 210}	6 – 12
Bone – fresh fracture ¹⁷⁰	5 – 10
Bone – spinal fusion ²¹¹	8
Skin – ulcers (electrode on wound) ^{100, 186, 187}	5 – 110
Skin – ulcers (electrode on intact skin) ^{188, 212}	20, 260
Skin – graft ¹⁹¹	0.1 – 0.2
Muscle - DOMS ²⁰²	20

The data allows some narrowing of the therapeutic window for this parameter, but there is significant variation in effective densities, even for a particular form of tissue damage in some cases. Nevertheless, there appears to be a pattern of lower densities being more effective for acute injuries (fresh fractures, fusions, skin grafts).

3.4.6 Conclusions

The accumulation of data from human trials suggests that MCT of certain parameters is capable of promoting healing in a range of tissues. It appears particularly suited as an adjunct treatment in cases where other forms of management have been unsuccessful. Whereas animal studies have focussed primarily on accelerating normal healing in acute lesions, the human trials have been more concerned with chronic lesions and dysfunctional healing. Once again there remains doubt about the parameters of the therapeutic window.

Study protocols have been directed more towards testing proprietary devices rather than systematically evaluating the influence of each parameter. Whilst this approach is scientifically unsatisfying, it may have some justification. Since the possible combinations of microcurrent parameters are virtually limitless, it is unfeasible to compare them all. Also, particularly where the electrode is not in direct contact with the lesion, the relationship between the applied current and that reaching the damaged tissue is neither constant nor necessarily predictable. This is true for current intensity, density, charge and energy delivered, and waveform. So it more practical to develop treatment protocols in an

evolutionary fashion, adjusting parameters for each form of tissue damage in the light of all available trial data. For the soft connective tissues, the particular concern of this investigation, that data is now considered.

3.5 HUMAN TRIALS WITH SOFT CONNECTIVE TISSUE

It was clear from an initial search of the literature that there are few published clinical trials of MCT for soft connective tissue. Therefore an in-depth search was conducted to obtain as much relevant evidence as possible. This formed the initial stage of a systematic review, whose purpose was to consider whether there is a case for the application of microcurrent to damaged soft connective tissue, and to identify areas that require further investigation. The specific questions addressed were:

- A.** What are the effects of microcurrent therapy on tissue healing and on clinical signs or symptoms following soft connective tissue damage?
- B.** Are these effects dependent on the treatment parameters or method of application?
- C.** Is microcurrent more effective when used in combination with other forms of treatment?
- D.** Are there any adverse effects of MCT?
- E.** What data is there regarding feasibility, cost, acceptability to patient and clinician of this treatment?

These questions reflect the clinical focus of this investigation, and its concerns with effectiveness, safety and practicality. The review process was based on recommendations made in the literature for the conduct of reviews²¹³⁻²¹⁵. Although well-conducted randomised controlled trials (RCTs) are thought to provide the best evidence for treatment effectiveness²¹⁶, other study designs can supply useful information about effects, safety, appropriateness and feasibility^{217, 218}. They may also provide indications of potential population subgroups with differential responses to treatment. These considerations are particularly important where a therapeutic application is novel and where few trials have yet been conducted. The standard of evidence provided by such studies may be lower than that of well-conducted trials, but not considering them risks ignoring potentially valuable data. This is particularly true of rehabilitation research where it may be very difficult to create a well-controlled trial that bears any resemblance to the clinical context in which a therapy may be employed²¹⁹. In such situations, careful consideration and weighting of multiple lines

of evidence may be the most appropriate and productive approach. It entails a more complex form of data analysis and quality scoring system, but the potential benefits suggested that this inclusive approach should be employed. Hence the review included both studies that used an RCT design, and those employing other experimental or quasi-experimental approaches.

3.5.1 Eligibility criteria

Studies types included were human and experimental, such as randomised controlled trials (RCTs), non-randomised or quasi-randomised controlled trials, controlled before and after studies, interrupted time series, cross-over or parallel arm studies, and prospective or retrospective case series or case studies involving an intervention.

The study intervention included some form of MCT as previously defined, applied to damaged soft connective tissue (comprising a primarily collagen-based matrix formed by cell phenotypes of the fibroblast). Any comparative trials using identical forms of MCT in all groups, as an adjunct to another treatment, were excluded because the design would not enable the effects of the microcurrent itself to be evaluated.

Included studies employed outcomes relating to any of the following: tissue healing, signs or symptoms of possible tissue damage, adverse events, treatment costs and user acceptability. Only studies published in English were considered, unless a summary or abstract allowing the necessary data to be extracted was available.

3.5.2 Search strategy and study selection

Multiple sources were searched in order to cover not only peer-reviewed and published papers, but also the grey literature. These included core and subject specific databases recommended by authorities for conducting reviews of clinical effectiveness studies^{220, 221}. The specific databases used were PubMed, EMBASE, AMED, Cinahl, ISI Web of Science, ChiroAccess, Google Scholar, OpenSIGLE (grey literature) and Theses.com, along with the following registers of trials: Cochrane Database, controlled-trials.com, Clinical Trials.gov, PEDro, DARE and Health Technology Assessments. The reference lists of included studies and those cited in publicity provided by manufacturers of commercial microcurrent devices were also searched, and the ISI Citation index was used to trace papers citing the studies included in the review. Grey literature, defined as “that which is produced on all levels of governmental, academics, business and industry in print and electronic formats, but which is not controlled by commercial publishers”^{cited in 222}, was thought to be of a potential value both

for correcting publication bias and to supplement the scant evidence that was uncovered during preliminary searches of the conventionally-published literature.

Because the terminology used to describe microcurrent is not used consistently in the literature, an iterative approach was adopted for the development of a search strategy. Three sets of search terms were used initially, identifying the therapy, the tissue or disorder, and the study design. Variants of the treatment terms failed to pick up several relevant papers, which used other phrases such as “electrical stimulation” or even “electromagnetic stimulation” as their key terms. Subsequent searches using these terms were very non-specific, however, and produced large numbers of irrelevant publications. Attempts to filter by connective tissue type or disorder met with only limited success, failing to exclude numerous studies concerned with other tissue types. Hence, a broad search strategy was adopted. The study design terms were based on published guidance for the identification of RCTs and studies using other experimental designs within the PubMed database^{223, 224}. The searches employed with each database are detailed in Appendix 1.

For conventionally published papers emerging from the search, title or abstracts were viewed to gauge whether the study was likely to meet the eligibility criteria. Screening of grey literature was based on viewing of any available information in the source. For both conventional and grey literature, if there was doubt about eligibility, attempts were made to obtain the full publication to screen for eligibility.

3.5.3 Quality Assessment

There are many assessment tools available for judging the quality of human studies, although few are supported by validity and reliability studies^{225, 226}. In the absence of a gold standard, the choice of quality criteria for this review was based on applicability to different study designs, coverage of key quality domains (internal validity, external validity and reporting^{226, 227}), and ease of use. No single tool meets all these criteria^{225, 226}, therefore several were drawn upon to create an evaluation instrument suitable for this review²²⁸⁻²³¹. A systematic review of study quality scales used with physiotherapeutic interventions suggests that additional factors, not addressed by any of these sources, should be taken into account when assessing the quality of physiotherapeutic clinical trials²²⁵. These included standardisation and precise description of the intervention, patient adherence to the protocol, and psychometric properties of outcome measures used. Whilst the importance of these features in quality assessment has not been proven, they have face validity for the purpose, particularly where multimodal interventions and multiple outcome measures are used.

Although it has been suggested that the blinding of allocation to groups in RCTs should be given particular weight^{232, 233}, no validated weighting systems are available for all the criteria included in this instrument, and so none was applied.

Trials involving a single group and those comparing outcomes for more than one group use different methodologies are not necessarily seeking to answer the same questions. Thus it is not appropriate to assess their quality by the same criteria. For instance, whilst a case series cannot provide robust evidence of efficacy, it may nevertheless be well-conducted and give high quality and valuable data about safety and feasibility. Therefore, a novel scheme was developed to enable both types of study to be evaluated. This had a core set of 11 criteria that were applied to all studies, and an additional seven criteria specifically for application to comparative studies.

The resulting quality criteria are presented in Table 3.2. A more detailed version of the tool, which was used in the review, is given in Appendix 2. The validity of this instrument was not assessed, although rationales for the inclusion of each criterion are provided in the cited references.

Table 3.2: Study quality assessment criteria

Criteria for all studies		
1	Eligibility criteria specified ^{230, 234-236}	2 = comprehensive statement of inclusion and exclusion criteria 1 = partial information about relevant eligibility criteria 0 = no information about eligibility criteria
2	Treatment fully described ^{234, 236}	2 = description allowing duplication of treatment provided 1 = partial description 0 = essential elements of description absent
3	Treatment standardised ^{225, 236}	2 = clear statement of how standardisation was achieved 1 = statement suggesting standardisation 0 = not standardised / unclear / no evidence presented
4	Key baseline characteristics stated ^{226, 236}	2 = data presented for key characteristics that might affect outcome 1 = data presented for some characteristics that might affect outcome 0 = no relevant data
5	Key outcome measures validated ^{225, 234}	2 = evidence given for valid use of key outcome measure for this application 1 = key outcome measure has face validity for this application 0 = no evidence of validity of application
6	Key outcome measures reliable ^{225, 234}	2 = evidence given for reliable use of key outcome measures for this application 1 = partial evidence regarding relevant reliability data presented 0 = reliability of application not established or unclear
7	Drops outs and Intention to	2 = statement that all received intended treatment, or ITT analysis

	treat analysis ^{230, 231, 234-236}	1 = clear statement of withdrawal numbers and reasons 0 = unclear or no information presented
8	Appropriate statistical analysis ^{230, 234, 236}	2 = apparently appropriate analysis used 1 = incomplete analysis presented 0 = inappropriate or no relevant analysis
9	Point & variability estimates for at least one key outcome ^{230, 235, 236}	2 = appropriate graphical or numerical data provided 1 = partial presentation of data 0 = inappropriate or no data
10	Key outcomes measured for >85% of subjects in each group ²³⁰	2 = numbers allocated and measured stated, and criterion satisfied 0 = cannot tell, or <85% in each group measured
11	No competing interests ²²⁸	2 = clear statement of no competing interests 0 = potential conflict / no statement / unclear

Additional criteria for experimental studies involving comparison between groups

12	Method of group assignment described ^{226, 228, 229, 236}	2 = full description allowing duplication 1 = partial description 0 = inadequate or no description
13	Satisfactory method of randomisation ^{230, 231, 235}	2 = clear evidence of satisfactory randomisation 1 = partial evidence of randomisation 0 = no evidence
14	Groups balanced on key baseline characteristics ^{226, 229, 230, 234-236}	2 = no significant difference on all key baseline characteristics of completers, or adjustment in analysis 1 = no significant difference on most key baseline characteristics of completers, 0 = not stated or differences not dealt with
15	Allocation concealment ^{230, 235, 236}	2 = clear evidence of satisfactory concealment 1 = partial evidence of concealment 0 = no evidence
16	Subjects blinded to treatment ^{230, 231, 235, 236}	2 = clear evidence of satisfactory concealment 1 = partial evidence of concealment 0 = no evidence
17	Therapists blinded to treatment ^{230, 235, 236}	2 = clear evidence of satisfactory concealment 1 = partial evidence of concealment 0 = no evidence
18	Assessors blinded to treatment ^{230, 231, 234-236}	2 = blinding clearly achieved 1 = partial evidence of blinding 0 = no evidence presented

The marking system meant that different study types had different maximum attainable quality scores (22 for single group studies and 36 for comparative studies). No quality threshold was set for inclusion in the synthesis, but scores were used in assessments of the strength of evidence for each of the questions posed by the review. Scores were converted to percentages of the maximum possible for that study type, and interpreted as follows: 70% or

above = good, 50-69% = fair, below 50% = poor. These criteria are arbitrary, but the upper threshold is the same as that used in some other systematic reviews of tennis elbow trials²³⁷,²³⁸; the lower thresholds are rather more conservative.

3.5.4 Data Extraction and analysis

The following data was extracted from included studies:

- Source: authors, year, title and publication for conventional literature; identifier, source and date obtained for other forms.
- Subjects: numbers, inclusion and exclusion criteria
- Methodology: basic design, group allocation method, blinding, intention to treat analysis, sample selection, baseline homogeneity (if applicable).
- Intervention: all microcurrent parameters including current intensity (average or peak), waveform description, frequency, pulse duration and repetition rate where applicable, whether current or voltage regulated; electrode description (material, size, placement); duration of application (per single application, number of applications, inter-application interval, total treatment period)
- Co-interventions and comparators: additional interventions, description of treatment given to other groups in study (if applicable)
- Outcomes: all outcomes measured, adverse events, values, statistical test results, departures from study protocol, conclusions reached.
- Conflicts of interest, funding
- Comments: any additional information deemed relevant.

Following this process, data was inspected and then synthesised or summarised so as to address each of the review questions in turn.

The review included trials using a variety of designs, and was concerned not only with clinical effectiveness but also with appropriateness (from the patient's point of view) and feasibility (of incorporation into clinical practice). Thus, a framework was required to judge the level of the evidence for these different issues. Such a framework has been proposed²¹⁸: it ranks the evidence on different types of questions into four categories - excellent, good, fair

and poor – according to the type of question being addressed and the type of study providing the evidence. So, for example, whilst systematic reviews and multicentre studies are necessary to provide an excellent standard of evidence on any clinical question, a good level of evidence – that can be used to inform clinical practice - can be obtained from both RCTs and observational studies. This schema was used, along with the methodological quality criteria described above, to rank the level of evidence emerging from this review.

3.5.5 Results

Figure 3.3 illustrates the search and filtering process that produced 20 studies for inclusion in the review.

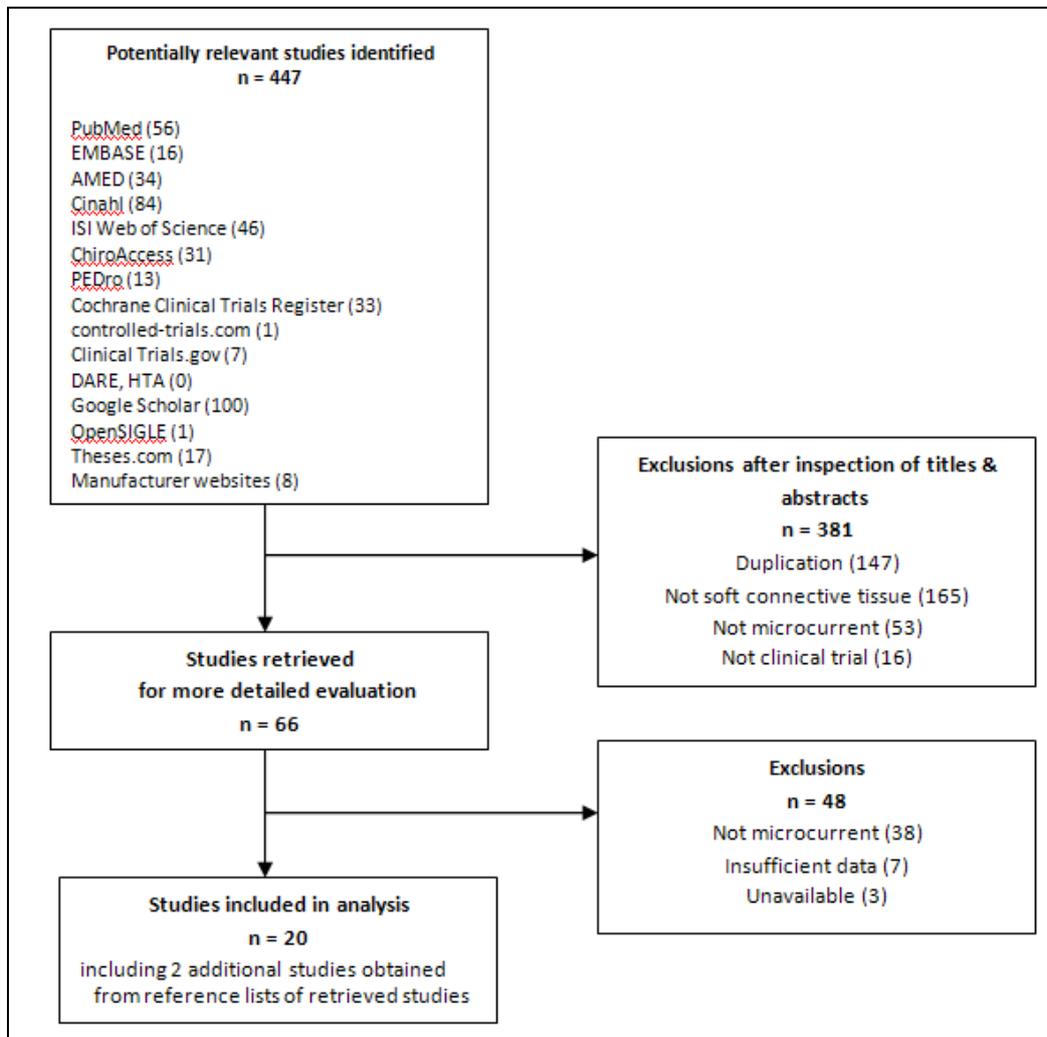


Figure 3.3: Search results and filtering process for systematic review of MCT trials

A search for publications citing any of the 20 included studies was made with the ISI citation tracker, but produced no new eligible studies. Two potentially relevant studies could not be traced^{239, 240}, and a third was unobtainable²⁴¹. Of the 20 eligible studies, 11 were listed in PubMed or Cinahl, five were obtained via Google Scholar, three from manufacturers' websites and one from reference lists of other publications. Two of them were grey literature: one was a conference abstract and one was a report based on a Masters thesis. A summary of extracted data and quality scoring for the included studies is presented in Table 3.3. More expansive descriptions of the studies, their quality scores, treatment parameters and outcomes are given in Tables 3.4, 3.5 and 3.6 respectively.

Table 3.3: Summary of characteristics of included studies

Study	n	Design	Target	Quality score (%)	Control	Current Intensity / μ A	Treatment Duration	Waveform	Co-intervention	Primary outcomes
Chapman-Jones & Hill (2002)	48	RCT	Chronic Achilles tendinopathy	36	Standard treatment	40	30 minutes/day for 14 days (total 7 hours)	monophasic square wave 10Hz	Eccentric exercises	Pain; stiffness
Cho et al (2007)	10	CS	Plantar fasciitis	18	na	60-160	>4 hours/day for 6 weeks (total > 168 hours)	Spike \sim 1Hz	ns	Post-exercise fatigue; Pain
El-Husseini et al (2007)	24	RCT	Post-operative pain after total knee replacement	28	Analgesic medication	10 / 10-937	Ns but apparently continuous for several days (total \sim 100hours)	DC or varying (form ns) 0.5-500Hz	Analgesic medication	Pain; wound healing
Ho et al (2007)	16	RCT	Lateral epicondylitis	39	Exercise programme	40 / 300	Several minutes 10 times in 3 weeks (total < 1hour)	Biphasic square wave 0.3 / 3 / 30Hz	Exercise programme	PPT; PFGS
Johannsen et al (1993)	16	RCT Cross-over	Chronic lateral epicondylitis	75	Sham MCT	0-300	Several minutes 10 sessions over 3 weeks (total < 1hour)	Ns but apparently biphasic	None	MGS; pain
Koopman et al (2009)	10	RCT Cross-over	Chronic nonspecific back pain	78	Sham MCT	25	Continuous 5 days (total \sim 120 hours)	Form ns manufacturer states f=0.5Hz	ns	Pain; QOL
Kulkarni & Smith (2001)	15	CS	Pain - various musculoskeletal	50	na	600	1 hour, 5/week for 3 weeks or until no pain (total <15 hours)	Ns but manufacturer states biphasic	Cranial Electro-stimulation Treatment in some cases	Pain; Side effects
Lennox et al (2002)	26	CS	Radiation-induced fibrosis in neck	59	na	typically 600	ns x2/day 5 days (total \sim <2hours)	AC 10 / 0.5-100Hz	None	Neck ROM
Lerner & Kirsch (1981)	40	RCT	Chronic back pain	33	Sham MCT	"variable subsensory microcurrent"	2 x 6 seconds, x3/week for 2 weeks (total 72 seconds)	Biphasic 0.5Hz	ns	Pain
Maenpaa et al (2004)	12	CS	Ankle contracture in cerebral palsy	50	na	300	Min 5 hours/week For average 22 treatments (total = ?few hours)	"constant slope-wave" 30Hz	None	Ankle ROM
Maugeri et al (1999)	19	CS	Acute arthrorheumatic pain	41	na	30	20 minutes every 2 days - 6 treatments (total = 2 hours)	ns	ns	Pain; Function

Study	n	Design	Target	Quality score (%)	Control	Current Intensity / μ A	Treatment Duration	Waveform	Co-intervention	Primary outcomes
McMakin (2004)	22	CS \oplus	Chronic low back myofascial pain	37	na	100	2-40 minutes up to x2/week, max 4 weeks (total = up to tens of hours)	pulsed DC modified to alternating ramped square wave	massage, manipulations as needed, other complementary therapies	Pain; Side effects
McMakin et al (2005)	54	CS	Fibromyalgia associated with cervical spine trauma	30	na	ns "polarised" microcurrent	ns	square wave 10 / 40Hz	ns	Pain
Noto & Grant (2009)	120	RCT	Pain - location not specified	6	a range of electro-therapies	600 according to manufacturer	treatment duration 15-20 minutes; number ns (total = ?)	Form ns 10Hz	None	Pain; Side effects
Rolle et al (1994)	31	RCT	Elbow tendinitis	70	Sham MCT	40-100	30 mins /day for 6 days (total = 3 hours)	Monophasic sloped 0.3-30Hz	Exercise programme	Pain
Sizer et al (2000)	41	RCT	postoperative pain after patellar tendon or anterior cruciate ligament reconstruction	33	Sham MCT	100	Minimum 1 hour/day, for 10 days (total > 10 hours)	ns	Standard physiotherapy rehabilitation programme	Pain medication; Pain
Smith (2001)	978	CS	Pain - various musculoskeletal	23	na	ns but up to 100 according to manufacturer	ns	Ns but biphasic according to manufacturer	ns	Patient-rated improvement
Stanish (1985)	>100	CS with comparison group	Patellar Tendon & cruciate ligament - post-surgery	14	Comparison with surgery only	20	ns but apparently continuous for several weeks (total ?>100 hours)	DC	Surgery	Time return to full weight-bearing and function
Tan et al (2000)	28	RCT Cross-over	Pain - various musculoskeletal	61	sham MCT	10-600	ns	ns but according to manufacturer biphasic 0.5Hz	"standard treatment protocols" but not described	Pain
Zimmerman & Lerner (1989)	42	RCT (3 groups)	Low back pain	39	Biofeedback; MCT+ biofeedback	200 / 500	30 minutes, 2/week for 10 weeks (total 10 hours)	ns but according to manufacturer biphasic 0.5Hz	None	Anxiety Pain

Abbreviations: CS = case series; MCT = microcurrent treatment; MGS = maximum grip strength; na = not applicable; ns = not specified; PFGS = pain-free grip strength; PPT = pressure pain threshold; QOL = quality of life; RCT = randomised control trial; ROM = range of movement;

Description of studies

Twenty studies met the eligibility criteria for inclusion in the review. Ten were RCTs, one was a non-randomised controlled trial and nine were case series. Table 3.4 provides descriptions of these studies. Tendons were the mostly common tissue type considered, being specifically investigated in four studies and possibly involved in one concerned with myotendinous contracture²⁴². In all these cases, the tendinopathy was chronic, with minimum or average symptom durations of greater than three months. Ligaments, fascia and bursae were explicitly treated in one study each; the others involved body parts that may have involved several forms of connective tissue (e.g. deep surgical wounds^{243, 244}, peri-arthritis¹⁰⁴, region-specific musculoskeletal pain²⁴⁵⁻²⁴⁹, and radiation-induced fibrosis²⁵⁰).

The most frequently employed outcome measure was pain, assessed by either patient-rated scales, pressure algometry or use of analgesic medication. Other measures included muscle strength and fatigue rates, joint range of movement, quality of life scores and global change ratings. Tissue was evaluated by sonography in one study²⁵¹ and histology in another¹⁴³. Haematology was used in one study to measure levels of inflammatory mediators²⁵².

Treatment descriptions were inadequate in every case. In particular, microcurrent waveforms were rarely fully described, and detailed descriptions of co-interventions such as exercise programmes were not provided. Current intensities varied between 16 and 600 μA , although it was often impossible to tell whether these were average or peak values. DC was employed in one study only; monophasic or biphasic waveforms were more common, with fixed frequencies of 0.3, 3 or 30 Hz used in several cases^{242, 253, 254}, and frequency modulation up to 100 Hz in another²⁵⁰. The use of current control to compensate for varying circuit impedance was rarely mentioned. Application of microcurrent was usually by adhesive pads or via probes that were held manually against the body surface and often repositioned during each treatment. Metal impregnated garments, graphite gloves and bare wire wrapped around the damaged tissue were alternative methods of application, being used in a single study each. Treatment durations varied from 20 minutes/day for six days, to continuous application for a month or more. Rationales for these treatment parameters were rarely given and in most cases investigators used proprietary microcurrent devices, following the suppliers' instructions. In some instances it was possible to obtain additional information from the manufacturers. Where this has been incorporated into the data table, it is remarked upon.

Table 3.4: Characteristics of included studies (M=MCT group, C=Control group, BC=baseline characteristics, BE=baseline equivalence, ns=not specified)

Chapman-Jones, D. and D. Hill (2002). "Novel microcurrent treatment is more effective than conventional therapy for chronic Achilles tendinopathy: randomised comparative trial." ²⁵¹	
Methods	RCT, block randomisation Sample size at entry: M 24, C 24 sonographic assessment blind to clinical findings, no other blinding
Target	Tendon - Chronic Achilles Tendinopathy
Participants	From hospitals (?Outpatients dept) Inc: TA pain, stiffness or ↓Function Exc: Treatment in previous month, Age < 18 years, tendon rupture, symptom duration < 3 months BC: 35 male, 29 bilateral, mean age 36/39 years BE: Similar age, sex and baseline severity
Interventions	MCT Co-intervention: Following treatment, progressive eccentric exercises (form and duration ns) Control: variable treatment depending on clinician but including progressive eccentric exercises
Outcomes	Clinician severity rating Sonography (0-9) ankle joint ROM patient-rating of pain, stiffness, function using bespoke ordinal scales Assessment at baseline, 3,6,8,12m 18 & 11 subjects assessed at 1 year
Notes	complex and unvalidated scoring systems for all outcomes incomplete baseline description Incomplete outcome reporting (e.g. sonography, function, ROM) control group treatment not standardised outcome statistics not reported at 3,6,9m No ITT analysis – drop outs at 1 st follow-up
Cho, M. S., R. J. Park, et al. (2007). "The Effect of Microcurrent-Inducing Shoes on Fatigue and Pain in Middle-Aged People with Plantar Fasciitis." ²⁵⁵	
Methods	Case Series
Target	Fascia - Plantar fasciitis
Participants	N = 10 Clinical Diagnosis BC: All over 50 years, 5 female
Interventions	MCT No vigorous exercise allowed
Outcomes	Post exercises fatigue using EMG activity after treadmill Pain (VAS) after 20' on treadmill No follow up
Notes	Method of diagnosis ns Little baseline information Microcurrent parameters not measured or justified Not clear circuit for charge flow No link established between fatigue OM and plantar fasciitis Poor reporting

El-Husseini, T., S. El-Kawy, et al. (2007). "Microcurrent skin patches for postoperative pain control in total knee arthroplasty: a pilot study." ²⁴⁴

Methods	RCT Sample size at entry: M 12, C 12
Target	Pain - following Total Knee Replacement
Participants	BC: ns
Interventions	MCT Co-intervention: Analgesic medication (tramadol) Control: analgesic medication
Outcomes	Pain (NRS) use of medication (mg/day) clinician rating of wound healing (1-3) no follow-up
Notes	non-parametric tests used but mostly unidentified

Ho, L. O., W. L. Kwong, et al. (2007). "Effectiveness of Microcurrent Therapy in the Management of Lateral Epicondylitis: A Pilot Study " ²⁵³

Methods	RCT, blinded random allocation Sample size at entry: M 8, C 8
Target	Tendon - Chronic Tennis elbow
Participants	Local Outpatients Dept Inc: Clinical diagnosis tennis elbow, symptom duration >3 months Exc: cervical spondylosis, elbow OA, Radial neuropathy, shoulder tendonitis, direct trauma to elbow, previous lateral elbow pain, previous steroid injection BC: 2 males, mean duration 6 months, mean Pain (VAS) = 6/10
Interventions	MCT Co-intervention; six weeks standardised exercise programme: stretch & strengthening. Instructions on pamphlet; diary of activity Control: exercise programme
Outcomes	Pressure pain threshold Pain-free grip strength (PFGS) Maximum grip strength (MGS), Pain on MGS (VAS) Recorded at baseline and 1, 2, 3 and 6w (follow-up 3 weeks)
Notes	MCT parameters and methods of application idiosyncratic and given no justification Randomisation methods ns Length or type of exercise programme ns Drop outs ns Baseline equivalence

Johannsen, F., A. Gam, et al. (1993). "Rebox: an adjunct in physical medicine" ²⁵⁶

Methods	RCT, cross-over Sample size at entry: M 7, C 9 Control: sham MCT 7 received MCT then placebo MCT; 9 received placebo MCT then MCT; one week washout between treatment periods
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Target	Tendon - Chronic tennis elbow
Participants	Local racquets clubs Inc: Clinical diagnosis of tennis elbow , Symptom duration>3m Exc: neck shoulder pain, neurological problems affecting arm, OA, reduced elbow ROM, steroid injection <3m BC: 10 males, median duration 6mo, mean Pain on lifting = 4-6/10
Interventions	MCT Co-intervention: maintain existing training load and avoid other treatment Control: sham MCT via dummy equipment
Outcomes	MGS Pain on MGS (VAS) Pain lifting lifting 2kg (VAS) Assessment before and after each treatment. Baseline equivalence on PVAS
Notes	Real sham MCT code held by manufacturer until after analysis so fully blinded Randomisation method ns

Koopman, J. S., D. H. Vrinten, et al. (2009). "Efficacy of microcurrent therapy in the treatment of chronic nonspecific back pain: a pilot study." ²⁴⁷

Methods	RCT - cross-over Sample size on entry M 5, C 5 5 days treatment, 9 days washout, 5 days other treatment blind allocation
Target	Pain – chronic Low Back pain
Participants	Recruited from hospital OPD Inc: Non-specific LBP, symptom duration>3months, PainVAS>4, adults <65years Exc: receiving other treatment except escape medication, connective tissue or neurological disease BC:4 males, mean age 50 years, mean duration 107months
Interventions	MCT Co-intervention: ns Control: sham MCT
Outcomes	Pain (VAS) Use of analgesia SF McGill Pain Questionnaire EuroQOL-5D. Patient-rated global improvement Adverse events follow up at 10 weeks
Notes	No drop outs

Kulkarni, A. D. and R. B. Smith (2001). "The use of microcurrent electrical therapy and cranial electrotherapy stimulation in pain control." ²⁴⁵

Methods	Case series Sample sized at entry: 15
Target	Pain – various musculoskeletal
Participants	Consecutive referrals to hospital pain clinic

	Inc: chronic pain in any area inc upper limb, back, knee; non-specific or diagnosed e.g. arthritis. BC: 5 males, mean age 50 years, duration 4 months -10 years
Interventions	MCT Co-intervention: Patients with depressive symptoms (19/20) also given Cranial Electrostimulation Treatment (5 in series only received CET) No pain medication given, participants asked not to take analgesics
Outcomes	Pain (VAS) Side effects Assessment each week until end of treatment No follow up
Notes	Several disorders; heterogeneous group PVAS scale defined differently than usual States treatment duration 1 hour but seems unlikely probes would be applied manually for that period. Most received CET also, so unclear contribution of MCT Most early drops out – few received full 3 weeks, but in several cases due to reduced pain Unknown if no analgesics rule obeyed
Lennox, A. J., J. P. Shafer, et al. (2002). "Pilot study of impedance-controlled microcurrent therapy for managing radiation-induced fibrosis in head-and-neck cancer patients" ²⁵⁰	
Methods	Case series Sample sized at entry: 26
Target	Connective tissue – radiation-induced fibrosis in neck
Participants	Inc: Head and neck cancer, >6mo since completed radiotherapy, with tissue discomfort or limitation caused by fibrosis Exc: pacemaker, Ca channel blocker, pregnancy, life expectancy<6mo, receiving physio or anti-inflammatory treatment BC : 14 males, mean ages in groups 52-63 years. Data also given for race, radiotherapy dose, time elapsed since radiotherapy
Interventions	MCT Co-intervention: none
Outcomes	Neck ROM using laser marker & scale, graded 0-3 by comparison with normal ROM for that age group, added for composite 0-9 score Questionnaire regarding symptoms patients thought due to radiotherapy (e.g. impaired speech, dry mouth) Adverse effects Assessment before, after & monthly for 3 month follow-up
Notes	Reliability of outcome measures (OMs) checked daily but method ns BC data tabulated for all patients Comprehensive treatment description, but MC waveforms not fully described No pre-assessment so unknown whether OMs were improving anyway. No testing of difference, only descriptive statistics Table showing subjective improvements does not allow for unchanged or worsening symptoms Not clear whether participants entered consecutively or selected Compliance during follow-up period ns

Lerner, F. N. and D. L. Kirsch (1981). "A double-blind comparative study of micro-stimulation and placebo effect in short term treatment of the chronic back pain patient." ²⁴⁸

Methods	Placebo controlled trial Sample size on entry M 20, C 20 group allocation on basis of baseline pain charts to obtain equivalence. Real and placebo microcurrent devices, assessors and patients blind to allocation
Target	Pain - Low Back Pain
Participants	Inc: chronic neuromusculoskeletal pain (>50h/wk), few if any remissions Exc: "significant complicating factors" BC:42% male, mean age 38 (19-63) years, 63% LBP, 37% neck & shoulder. Average pain=1.3/5.
Interventions	MCT Control: sham MCT Co-intervention: ns
Outcomes	Pain (NRS 0-5) Assessment hourly for 2 weeks prior to treatment, waking hours; completed charts during treatments, and at 2 weeks and two months after treatment complete
Notes	Unclear selection process Low level average baseline pain No statistical analysis

Maenpaa, H., R. Jaakkola, et al. (2004). "Does microcurrent stimulation increase the range of movement of ankle dorsiflexion in children with cerebral palsy?" ²⁴²

Methods	Case series Monitoring for 4 weeks, then 4 weeks treatment Sample size: 12
Target	Myotendinous contracture in cerebral palsy
Participants	All meeting criteria from referrals to hospital department over specified period. Inc: Children with Cerebral Palsy, >4y old, Dorsiflexion<0°. symptom duration>3mo, no benefit from botox or surgery BC: 7 males, mean age 10 years BE: characteristics "somewhat uniform"
Interventions	MCT Co-intervention: none
Outcomes	Active & passive ankle ROM using fixed protocol One leg standing time One leg hops number. Acceptability to patients and parents Assessment 4 weeks pre treatment, pre and post treatment
Notes	Box plots but no numerical tabulation of mean changes Suggested MCT broke down collagen formation (improved balance with less muscle collagen - referenced) Unclear if changes are clinically significant Compliance not described

Maugeri, D., M. S. Russo, et al. (1999). "Electroionotherapy in acute arthrorheumatic pain" ¹⁰⁴

Methods	Case series No blinding Sample size on entry: 19
Target	Pain – various musculoskeletal
Participants	Unclear how recruited Inc: arthrorheumatic pain inc cervical OA scapulo-humeral OA, peri-arthritis, torn muscle, bursitis, lumbar discopathy, Exc: other significant health problems, pacemaker BC: 7 males, mean age 58 years, mean pain 3.4/5
Interventions	MCT Co-intervention: ns
Outcomes	Pain (VAS) Function (VAS 0-5) Use of analgesics pre and post treatment No follow up
Notes	Poorly described device and parameters

McMakin, C. R. (2004). "Microcurrent therapy: a novel treatment method for chronic low back myofascial pain." ²⁴⁶

Methods	Case series – retrospective review of case notes
Target	Pain - Chronic low back myofascial pain
Participants	N = 22 on entry Exc: facet or disc dysfunction, neuropathy, severe arthritic change. BC: most pain result of prior trauma or overuse, mean duration 8.8 years..
Interventions	MCT Co-intervention: massage, manipulations as needed, other complementary therapies
Outcomes	Pain (VAS 0-10) Side effects 128/137 completed treatment.
Notes	Not clear why only cited data for 22 chronic patients, not for larger group from which sample was selected Uncontrolled co-interventions Poor BC descriptions

McMakin, C. R., W. M. Gregory, et al. (2005). "Cytokine changes with microcurrent treatment of fibromyalgia associated with cervical spine trauma." ²⁵²

Methods	Case series - retrospective analysis of data Sample size: 54
Target	Pain - Fibromyalgia associated with cervical spine trauma
Participants	Inc: Initial testing for pain reduction by treatment, meeting American College of Rheumatologists diagnosis criteria for fibromyalgia BC: mean age 44 years, mean duration 9.5 years, mean PVAS 7.3/10
Interventions	MCT Co-intervention: ns

Outcomes	Pain (VAS 0-10) Cytokine & peptide levels in 6 patients (no SS difference from others in age or duration). Compared blood results with a single control, a person with regional myofascial pain syndrome not meeting ACR diagnosis criteria for fibromyalgia (control was also treated); Presence of taut bands and active Trigger Points Adverse events
Notes	13 non-completers
Noto, K. and P. Grant. (2009). "Comparative study of micro-amperage neural stimulation and conventional physical therapy modalities." ¹⁰²	
Methods	RCT Random assignment by referring physician Sample size on entry M 60, C 60
Target	Pain – location not specified
Participants	Patients from one clinic Inc: seeking treatment for pain BC: ns
Interventions	MCT Control : treated with a range of electrophysical modalities including ultrasound, hot packs – all provided by same physiotherapist Co-intervention: none
Outcomes	Questionnaire covering type of pain, intensity pre- and post-treatment Number of treatment sessions to achieve pain relief Side effects total cost patient rating of overall effectiveness.
Notes	Brief report of Masters thesis No data on patient characteristics ?Use of inappropriate statistical test
Rolle, W. C., G. Alon, et al. (1994). "Comparison of subliminal and placebo stimulation in the management of elbow tendinitis." ²⁵⁴	
Methods	Placebo RCT Patient, therapist and assessor blinded to allocation and treatment Sample size on entry: M 16, C 15
Target	Tendon - Chronic Tennis elbow
Participants	Recruitment ns Inc: clinical diagnosis of tennis elbow by physician BC: 19 males, mean age 40/46 years, mean symptom duration 7 (0.75-25) months (pain ns)
Interventions	MCT Control: sham MCT Co-intervention: Daily exercises program 10-15min + icing
Outcomes	MGS Pain at rest and on several provocation tests – average (VAS) 7 point "general pain scale" Assessment: Pre & post 3 treatments, 6 treatments, 1 & 6 weeks later

Notes	<p>Method of blinding described and adequate</p> <p>BC equivalence</p> <p>Reliability of MGS testing assessed with healthy volunteers</p> <p>Incomplete data at 6 weeks so not analysed, no ITT. Reasons given for missing data.</p> <p>Incomplete waveform description</p> <p>Appropriate statistical analysis</p> <p>Suggested long phase duration may result in high impedance and affect current (unclear if current controlled)</p> <p>Minimal eligibility criteria</p> <p>Co-intervention not controlled</p> <p>Conclusions only for short term</p>
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Sizer, P., S. Sawyer, et al. (2000). The effect of microcurrent stimulation on postoperative pain after patellar tendon-bone anterior cruciate ligament reconstruction. ²⁴³

Methods	<p>Placebo RCT</p> <p>Blind and random allocation – method ns</p> <p>Sample size on entry: M 25, C 16</p>
Target	Ligament – Anterior cruciate ligament repair
Participants	BC: mean age 21 years, 54% male
Interventions	<p>MCT</p> <p>Control: Sham MCT</p> <p>Co-intervention: Standard physiotherapy rehabilitation programme</p>
Outcomes	<p>Pain medication intake</p> <p>Pain (NRS)</p>
Notes	<p>Conference abstract</p> <p>Potentially well-conducted but insufficient data in abstract.</p> <p>Patient-completed log book of frequency of use</p>

Smith, R. B. (2001). "Is microcurrent stimulation effective in pain management? An additional perspective." ²⁵⁷

Methods	<p>Case series</p> <p>Retrospective analysis of warranty cards sent to manufacturer of MCT device, with optional medical data</p> <p>Sample size: 978 out of 2500 records inspected, sub-grouped musculoskeletal cases by region.</p>
Target	Pain – various musculoskeletal
Participants	<p>Inc: musculoskeletal pain, MCT use for at least 3 weeks</p> <p>BC of 1949 pts with pain as primary diagnosis: 28% male, mean age 50 (15-92) years</p>
Interventions	<p>MCT</p> <p>Co-intervention: ns</p>
Outcomes	Patient-rated symptom improvement scale (slight / fair / moderate / marked)
Notes	<p>Baseline pain ns</p> <p>OM does not provide for no improvement / worse</p> <p>Unknown how many used cranial electrostimulation rather than MCT</p> <p>Writer is an employee of device manufacturer</p>

Stanish, W. (1985). "The use of electricity in ligament and tendon repair " 143	
Methods	Case series with comparison group Sample size >100
Target	Patellar Tendon & cruciate ligament – post-surgery
Participants	Inc: cruciate Ligament or Achilles tendon repair BC: ns
Interventions	MCT Comparison group: surgery but no MCT Co-intervention: compression bandage & slab 10-14 days, then Range of movement & strengthening exercises
Outcomes	Time return to full weight-bearing and function Histological analysis of 45 reconstructed ligaments Side effects Assessment: ns, but histology 9 months after surgery
Notes	little numerical data is provided for scrutiny. No statistics, no blinding MCT adherence guaranteed as implanted, exercises adherence unknown
Tan, G., T. Monga, et al. (2000). "Efficacy of microcurrent electrical stimulation on pain severity, psychological distress, and disability." 258	
Methods	RCT: cross-over, randomised 2 month washout period Sample size on entry: 14+14 Assessors blinded to treatment
Target	Pain – various musculoskeletal
Participants	Hospital OPD, mostly army veterans Inc: Primarily musculoskeletal pain, >6mo duration, Exc: other treatments other than analgesia, pregnancy, fibromyalgia, pacemaker, inaccessible surgical scar, chronic psychiatric problem as main complaint BC: 91% male, age 56 years, mean duration 15 (4-45) years, 64% multiple pain sites, back pain most common, PVAS (real 2.6/5; sham 3.2/5) - data for completers only BE: not addressed
Interventions	MCT Co-intervention: standard treatment protocols but not described Control: sham MCT Analgesia medication + Cranial ElectroStimulation for 20 minutes each treatment (attached to ear lobes)
Outcomes	Pain in 3 worst sites (VAS 0-5) Multidimensional pain inventory (MPI) including psychological distress and subscales; Sickness impact profile Roland Scale (SIPR) including disability Assessment: pre+post 1 st treatment, 2 months after 1 st Rx, post 2 nd treatment and 2 months after 2 nd treatment.
Notes	MCT parameters incomplete Random assignment - method ns Large loss to follow-up. No ITT SIPR & MPI scales: cited validity and reliability evidence No monitoring/reporting of medication Incomplete description of pain sites

Zimmerman, S. I. and F. N. Lerner (1989). "Biofeedback and electromedicine: Reduce the cycle of pain-spasm-pain in low-back patients." ²⁴⁹	
Methods	RCT 3 groups: MCT (13), Biofeedback (BF) (14), MCT+BF (15) Random assignment (method ns)
Target	Pain - Low Back
Participants	Recruited from posters in several medical centres Inc: Physician referral for LBP & spasm Exc: pregnancy, heart disease, psychosis, diabetes, epilepsy, substance addiction, other treatment at time of study inc analgesic medication BC: 62% male, mean age 41 years; pain approx 4.2/10 BE: similar demographics but baseline pain ns; SS differences in age between two groups
Interventions	MCT group: 30mins, x2/week (3 days apart) for 10weeks MCT+BF: as for MCT but x1/week each modality BF: as for MCT. Audio feedback on paraspinal muscle activity. Co-intervention: none
Outcomes	Subjective Units of Disturbance Scale (anxiety) Daily Pain (NRS 0-10) Trunk mobility Subjective Q&A Assessment at 5 th ,10 th ,15 th , 20 th sessions (10 weeks in total)
Notes	Trunk mobility OM not clearly described No variability estimates 1 biofeedback & 2 MCT failed to complete – reasons not given

Study quality

Table 3.5 presents the quality assessment scores given to each study. Methodological and reporting quality were generally low, even for the single group studies which were assessed against less stringent criteria. Three of the RCTs had good methodological and reporting scores^{247, 254, 256}; two of these were concerned with tennis elbow, the other with non-specific back pain. The other RCTs scored poorly, as did the single non-randomised comparative study. Three of the case series were of moderate quality^{242, 245, 250}, the others were judged poor. Low scores were often a result of incomplete reporting, particularly regarding treatment parameters and standardisation, validity and reliability of outcome measures, blinding and randomisation procedures, and missing data.

Table 3.5: Methodological and reporting quality scores of included studies

Study	quality criterion score																		Total score	Rating
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18		
251	2	1	0	1	1	0	0	1	2	0	0	1	2	1	0	0	0	1	13/36 (36%)	Poor
255	1	0	0	0	1	0	0	0	2	0	0	4/22 (18%)	Poor							
244	1	1	1	0	1	0	0	2	2	0	0	1	1	0	0	0	0	0	10/36 (28%)	Poor
253	2	1	1	2	1	0	0	2	2	0	0	1	0	2	0	0	0	0	14/36 (39%)	Poor
256	2	1	1	2	1	0	1	2	2	2	2	1	1	1	2	2	2	2	27/36 (75%)	Good
247	2	1	2	2	2	1	2	2	2	2	0	1	1	2	2	2	2	2	28/36 (78%)	Good
245	1	1	1	1	1	0	1	1	2	2	0	11/22 (50%)	Fair							
250	1	1	1	2	1	1	2	0	2	2	0	13/22 (59%)	Fair							
248	1	0	1	1	1	0	0	0	0	0	0	1	0	0	2	2	2	1	12/36 (33%)	Poor
242	2	1	0	1	1	0	1	1	2	2	0	11/22 (50%)	Fair							
104	1	0	1	1	1	0	1	1	1	2	0	9/22 (41%)	Poor							
246	1	1	0	1	1	0	0	1	1	2	0	8/22 (37%)	Poor							
252	1	0	0	0	1	1	0	2	1	0	0	7/22 (30%)	Poor							
102	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	2/36 (6%)	Poor
254	1	1	2	2	1	0	1	2	1	0	0	2	2	2	2	2	2	2	25/36 (70%)	Good
243	1	1	1	1	1	0	0	1	1	0	0	1	1	0	1	1	1	0	12/36 (33%)	Poor
257	1	0	0	1	1	0	0	1	1	0	0	5/22 (23%)	Poor							
143	1	1	0	0	1	0	0	0	0	0	0	3/22 (14%)	Poor							
258	2	0	1	2	2	1	1	2	2	0	0	1	1	0	1	2	2	2	22/36 (61%)	Fair
249	2	1	1	1	1	0	1	2	1	2	0	1	1	0	0	0	0	0	14/36 (39%)	Poor

Findings

Although several studies used or appeared to use the same device to deliver MCT, treatment parameters were never the same and so no meta-analysis of data was attempted. Table 3.6 summarises the treatment parameters and outcomes obtained in each study. This provides data relating to review questions (a) and (b) concerning treatment effects and parameter dependence.

Table 3.6: Summary of MCT parameters and outcomes in included studies (CR=current regulated, ns=not specified; SS= statistically significant)

Parameters	Outcomes
251	
<i>Face & body protector</i> CR 40µA, 10Hz, modified monophasic square wave 2 surface carbon fibre electrodes, placed medial lateral to lesion + gel 30 minutes/day for 14 days.	Non parametric tests: SS greater improvement in pain, stiffness and clinician assessment at 1 year No results presented for earlier assessments Sonographic evidence of tissue change "in agreement" with other measures at 1 year
255	
<i>G-man</i> 60-160µA Piezoelectric pulsed by footfall so ~1Hz From shoe heel to sole via conducting sock Wear shoes >4 hours/day for 6weeks	SS reductions in pain & Tibialis Anterior fatigue No SS reduction in soleus fatigue
244	
<i>Painmaster patch</i> Parameters ns but manufacturer literature states either DC 10µA or varying 10-937µA 0.5-500Hz	SS lower pain SS and clinically significant reductions in use of analgesic medication in treatment group on each day Wound healing better in treatment group at end of period No follow-up
253	
<i>Precision micro (precision electronics, usa)</i> 40 µA or 300 µA 0.3, 3 and 30Hz Biphasic square wave (50% duty cycle) Apparently CR Via probes contacting the skin at various points on the elbow and forearm Several minutes 10 times in three weeks.	All participants improved but no significant differences between groups recorded on any of the outcome measures.
256	
<i>Rebox</i> 0-300µA 200-5000Hz Modulation ns Biphasic Waveform ns Pin electrodes, method of application unspecified Several minutes 10 sessions over 3 weeks	SS but clinically insignificant improvements in MGS, PVAS on MGS trial and when lifting 2kg, after MCT compared sham MCT
247	
<i>Pain away patch</i> 25µA, 3V Paper states 71.5kHz but manufacturer states f=0.5Hz Surface patches on either side of spine at level of pain Continuous 5 days	MCT produced greater improvements in Pain, use of analgesia, SF mcgill Pain Questionnaire, euroqol-5D and Patient-rated global improvement, compared to control period, but difference were not SS. No adverse events reported

Parameters	Outcomes
245	
<i>Alphastim 100</i> 600µA Probes either side of painful area, repositioned every 10s after bleep from device; or adhesive electrodes 1 hour, 5/week for 3 weeks or until no pain	Substantial reductions in pain for most patients: mean 52% for CET + patches (n=7), 85% CET + probes (n=7),
250	
<i>Electromyopulse 75F</i> Current at highest tolerable, typically 600µA, AC 0.5-100Hz Then <i>electroacroscope 80L</i> 600 µA, 10Hz CR, "rapid rise time" Via conductive gel-covered roller Calculated $\rho = 16\mu\text{A}/\text{cm}^2$; First 20 mins used Myoscope and Fixed electrode taped to shoulder blade Then 10mins using Acuscope and hands on 2 fixed electrode plates. Followed by 1 min with named after-treatment cream rather than gel on roller x2/day for 5 days (4-5 hour intervals)	Improvements in ROM, best for more severely effected (49-65%), sustained in longer term Improvements in radiotherapy side effects especially stiffness discomfort All patients completed
248	
Prototype of <i>Alphastim</i> Biphasic current "variable subsensory microcurrent" Maximum available current, lowest frequency (0.5 Hz) Use of probes to locate areas of low conductivity Stimulation with probes at 8 pairs of sites either side of spine. 2 x 6 seconds, x3/week for 2 weeks (total 72 seconds).	Initial pain reductions in each group, gradual return to baseline level in placebo group, but sustained reduction in real MCT group (from 1.3/5 to 0.5/5) % of people in each group with different treatment effects: >50% real MCT achieved "good" at each time point; 90% failure in placebo group at follow-up
242	
<i>Micro 100 dual channel</i> 300µA constant slope-wave current, 30Hz. Adhesive electrodes, 2 anodes on gastrocnemius bellies, cathodes either side of achilles tendon At least 5 hours/week Treatment at home, provided by parents	Average number of treatments =22 SS improvements in most ROM measures and one leg standing time but not in active dorsiflexion with knee extended or in number of hops.
104	
<i>Bio-ejt be101</i> States produces ion discharge in air and about 30µA current in tissue via high voltage electrode 2 transducers 20 minutes every 2 days – 6 treatments	SS improvement in pain and functional measures, but mean change values not reported Reduction in analgesia use (but low at baseline)
246	
Device ns 100µA pulsed DC modified to alternating ramped square wave Graphite conductive gloves placed on skin either side of	SS and clinically significant reductions in pain for 22 chronic cases (6.5-1.7/10) after mean 5.6 treatments over 6 weeks.

Parameters	Outcomes
torso 2-40 minutes up to x2/week reduced as pain reduced, halted when no pain for 4 weeks.	1 patient could not tolerate and discontinued after 4 weeks; other effects: muscle spasm, hyperaesthesia
252	
Device ns 2-channel square wave 10 and 40Hz (determined empirically) Patients given pocket-sized unit with “polarised” microcurrent 2 adhesive electrodes either side of neck, 2 on soles of feet. Instructed to use at home to keep P<3/10. Initial testing by graphite gloves for 90 minutes; more than one treatment in clinic but number ns. Duration ns, but text suggests several months	SS and clinically significant reduction in Pain (7.3 to 1.3/10) SS reduction in serum cytokine levels compared to control 51 relapse, 13 non-completers
102	
<i>Electroacroscope 80</i> Parameters ns. Parameter information from manufacturer and other publications: 600µA, 10Hz, CR; probes or pad electrodes; treatment duration 15-20 minutes	Fewer treatment sessions, lower cost, fewer side effects and higher patient rating of effectiveness in MCT group Use Chi square test but not clear how this supports the conclusion of statistically significant differences between group outcomes.
254	
<i>Myomatic stimulator</i> Monophasic “sloped”, 0.3-30Hz, 40-100µA, 1.67-16.7ms phase duration, polarity reversal every 2.5s 10 minutes with probes, 20 minutes with pads Initially applied with probes various sited around painful area, then 4.5cm square polymer pads over lateral and medial epicondyles Apparently daily treatment over 6 days	Improvements in both groups on all outcome measures but no SS difference between groups
243	
<i>Alphastim 100</i> 100µA, 0.5Hz, 50% duty cycle “subsensory” Use as needed for 1 hour, minimum 30 minutes between treatments for 10 days	SS lower pain levels each day in real MCT group compared to placebo Other oms not reported
257	
<i>Alphastim</i> Parameters ns For whole study group, mean period of use 14.7 weeks (3 weeks -5 years) No other data given: may have used probes, patches or ear clips	% In each category of improvement given for back/neck/limbs. All improved – 75% moderate or marked in each category. No statistical tests.
143	
<i>Osteostim hs12 (telectronics)</i> 20µA DC current controlled Assuming wire diameter 1mm, $\rho = 2.5\mu\text{A}/\text{cm}^2$ DC unreported time, presumably several weeks	Accelerated recovery compared to non-MCT patients: “most” returned to full function in 6 months compared to typical 18 months for conventional treatment. Histology showed tissue revascularised with mature

Parameters	Outcomes
Cathode 25cm titanium wire wrapped around structure; battery is anode taped outside body Timings ns	and well organised collagen at 6 months. No statistical tests
258	
<i>Alphastim 100</i> 10-600µA 0.5 Hz Probes applied to scar tissue if present (time ns), followed by application to all pain sites (time ns) 12 sessions in total (6 real 6 sham)	No SS differences in any variable within and between sham and real MCT groups 11/28 completed. Losses due to length of study, scheduling conflicts, use of other treatments.
249	
<i>Alphastim 350</i> Initially 200µA, then 500µA 0.5Hz Via adhesive pads, either side of spine at L3-5 on erector spinae 30 minutes, 2/week for 10 weeks	SS trunk mobility gains in all groups: BF/MCT group best, MCT better than BF at mid-point but not SS at end. SS decreases in pain in groups, clinically significant in BF/MCT and MCT groups by end of study Improvements in psycho-emotional scales in all groups, best in BF/MCT. 1 biofeedback & 2 MCT failed to complete – reasons not given

Having extracted the data and assessed the quality of the evidence from the selected trials, it was possible to provide responses to the questions set out by the review:

(a) What are the effects of microcurrent therapy on tissue healing and on clinical signs or symptoms following soft connective tissue damage?

The three good quality RCTs employed different microcurrent devices and treatment protocols. Two were concerned with chronic tennis elbow and gave limited evidence of benefit in the short term. In one²⁵⁴, pain levels decreased in the MCT groups more than in the placebo MCT groups, although gains were not statistically significant. The study was small and likely to be underpowered, therefore risking type II error. In the second (larger) study, grip-strength, pain on gripping and lifting and daily impairment improved more with real than placebo MCT, but the differences were regarded as clinically insignificant²⁵⁶. The third (small) trial concerned chronic low back pain²⁴⁷. There was significantly less use of analgesics, and non-significant trends to improved pain, quality of life and global assessments in the MCT group compared to the placebo MCT group. The longest follow-up period in these trials was 10 weeks²⁴⁷, so no good evidence is available regarding long term-effectiveness on any outcome measure.

One fair quality RCT found no significant differences in pain and disability between real and sham MCT groups of patients with chronic musculoskeletal (mostly lumbar) pain²⁵⁸. This trial had greater than 50% loss of participants by final assessment and there may have been significant differences in baseline pain scores between the groups – this was not tested or commented upon by the authors. Another fair quality pilot RCT found that MCT produced significant improvements in cervical range of movement, previously limited by radiation-induced fibrosis²⁵⁰. It is not clear whether this was secondary to pain reduction or tissue changes.

The remaining controlled trials and all of the case series investigations concluded that MCT was capable of improving outcomes, which mostly related to pain or function. Two studies measuring outcomes directly related to tissue status – sonography²⁵¹ and histology¹⁴³ - concluded that MCT could accelerate tendon healing, but both had low quality scores and so may be biased. Another poor quality uncontrolled study found substantial reductions in serum inflammatory cytokine levels²⁵² following MCT for fibromyalgia caused by cervical spine trauma. These correlated with local pain reduction, but connective tissue damage may not have been the source of pain.

In summary, there is good but limited evidence that some forms of MCT can provide marginal clinical benefits in tennis elbow and low back pain, but the evidence regarding its effects on soft connective tissue healing is poor.

(b) Are these effects dependent on the treatment parameters or method of application?

No single study compared different forms of microcurrent with the same population and, because of the heterogeneity of the study protocols, it is not possible to consider the relative effectiveness of different microcurrent parameter combinations. The good quality trials used both monophasic and biphasic currents with fixed or varying frequencies between 0.3 and 5000 Hz, a variety of waveforms, and current intensities between 25 and 300 μA , and total treatment times between a few minutes and 5 days. Across the range of studies, where tissue healing was being monitored in some way, treatments judged to be effective were applied for longer period of time, often tens of hours in total. Where shorter application times were deemed effective, this was generally in terms of short-term pain reductions. Where the necessary data was provided, the current density of possibly effective forms of MCT were calculated, and are presented in Table 3.7. These are of the same order of magnitude as those that were found effective for other forms of tissue (see the earlier Table 3.1). It is interesting to note that, in contrast to the data for skin and bone injuries, a higher current density was

effective for the acute injury (surgically repaired tendon or ligament¹⁴³) than the chronic tendinopathy²⁵¹. However, both studies from which this data is drawn had low quality scores.

Table 3.7: Current density values calculated from trials suggesting MCT effectiveness

Tissue - lesion	Current density at electrode ($\mu\text{A}/\text{cm}^2$)
Tendon – surface electrodes ²⁵¹	1.6
Fibrosis – surface roller electrode ²⁵⁰	16
Myocontracture ²⁴²	6
Tendon/Ligament – wire electrode wrap ¹⁴³	2.5

Therefore it is concluded that there is fair evidence that treatment parameters can influence the effectiveness of treatment, but insufficient evidence to prefer one set of parameters over another.

(c) Is microcurrent more effective when used in combination with other forms of treatment?

Where MCT was applied to musculo-tendinous structures, it was normally accompanied or followed by a programme of exercise, including stretching and/or strengthening, but none was described in any detail. In two case where microcurrent was used to treat pain, analgesic medication was also provided^{244, 258}. One study also provided manual therapy and various forms of complementary therapy²⁴⁶. No study compared the same form of MCT with and without a co-intervention, so as yet there is no evidence regarding the issue of whether MCT is more effective when used in combination with another treatment.

(d) Are there any adverse effects of MCT?

Side effects or adverse events were addressed in seven studies and were generally rare. In one²⁴⁶, muscle spasm was observed in 2/22 subjects during or after treatment, and numbness and hyperaesthesia when applied to the neck of one person with a history of spinal cord injury. In another²⁴², 6/12 subjects reported warmth in the treated area after treatment. In the only investigation using constant 20 μA continuously for several weeks¹⁴³, delivered via a surface and an implanted electrode, skin ulceration was reported in less than 4% of subjects. Where only surface electrodes were used, so such effect was reported. Standard contraindications to electrostimulation – including pregnancy and presence of cardiac pacemakers – were applied in some cases, though these appear to be precautionary rather than evidence-based in the case of MCT. Thus, there is a good standard of evidence

that, when applied via surface (rather than implanted) electrodes, MCT is safe and has few and minor side effects.

(e) What data is there regarding feasibility, cost, acceptability to patient and clinician of this treatment?

One poorly-rated RCT¹⁰² reported that MCT required significantly fewer treatment sessions and lower cost than a combination of other electrophysical modalities. In another, involving parents treating children at home²⁴², both reported that the treatment was simple and convenient to deliver. Microcurrent devices varied considerably in design and included adhesive patches containing all necessary circuitry, portable battery-powered devices connected to the tissue via adhesive electrodes, and non-portable generators delivering current through hand-held probes or conductive gloves worn by the therapist. Some allowed the patient to treat themselves whilst engaged in daily activities, whereas others required regular treatment visits to a clinician. Hence there is limited and poor-to-fair evidence that some forms of MCT are both feasible and appropriate forms of treatment

3.5.6 Discussion

The majority of these studies reached positive conclusions regarding the efficacy of MCT, either in reducing short term pain in certain musculoskeletal disorders, or promoting tendon and ligament healing and return to function in the medium to longer term. However, the available evidence is limited and generally of low quality, so it is not possible to be confident in these conclusions or about the most effective parameter combination. Most of the studies involved treatment of a condition or body part encompassing several tissue types. However, tendon lesions were the specific focus of several. Those concluding that MCT can be beneficial used current intensities between 40 μ A and 300 μ A and DC or monophasic waveforms with frequencies below 100 Hz in most cases, but higher in some. Application was generally by surface electrodes, which is advantageous because it avoids the risks of trauma and infection associated with implanted electrodes. Total treatment times in these studies varied, but were rarely longer than about 10 hours. The two tendon studies that showed no benefit of MCT for tendinopathy used much shorter treatment times and biphasic or polarity-reversing currents. Although these data provide some hints of what type of microcurrent might be more effective, in truth the evidence is not robust enough to rule in or out any particular combination evaluated. This unsatisfactory situation may only be remedied by the conduct of further and higher quality trials.

The analgesic effect of microcurrent was the outcome most commonly measured. Signs of tissue healing were assessed in only two studies, using sonography or histology. Pain and function, whilst not necessarily indicators of healing, are clinically significant outcomes and a range of instruments were used to measure them. The rarity and mildness of adverse events associated with the use of MCT with surface-mounted electrodes is encouraging; likewise the findings of several studies that the treatment was acceptable to patients and of lower cost than some other forms of treatment. The inclusion of a wider range of study methodologies than is common in systematic reviews provided useful data in these regards.

Although three studies^{102, 143, 255} had quality scores lower than 20%, and cannot be regarded as providing credible evidence regarding treatment efficacy, their inclusion in the review is justified on other grounds. They illustrate the range of delivery systems that are available (including a shoe-mounted piezo-electric device²⁵⁵). Two considered side-effects^{102, 143}, and one represented the only attempt amongst all the studies to address cost-effectiveness by comparison with conventional treatment¹⁰². These are important considerations in the evaluation of MCT and, in spite of their low quality, these studies provide information that can be used in the planning of a more robust trial.

The review methodology adopted has a number of limitations that may impact on its findings. The application of eligibility and quality criteria was carried out by a single investigator; ideally another rater would have used the same process to establish and improve the reliability of assessment. The quality criteria checklist, although based on existing validated instruments, was not independently validated and its reliability has not been established. Application of some items was problematic, for instance rating treatment standardisation: if MCT was applied for as long as it took to obtain a satisfactory outcome in each case, does this constitute standardisation? Also, key prognostic indicators are not always obvious for a given disorder, so the comparability of key baseline characteristics could not be guaranteed. Low methodological scores often resulted from poor reporting; the methodology used may have been better than these scores suggest in some cases, and the conclusions more robust than they appear. Some studies with low methodological scores may have been optimal for their design – for instance, blinding may have been impossible to achieve in some cases. The limitations of word-counts in journals may also have prevented comprehensive reporting of significant methodological features. These issues relate to items that appear in other commonly-used quality checklists, and so would have been present whichever one was employed. Finally, assessment of the potential impact of publication bias on findings of systematic reviews has been recommended^{214, 259}, but in this case the heterogeneity of the studies means that formal analysis, for example using a funnel plot, was

inappropriate²⁶⁰. The broad search strategy uncovered several items of grey literature meeting the eligibility criteria, and these may have helped reduce publication bias²⁶¹, although their low scores lessen the value of their data.

3.6 CONCLUSIONS

The narrative review of evidence from cell, tissue and animal studies, and from human trials involving bone and skin, suggested that microcurrent has the capacity to promote and enhance the healing process in a range of tissue types. The systematic review demonstrated that the case for its application to damaged soft connective tissues is much less clear. The quality of clinical trial evidence is generally poor, and the few good quality studies use different treatment parameters, so are not amenable to a meta-analysis that might enhance their power. However, poor reporting and small sample sizes may mask potentially significant findings. Trends to better outcomes have been observed in several good and fair quality trials; side effects of treatment are few and usually minor, and some forms of MCT permit patient-controlled, home-based treatment. If effective, they might offer substantial costs savings over other resource-intensive therapies. These considerations suggest that further, higher quality clinical studies are justified.

Many areas of uncertainty remain, and require investigation. Although tendons are the form of tissue most commonly examined, other collagen-based tissue have similar healing pathways^{262, 263} and so might also be expected to respond to MCT. Trials of MCT with these types of tissue are warranted. Most of the studies reviewed were concerned with chronic musculoskeletal disorders rather than acute injuries or the acceleration of normal healing, so little is known about the potential of MCT in these contexts. Pain and function were the most-commonly measured outcome variables. The trials that considered outcomes directly related to tissue healing were of poor quality, and so it is not clear whether MCT can influence healing in these cases. If the potential of MCT to promote healing in soft connective tissues is to be investigated, suitable outcome variables must be included in the protocol. Finally, the uncertainty over the relative benefits of different types of microcurrent and treatment parameters suggests that these require more systematic examination for each potential application.

Given these issues, proceeding directly to a clinical trial would be problematic. A number of preliminary questions require responses first:

- which soft connective tissue disorders are most likely to respond to MCT? Tendons are the specific tissues for which most supportive evidence is available, but there are many types of tendon disorder, some of which may already have effective management strategies. Other types of soft connective tissue may present a greater challenge to the affected individual and the clinician. Therefore, some consideration of clinical priority is appropriate.
- What combination of treatment parameters is most likely to be effective? None of the reviewed trials formally compared the effects of different types of microcurrent, even though the therapeutic window remains obscure. Some preliminary comparison of those parameters supported by existing evidence could help clarify this issue, establish an effect size, and so provide a firmer basis for using a particular type of MCT in an adequately-powered trial.
- What outcome measures will provide the most useful information about tissue healing and be clinically relevant? A combination of measures is likely to be necessary, and those selected should be of proven validity, reliability and responsiveness, so as to provide a comprehensive and credible data set.

Further literature reviews and original experimental work were conducted to address these questions, and these are reported in subsequent chapters.

Chapter 4

Selecting a disorder to treat

4.1 INTRODUCTION

The preceding chapters have suggested that MCT may assist healing and reduce symptoms in a range of musculoskeletal disorders, particularly where other forms of treatment have been unsuccessful. However, the effects of treatment appear to vary with the type of damage. For instance, fresh fractures may not respond as successfully to DC MCT as chronic ones¹⁷¹, and different forms of skin ulcer may respond best to different types of MCT^{82, 194}. The same may be true of the soft connective tissues, so that effectiveness with one form of tissue damage does not necessarily imply effectiveness with others. Therefore, for the purposes of this investigation, it was necessary to focus on a particular disorder and measure the effects of a specific type of MCT on it. Although any conclusions would apply to that application alone, they might have implications for the treatment of other disorders. This chapter describes the work done to select a soft connective tissue disorder for use in a clinical trial of MCT.

The chapter begins by identifying the criteria that were used to govern the choice. This is followed by a description of a survey of practising musculoskeletal physiotherapists, which was used to prioritise a range of possible disorders. The three disorders assigned the highest priority by the survey are then compared using additional information taken from the literature. The chapter ends with a discussion of the data collected, leading to the choice of a single disorder to treat – chronic tennis elbow.

4.2 CRITERIA FOR THE SELECTION OF A DISORDER

Several international reports have drawn up priorities for research into the treatment of musculoskeletal disorders. They have used prevalence, personal and societal impact, and resistance to existing management strategies as criteria for their selection²⁶⁴⁻²⁶⁶. These were adopted for the purposes of this investigation, but several other criteria were also identified: ideally there would already be some evidence to support the application of MCT to that

particular disorder; since tissue healing is a particular concern of this investigation, there should be identifiable tissue damage to some form of soft connective tissue; the damage should be capable of being assessed and monitored experimentally; and the disorder should be feasible for use in this investigation. These criteria are summarised in Table 4.1.

Table 4.1: Criteria used to select disorder for treatment in this investigation

Criterion	Explanation
A Prevalence	Commonly occurring, so that the treatment might have wide application were it to prove beneficial
B Impact	Presenting a significant problem to those affected, in terms of symptoms and functional compromise, or to the wider society through loss of productivity or treatment expense
C Recalcitrance	Resistant to existing management strategies, either by a poor or slow response, a tendency to recurrence or to chronicity
D Identifiable soft connective tissue damage	Involving damage to tissue composed of a collagen-based matrix manufactured by phenotypes of the fibroblast cell, which have a common healing pathway
E Potential response to MCT	Evidence that MCT might promote healing or symptom alleviation in this particular disorder
F Feasibility for trial	Local availability of affected individuals; reliably diagnosed; amenable to assessment and monitoring of tissue damage.

There are many forms of tissue damage that might respond to MCT, but these criteria excluded a number of them, for instance those primarily affecting bone, hard cartilage, muscle, nerve or epithelia, which differ significantly from the soft connective tissues in cell type and healing physiology^{267, 268} (ch 5). Non-specific disorders, such as complex regional pain syndrome and low back pain, are also excluded because in these cases tissue damage may be absent or impossible to identify^{269, 270}. These exclusions leave a number of common and debilitating disorders that might meet the criteria. Table 4.2 lists 20 of them, identified by consulting a range of musculoskeletal textbooks and epidemiological studies²⁷¹⁻²⁷⁵.

Table 4.2: Common soft connective tissue disorders identified for possible use in trial

Rotator cuff tendinopathy	Knee bursitis
Frozen shoulder	Adductor tendinopathy
Bicipital tendinopathy	Patellar tendinopathy
Tennis elbow	Quadriceps tendinopathy
Golfer's elbow	Knee cysts
Wrist tendinopathy	Iliotibial band syndrome
Carpal tunnel syndrome	Achilles tendinopathy
Trochanteric bursitis	Knee collateral ligament lesion
Knee cruciate ligament lesion	Ankle ligament lesion
Hamstring tendinopathy	Plantar fasciitis

The list required further filtering in order to select the most appropriate disorder for use in the trial. A survey of clinicians was used as the first step in this process, and a description of this work follows.

4.3 SURVEY OF CLINICIANS

4.3.1 Introduction

The main purpose of the survey was to prioritise the disorders identified in Table 4.2 by current clinical criteria, drawing on the experience and opinions of health practitioners who treat them. Data regarding prevalence and impact is available in the literature for some of these disorders; a survey of clinicians was conducted to rate those that are sufficiently troublesome to lead people to seek help from a healthcare professional. The survey was also used to highlight issues in diagnosis of the disorders, which might inform construction of the trial protocol; and to identify the strategies most commonly adopted in their management, including the use of electrotherapy. The objectives of the survey were therefore to:

- rank the soft tissue disorders by clinicians' opinions of how commonly they are seen in practice, the problems they cause patients and their recalcitrance to treatment;
- identify issues in diagnosis and management;
- gauge whether clinicians might employ a novel electrotherapy in their management.

4.3.2 Methods and materials

A two-phase process was adopted: in the first phase, a structured postal questionnaire was used to facilitate data collection from a sample large enough to enable a quantitative analysis with some capacity for generalisation; in the second phase, semi-structured telephone interviews were conducted with a sub-sample of questionnaire respondents. Its aim was to obtain more detailed information about management of the highest-ranked disorders. Interviews are useful for deepening the coverage and exploring the meaning of data obtained by quantitative instruments^{276 (ch1)}. When conducted by telephone, they allow involvement by respondents from a wider area and use fewer resources than face-to-face interviews or a focus group. Approval for both phases of the study was obtained by the University of Hertfordshire School of Health and Emergency Professions Ethics Committee. Consultation with the relevant authorities established that the study constituted an audit, and so approval via the NHS Ethics mechanism was not required (see Appendix 3 for documentation).

4.3.3 Participants and recruitment

Orthopaedic specialists, physiotherapists, sports therapists and osteopaths were considered as possible target populations. Musculoskeletal physiotherapists were chosen because they assess and treat many of the listed soft tissue disorders and they spend enough time with patients to gain an appreciation of their experience of the disorders. Using this group also had methodological advantages. A database of physiotherapist names, specialties, institutions and addresses was available; clinicians might be likely to respond to a survey conducted by a member of their own professional group; and through the survey, contacts would be made with departments who might later collaborate in a clinical trial of MCT. The database provides clinical placement information for physiotherapy students in the Southeast of England, and aims to include all NHS services and a number of private practices in the region. It was used to identify contacts in all 193 outpatient musculoskeletal clinics listed. They were sent the questionnaire and a covering letter stating the inclusion criteria: that respondents must be physiotherapists registered with the UK Health Professions Council, and have a minimum of 2 years' full-time equivalent experience treating musculoskeletal disorders. Ethical approval was given on condition that no reminder could be sent because the letter asked recipients to pass on the questionnaire to another clinician if they were unable or unwilling to complete it.

Once analysis of Phase 1 data was complete, all respondents who had indicated on the questionnaire their willingness to be involved in Phase 2 interviews, and who had had chosen at least two out of the three most highly-rated disorders, were re-contacted and invited to be interviewed. These clinicians had experience managing the most recalcitrant disorders and so could discuss their features, diagnosis and management in detail. The necessary sample size to achieve data redundancy varies²⁷⁷, but 12 interviews from a relatively homogeneous sample are considered to be adequate²⁷⁸, so this was sought as a minimum number.

4.3.4 Phase 1 – Postal questionnaire

No existing validated questionnaire was found that aimed to collect the data sought by this survey, and so an original format was created. The first version listed the disorders and asked the respondent to rate them by frequency of presentation, severity of impact on the patient, resources used and responsiveness to treatment, using a 5-point Likert scale. This was piloted with four academics who were also practising physiotherapists, and its format was revised following their feedback. Allocating scores to 20 disorders by four different criteria was judged too onerous and potentially confusing. The revised version asked respondents to choose at least 5 disorders and to score them on three criteria. Space was given to enable addition of any missing disorder they felt should be included. Questions were added to establish the length of experience in musculoskeletal physiotherapy, broad classification of the patient demographic, current use of electrotherapies in the management of the selected disorders, and to seek permission for possible inclusion in phase 2 of the survey. The revised version was piloted by sending it to 10 clinicians (selected from the database described earlier using a computerised random number generator). The standard covering letter was sent to them with a note explaining that they were in the pilot group, and a stamped addressed envelope was included, as well as an option to receive and respond to the questionnaire by email if preferred. Six questionnaires were returned. They were fully completed and no further changes in format were judged necessary, so the package was then mailed to the rest of the sample. A copy of the questionnaire is provided in Appendix 3.

4.3.5 Phase 2 – Telephone interviews

The interview was semi-structured, and comprised several predetermined open-ended questions, with follow-up questions allowed to clarify and deepen responses. Only the top three disorders identified by the questionnaire survey were considered in the interview. The starter questions were, for each disorder

- What are the main problems it causes for patients?
- How do you diagnose it?
- How do you manage the disorder?
- Are there any constraints on management (e.g. time, equipment, knowledge)
- Do you find that some presentations are more resistant to treatment than others?
- What outcome measures do you use to gauge success of treatment?
- Any other issues / comments?

The interview was recorded electronically to facilitate subsequent analysis. This format was piloted with an experienced clinician-academic and who had previously commented on the first draft of the questionnaire. The process was judged satisfactory and no amendments were made.

4.3.6 Data Analysis

Questionnaire data was analysed through descriptive statistics. The proportion of respondents voting for each disorder was calculated, and points assigned for frequency of presentation, impact on patient and recalcitrance to treatment were summed in each case. Although comparisons of total rather than average score gives more weight to disorders that were chosen by more respondents, using mean scores would give undue weight to disorders that few respondents reported as problematic. Therefore, the former method of data analysis was used.

Recordings of the qualitative interviews were listened to twice. A table was constructed of responses to initial questions, and common themes were identified. On second review, statements relating to these themes were noted so that areas of agreement and disagreement could be illustrated. An account of emergent themes, accompanied by supporting quotations,

was viewed by an academic with experience in qualitative analysis as a check on the interpretation.

4.3.7 Results

Questionnaire

The postal questionnaire survey was conducted during July and August 2007. From 197 questionnaires sent, 93 were completed and returned, representing a response rate of 48%. The mean experience of respondents in musculoskeletal physiotherapy was 10.7 (SD 7.5) full-time equivalent years. NHS clinics were the main workplace of 88 (95%) of the respondents; the remainder worked exclusively in private practice. The predominant patient group seen in clinic was reported by 24% of respondents as elderly, 18% as manual workers, 4% athletes or military personnel and 1% as refugees. The remaining 53% did not specify any dominant group amongst their patients.

Figure 4.1 shows the proportion of the sample identifying identified each disorder as problematic in terms of the three criteria. The top three disorders - frozen shoulder, plantar fasciitis and tennis elbow - were each chosen by more than 55% of respondents. The various tendinopathies were the mostly commonly cited disorders: 97% of respondents chose at least one form of tendinopathy.

Figure 4.2 plots the sums of points allocated by all respondents for the top 10 disorders. Ranking disorders by points on each criterion places them in a similar order to that of Figure 4.2, the main exception being rotator cuff tendinopathy, which ranks fourth in terms of frequency of presentation. Frozen shoulder, plantar fasciitis and tennis elbow are the most problematic disorders in terms of the proportion of respondents voting for them, and of the combined scores of respondents for frequency of presentation, severity of symptoms and recalcitrance to treatment.

Figure 4.3 demonstrates the relative popularity of different electrophysical modalities in the treatment of the ten most recalcitrant disorders. Ultrasound was by far the most popular modality, being used by more than half of respondents for most disorders. The main exceptions were frozen shoulder, for which ultrasound was used by only 17% of those identifying it as a problematic disorder, and carpal tunnel syndrome, with 33% usage. Laser was also used in a majority of cases, although to a much lesser extent than ultrasound. The other modalities were reported as used by less than 10% of respondents for most disorders, the main exception being pulsed short wave therapy, which was used by 28% of those

choosing trochanteric bursitis. A small number of respondents indicated using 'other' modalities, but did not specify what they were.

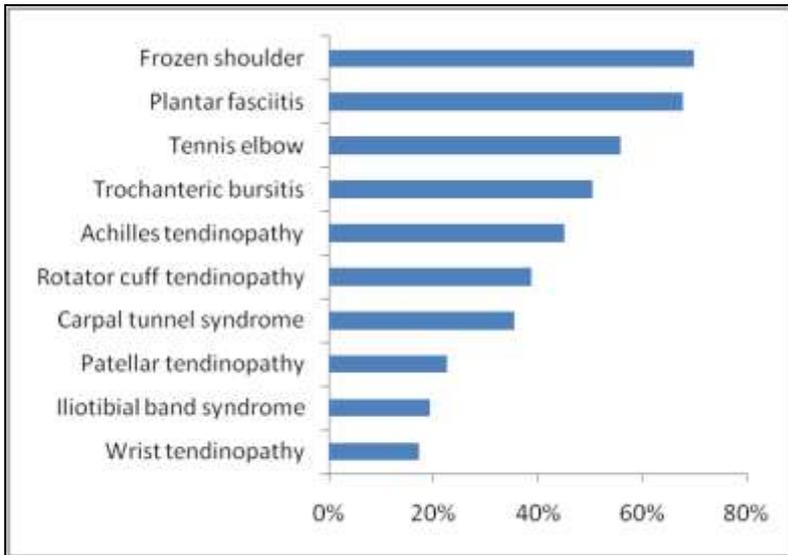


Figure 4.1: Proportion of respondents identifying top 10 problematic disorders

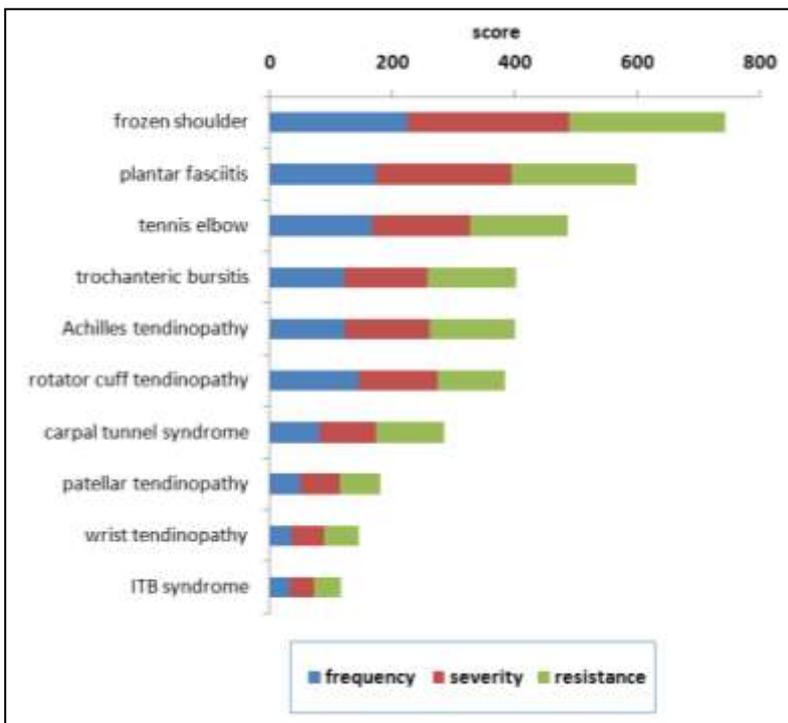


Figure 4.2: Scores for frequency of presentation, severity and recalcitrance to treatment of top 10 disorders.

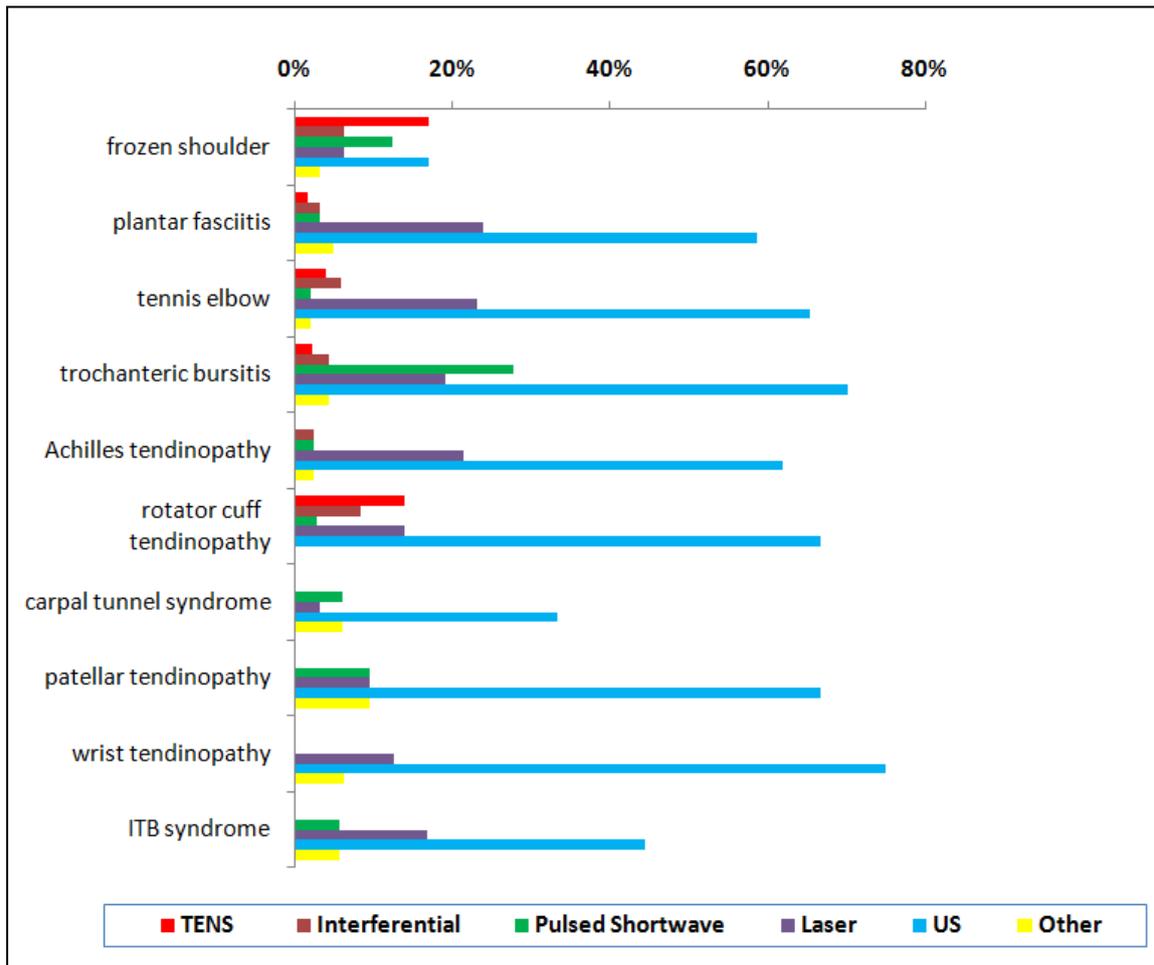


Figure 4.3: Choice of electrotherapeutic modalities in treatment of top 10 recalcitrant disorders.

Telephone interviews

In the second phase, 15 people were interviewed during the period August - September 2007. Interviews lasted between 15 and 20 minutes. The mean experience of the interviewees in musculoskeletal physiotherapy was 13.3 ± 7.9 years. A summary of responses is presented in Table 4.3.

There was broad consensus on most questions. For all three disorders pain was usually stated as the main problem for patients, although for frozen shoulder this was primarily in stage 1. Functional limitation severe enough to cause time off work was mentioned primarily for tennis elbow, and occasionally for plantar fasciitis. Once the pain of tennis elbow had diminished, patients were seen as unlikely to address the factors that might result in its recurrence. For frozen shoulder, limitation in activities of daily living in stage 1 appeared to be more significant than work-related problems. A concern was expressed that chronicity might be promoted by the centralisation of pain and the impact of psychosocial factors. These

may conspire to delay resolution as maladaptive patterns of behaviour and movement are not conducive to healing processes.

Table 4.3: Summary of responses to telephone survey questions concerning top three recalcitrant disorders

Frozen shoulder	Tennis elbow	Plantar fasciitis
<i>Issues in differential diagnosis</i>		
Rotator cuff problems, impingement, calcific tendinitis, cervical spine problems, poor scapular tracking Misdiagnosis in stage 1 can lead to inappropriate treatment Diagnosis easier in stiff phase some felt virtually impossible to identify structure at fault without imaging.	Neural dynamics Cervical spine problems Annular ligament Thoracic problem especially if symptoms bilateral	Neural dynamics Achilles tendinitis
<i>Main problems for the patient</i>		
Pain, particularly in stage 1 when may be in all directions Disturbs sleep Loss of movement Functional limitation (less of a problem than the pain)	Pain ↓grip strength Functional limitation leading to time off work and sports	Pain Functional limitation sometimes leading to time off work if on feet
<i>Management strategies commonly adopted</i>		
Painful phase – refer for injection, scapular setting, education & advice, reassurance that it will get better; use of electrotherapy (TENS) & acupuncture for pain Stiff phase - for most therapists, see once or twice to show self-management, stretches; for some, soft tissue release, muscle balance, scapular tracking, joint mobilisation, sustained joint glides Treat co-factors such as spinal, muscular, neural problems	Cryotherapy Taping, strapping Home exercises, stretch and strengthening (especially eccentric) Manual therapy (deep frictions, massage, mobilisations with movement) Electrotherapy (most commonly ultrasound) Lifestyle, work adaptation Education about disorder Treat co-factors such as spinal, neural problems Refer for corticosteroid Injection	Exercise (especially stretching) Cryotherapy Trigger points Addressing problems higher up (e.g core stability) Electrotherapy (most commonly ultrasound) Lifestyle, work adaptation Education about disorder Treat co-factors such as muscular, neural problems Refer for corticosteroid injection Refer to podiatry for more expert biomechanical assessment – often big improvement after orthotics sorted

Frozen shoulder	Tennis elbow	Plantar fasciitis
<i>Less responsive presentations</i>		
In painful phase, only symptomatic relief seen as possible. (Minority said could prepare for later impact on quality of life)	Chronic phase	Chronic phase
In stiff phase, disorder seen as virtually impervious to treatment by most interviewees		
<i>Factors limiting their successful management</i>		
Inadequate differential diagnosis leading to inappropriate management	Inadequate differential diagnosis leading to inappropriate management	Focus on symptoms rather than causes
Some felt could have more impact if saw patients more; others thought resources not an issue	Difficulty identifying and addressing all contributory factors	Difficulty identifying and addressing all contributory factors
Only seen when already in chronic phase	Only seen when already in chronic phase – seen as a low priority by referring GPs.	Centralisation of pain in chronic cases
Age-related degeneration may limit response to therapy	Centralisation of pain in chronic cases	Lack of biomechanics skills of clinician
Therapist tendency not to look deeper for related problems.	Tendency to re-injure: difficult to get patients to rest the area or change work patterns / lifestyle	If referred to podiatrist, attention may not be given to neurodynamics or muscle balance work
	Contributory co-morbidities e.g. Diabetes	Contributory co-morbidities e.g. Diabetes
	Psychosocial contribution	

Differential diagnosis was recognised by many participants as most challenging for frozen shoulder, although diagnosis of the other disorders was not regarded as always straightforward. Neural involvement was often cited as an issue with all three disorders, and muscle balance was mentioned for frozen shoulder and tennis elbow. Non-response to treatment was sometimes seen as arising from misdiagnosis, particularly in the case of the first stage of frozen shoulder, when limitation of movement might not follow a capsular pattern and pain could be impossible to localise. Less experienced clinicians were judged prone to treat frozen shoulder as a rotator cuff lesion and so exacerbate the problem. Unrecognised neural involvement in all three disorders was suggested by some respondents as accounting for their apparent recalcitrance.

The stage of the disorder was universally recognised as key to its response to treatment. All agreed that tennis elbow and plantar fasciitis were most resistant when they became chronic. For NHS clinicians this was a particular problem as these disorders were often chronic by the

time they were seen. For frozen shoulder the situation was more complicated: a majority felt that in its acute phase (stage 1 or the painful stage) only education and advice were appropriate and that manual therapy was virtually contraindicated, either by the pain it could cause or its 'proven' inefficacy. Some respondents felt that in later stages the disorder was more amenable to treatment, and that sustained improvements were possible; others stated that the course of the disorder could not be influenced by treatment at all, and that all clinicians could offer were coping strategies.

A range of treatment options were described for all the disorders. The most common were education about the disorder and advice on coping strategies. For tennis elbow and plantar fasciitis, addressing aetiological factors such as faulty biomechanics, footwear and ergonomics were cited. Adverse neurodynamics, muscle imbalance and trigger points were named as contributory or co-existing features that would be treated for all disorders. Where electrotherapy was used it was primarily for analgesia, or for encouraging the resolution of inflammation in the acute phase of the disorders. Only one mentioned its capacity to influence tissue healing. Referral for corticosteroid injections were often suggested, either immediately (usually in the case of frozen shoulder) or when conservative approaches were ineffective. Many respondents expressed the view that current physiotherapeutic interventions are primarily aimed at enabling the patient to adapt to and compensate for the effects of the disorder, rather than changing its course. This was especially so for frozen shoulder, but for some therapists was also true for the other disorders. Several spoke of the need to let the pathology run its own course in the knowledge that in most cases it is self-limiting.

For plantar fasciitis and tennis elbow, ongoing aggravation of the affected structure was cited most commonly as a factor limiting resolution. The range of inter-related contributory factors that may not be diagnosed or easily treated was often mentioned as a reason for recalcitrance with all the disorders. For NHS clinicians, funding issues and waiting list pressures were regarded as disincentives to addressing these factors.

Overall, the opinions expressed concurred with the finding of the questionnaire, that frozen shoulder is the disorder that is least amenable to treatment, especially in its initial painful stage but, for many clinicians, also in later stages. The majority opinion was that physiotherapy treatment could not impact upon the course of the disease. Whilst tennis elbow and plantar fasciitis were thought to be more responsive to treatment, the general feeling was that these disorders also had a natural history whose course was difficult to shorten by therapeutic intervention. They also had the added complication of being prone to

're-ignition' by repeated microtrauma from movements carried out in work or recreational activities.

4.3.8 Discussion

Data from the survey provides a range of clinical insights of value to this investigation. Frozen shoulder, plantar fasciitis and tennis elbow are judged as the most problematic soft connective tissue disorders in terms of both proportion of respondents voting for them, and their combined scores for frequency of presentation, severity of symptoms and resistance to treatment. Hence, these are all worthwhile candidates for use in a clinical trial of MCT. The tendinopathies were consistent high-scorers, and so if MCT were shown to be effective in the management of such disorders, it could have a substantial clinical impact.

The survey suggests that electrotherapies are widely used in the management of these disorders by this group of practitioners, although they appear to have limited success. Their potential for influencing the healing process appears to be under-appreciated. Usage is particularly high for the various tendinopathies, but much lower with frozen shoulder. The fact that modality choices varied significantly with disorder suggests that clinicians are not applying them indiscriminately, although usage is not necessarily in accord with experimental evidence. For example, trial evidence suggests that ultrasound may be beneficial for carpal tunnel syndrome²⁷⁹, yet respondents use it less frequently for this disorder than for others for which the evidence base is no stronger²⁸⁰, a finding confirmed by other investigators²⁸¹. So, even if MCT were demonstrated to be effective in the treatment of these disorders, this would not guarantee its incorporation into practice. Additional evidence, for example regarding its cost-effectiveness and potential for home-based treatment, might also need to be generated.

Information provided by the interviews suggests that accurate diagnosis and timing of interventions are seen as key to effective management of the disorders. Differential diagnosis, identification of concurrent pathologies and timing of interventions are also recognised in the literature as significant issues for the top three disorders²⁸²⁻²⁸⁶. Therefore these require careful consideration in a trial protocol.

The survey had a number of limitations. The choice of physiotherapists as the target population meant that the views of other clinicians were not sought. Disorders regarded by physiotherapists as resistant to treatment might respond more readily when managed by other health professionals, as evidenced by referrals of cases with plantar fasciitis to podiatry reported by some respondents.

The questionnaire return rate of 48% is at the lower end of rates typical for research published in medical journals²⁸⁷. Low response rates increase the risk of a non-representative sample generating skewed data due to non-response bias²⁸⁸, but estimates of an acceptable rate vary^{287, 289}. Non-response bias is not an issue if the responders and non-responders are similar in profile²⁸⁸. In this survey, the sample was homogeneous in respect to profession, specialty and minimum experience. Non-responders who did not have these characteristics would have been excluded from the study. The geographical spread of clinics appeared as broad as the original sample, with institutions from all over the region included in the returns. Taking these factors into account, there is no evidence to suggest that non-respondents might have identified and prioritised recalcitrant disorders differently. For the interviews, the sample was purposive rather than randomly selected, and was not intended to be statistically representative of the population from which it was drawn. The sample size for this phase appeared justified on the basis of informational redundancy, since the last few interviews mainly confirmed what had already been articulated by earlier interviewees.

The variables - frequency of presentation, severity of impact on patient and resistance to treatment - were amenable to different interpretations, and no formal checks were made to ensure that a common understanding existed within the sample. Feedback from the initial consultation and pilot mailing did not highlight this as an issue, however, and there appeared to be no ambiguity in their interpretation by respondents in the follow-up interviews.

Because of resource limitations, analysis of the recorded interviews was conducted by only one investigator. Ideally, the process would have been conducted by an additional person to check for potential errors and bias, and to seek agreement on interpretation²⁹⁰. On the other hand, the issues raised by the interviews served mainly to highlight areas that required further consideration in planning later experimental work, and did not change the findings of the larger, quantitative survey.

4.3.9 Conclusions

The survey served the useful purpose of bringing current clinical experience and opinion to bear on the process of selection of a disorder to treat, narrowing the choice from twenty to three. It also provided information relevant to the conduct of later experimental work, particularly regarding the challenges of diagnosis and patient selection. An account of the survey has been published²⁹¹.

4.4 DATA FROM THE LITERATURE

The survey of clinicians enabled a more focussed review of the literature to be conducted, by considering evidence relating particularly to frozen shoulder, tennis elbow and plantar fasciitis. Information was sought relating to the criteria set out in Table 4.1, so that a comprehensive rationale could be provided for the choice of a single disorder for treatment.

4.4.1 Prevalence

The prevalence of frozen shoulder is estimated to be in the range 2 – 5%, affecting people primarily in their 50s, women more than men^{292, 293}. The non-dominant shoulder is slightly more likely to be affected, and recurrence in the same limb is highly unusual²⁹⁴, although the contralateral limb is subsequently affected in up to 34% of cases^{295, 296}. The disorder is often described as self-limiting^{294, 295, 297}, but residual discomfort and loss of movement is common years after its supposed-resolution^{295, 298}. In its primary form it is idiopathic, but it may be secondary to diabetes, thyroid disease, autoimmune disease, hemiplegia and prolonged immobilisation²⁹⁴. A strong correlation has been observed between the incidence of frozen shoulder and Dupuytren's disease, to which it is histopathologically similar^{299, 300}. The disorder can follow surgery and trauma, but repetitive strain has not been identified as a contributory factor.

Epidemiological data for plantar fasciitis are scarce. No prevalence figures could be found, although a lifetime incidence of 10% in the USA is claimed³⁰¹ (but not substantiated). Its distribution in the population is disputed³⁰², but it appears to be most common in middle-aged women and younger male runners²⁸⁶. One study³⁰³ found that the disorder usually resolved completely if conservative treatment commenced within 6 weeks of onset, but that 20% of cases were still troublesome after 4 years. Significant risk factors include adverse biomechanics, unsuitable footwear, the presence of bony spurs, obesity and standing for long periods³⁰⁴. The disorder is usually described as a result of cumulative stress causing micro-tears in the plantar fascia^{283, 286}, and in this sense it is a repetitive strain disorder.

Prevalence rates of 1 – 3% are reported for tennis elbow in the general population, although rates for specific occupational and sporting groups can be much higher (15% and 50% respectively)^{305, 306}. Its peak occurrence is within the fourth and fifth decades, with dominant arm involvement twice as frequent as non-dominant^{307, 308}. Recurrence rates appear to be high, with two studies^{309, 310} finding that more than 50% of patients suffered recurrence, although they do not specify with what severity. A third study³¹¹ found that up to 12% of

their sample suffered recurrence of severe pain and disability. Tennis elbow is – at least in part - a repetitive strain disorder, with frequent patterned loading of the upper limb in work or sport being a primary risk factor³⁰⁷.

The figures provided here must be regarded with some caution as there are significant variations in the values provided by original epidemiological studies. The prevalence rates for tennis elbow in the general population are given as 1.1 – 1.3% in one study³¹² and 10.4 – 11.6% in another³¹³. The studies looked at the UK and Holland respectively, but the discrepancy seems unlikely due to population differences. Reported chronic repetitive strain injuries, particularly of the upper limb, have increased dramatically over recent decades ^{274, 314}. This may be because of previous under-reporting or could reflect real increases due, for example, to productivity pressures in the workplace, increased participation in sports, and rapid industrialisation in developing countries. Of the three recalcitrant disorders considered, this is of particular relevance to tennis elbow, a repetitive strain injury of the upper limb.

These data do not provide incontrovertible evidence as to which disorder is more common. Frozen shoulder may be more prevalent, but tennis elbow is likely to be on the increase.

4.4.2 Impact

There is very little published information on personal and economic costs specific to each disorder, either of treatment or in terms of lost income and production. Most relevant surveys only provide data by anatomical region (e.g. neck and shoulder, upper limb)^{272, 315} or general pathology (e.g. tendonitis, rheumatoid arthritis) ³¹⁶.

At the personal level, all three disorders can cause severe pain for the sufferer, and this may be significantly disabling in their earlier stages. The pain experienced during stage 1 frozen shoulder can considerably limit the movement available at the joint and so impact on activities of daily living such as dressing and reaching. Undoubtedly the ability to do manual work is affected by this disorder, but the literature tends not to address this. Although pain and restricted motion may persist, functional restriction is not marked in late stage frozen shoulder ^{295, 317}.

Prolonged discomfort and residual functional limitations are common with tennis elbow, though this often goes unrecognised by clinicians: one study found that more than 50% of patients with the disorder had persistent discomfort after a year, with some changing occupations or stopping sporting activities³¹¹. Another reported that nearly a third of

workers affected by tennis elbow in highly repetitive manual occupations were absent for 12 weeks or more as a result of it³¹⁸. Approximately 1 million patient visits per year were made in 1995 – 2000 for plantar fasciitis in the United States³¹⁹, though the associated costs have not been quantified.

A particular problem with both tennis elbow and plantar fasciitis is that if predisposing mechanical problems such as repetitive movements and adverse biomechanics are not addressed, the disorders may deteriorate or reoccur^{283, 302, 307, 320}. Reducing these contributory factors may be difficult as they could be integral to the patient's work or recreational activities.

4.4.3 Recalcitrance

Myriad treatment options are available for each of the disorders, though the evidence-base for many of them is limited. Options that have most commonly been advocated in the literature for the management of each disorder are presented in Table 4.4.

There are several systematic reviews looking at specific interventions for frozen shoulder. Two considering the use of oral or injected steroids^{321, 322} found a short term benefit in pain reduction and range of motion, but no long term benefit. A review of physiotherapeutic interventions³²³, including manual therapy, exercise and electrotherapy, found some evidence of benefit for all treatments but is critical of the quality of the studies reviewed. Aggressive stretching or manual therapy may be counter-productive in stage 1 of the disorder³²⁴. No interventions appear to make a long-term difference, although there is expert agreement that surgical interventions for refractory frozen shoulder are most successful if followed by physiotherapy³²⁵. One review²⁹⁶ notes that studies do not compare treatments with the natural history of the disorder and so cannot say whether resolution is spontaneous or due to treatment.

Systematic reviews of treatments available for plantar fasciitis ^{301, 326} indicate that steroid injections may be of some benefit in the short term, but can may lead to long term complications such as plantar fascia rupture; stretching exercises are helpful for pain reduction and orthoses are often helpful, especially to people who stand for long periods. No evidence was found to support the use of ultrasound, and results for extracorporeal shockwave therapy (ESWT) were equivocal. Different outcomes in studies of ESWT may be dependent on dose and patient selection^{301, 327, 328}. Most treatments appear to be aimed at analgesia or reduction of tissue stress^{283, 329}, although ESWT is also proposed to stimulate healing³³⁰.

Systematic review of treatments for tennis elbow^{305, 306} have concluded that corticosteroid injections are likely to be beneficial in the short term, and that ESWT is unlikely to be of benefit, but could not draw any conclusions about the efficacy of mobilisations, exercise, orthoses or surgery. They suggest that no treatments have proven long term benefit. However three studies comparing physiotherapy with injections³³¹⁻³³³ concluded that the former was more effective in the longer term, and found that corticosteroids can result in high recurrence rates and delay recovery. A review of 23 RCTs investigating a range of physiotherapy interventions found contradictory results that meant none could be endorsed apart from ultrasound, for which there was weak evidence in favour³³⁴.

Table 4.4: Management options for treatment of recalcitrant disorders

Frozen shoulder ^{296, 323, 324}	Plantar fasciitis ^{283, 301, 326}	Tennis elbow ^{285, 305, 335}
analgesia (NSAIDs, acupuncture, TENS, nerve block)	analgesia (NSAIDs, acupuncture)	analgesia (NSAIDs, acupuncture)
cryotherapy	cryotherapy	cryotherapy
corticosteroid injections	corticosteroid injections	corticosteroid injections
manual therapy (stretches, joint mobilisation)	rest	orthoses
exercises	self-stretching	electrotherapy (laser, ultrasound, pulsed shortwave, extra-corporeal shockwave therapy, phonophoresis)
hydrotherapy	manual therapy	exercises
electrotherapy (laser)	orthoses	manual therapy (frictions, joint mobilisation, manipulation, mobilisations with movement)
education and advice	heel pads	taping
activity modification	casting, night splints	platelet-rich plasma
distension arthrography	taping	education and advice
surgery (manipulation, capsular release, decompression)	electrotherapy (extra-corporeal shockwave therapy, ultrasound)	relative rest
supervised neglect	education and advice	surgery (tendon release, neural decompression)
	surgery (partial fasciotomy)	

The literature suggests that in most case the symptoms caused by these disorders may be expected to resolve, albeit incompletely, irrespective of treatment offered^{294, 301, 335}. An effective treatment should therefore either cause quicker resolution of the disorder or reduce its impact during its course, compared to a wait-and-see approach, but trials rarely make this type of comparison. (This issue is revisited in Chapters 7 and 8, when the results of the trials conducted in this investigation are discussed.) Published trials reach inconsistent conclusions, suggesting variable success rates for each form of treatment, and often limited long term benefit^{283, 301, 305, 306, 324, 325, 329}. The quality of trials or of their reporting is frequently judged inadequate.

There is little evidence available to identify which patients are more or less likely to respond to a particular form of conservative therapy. No specific prognostic indicators for frozen shoulder could be found. Its time-course is very unpredictable, with quite different durations of each stage claimed by different authors²⁹³⁻²⁹⁶. Staging systems do not appear to be incorporated into clinical trials and may be perceived as of limited value in empirical research. A review of literature on plantar fasciitis found many risk factors but none that reliably predicted clinical outcome²⁸³. Since repetitive microtrauma is often a factor in the development of both tennis elbow and plantar fasciitis^{283, 285}, continued stress on the affected site may cause re-injury and confound therapeutic efficacy, whatever treatment is applied. For tennis elbow, manual work and weekly participation in racquet sports were found predictive of negative outcomes in two studies^{336, 337}. A later sub-group analysis of trials of conservative treatment found that type of employment had minimal impact on outcome³³⁸, but the nature of the manual work was not specified, nor whether participants modified their activities to protect the vulnerable site. Symptom duration of more than three months has been found predictive of worse outcome with this disorder³³⁹.

4.4.4 Potential response to MCT

This criterion was considered in detail in the previous chapter. The weight of available evidence is most relevant to tendons and, by implication, to tennis elbow. However there are several caveats to consider. Findings from experiments involving animal tendons or tenocytes in vitro cannot be assumed to apply to the common extensor humans tendon in vivo. Actually since tendons and ligaments form part of the rotator interval, the structure affected in frozen shoulder³⁴⁰, these findings might arguably have relevance to that disorder. Also, in these investigations soft tissue damage was induced artificially and treatment was of an acute lesion. Therefore they cannot be regarded as directly applicable to the disorders of interest, which are normally characterised by insidious onset and often treated when chronic.

Since microcurrent can promote healing in non-uniting fractures and chronic skin ulcers, it has been argued that it can help with dysfunctional healing in other tissues – such as tendons, ligaments and cartilage^{113, 143, 171, 341}. The argument might be extended to joint capsules and fascia, and so include the disorders of interest here. However this line of reasoning makes a number of leaps of faith and may be challenged at several junctures. Pathological features and repair processes – both normal and disrupted – are not identical in the different tissue types, nor in the variety of disorders that affect them. Frozen shoulder commences with an inflammatory response in the synovium followed by a reactive fibroplasia in the joint

capsule, with excess production of collagen and increased numbers of myofibroblasts^{292, 300}, whereas tennis elbow is often characterised by micro-damage of already degenerate tendon tissue resulting in poorly organised and inferior quality collagen³²⁰. The former disorder leads to contracture of the affected tissue²⁹⁴, the latter normally does not. In other words, the pathophysiologies are not the same. On the other hand fibroblastic proliferation and tissue thickening are common to these disorders, and are also seen in plantar fasciitis³⁴². Matrix calcification and hypervascularity typical of granulation tissue can also be found in all three disorders^{300, 320, 343}.

4.4.5 Feasibility and methodological issues

Formulation of a feasible trial protocol requires that practical considerations and resource constraints be taken into account. These included availability of a study sample, time and funding, and the expertise of the investigator. Methodological rigour is enhanced by having a well-defined study population, recognition of prognostic factors, the identification and control of potential confounders, and the availability of valid and reliable outcome measures.

Case definitions are available for frozen shoulder and tennis elbow, although different studies sometimes adopt different versions^{344, 345}; none could be found specifically for plantar fasciitis. Diagnosis of frozen shoulder can be problematic^{282, 346}, especially in its early stages when pain may limit all movements. It may be mistaken for rotator cuff tendinopathy or impingement²⁸⁴. However when stiffness becomes the predominant feature, restriction of active and passive movement in a capsular pattern is more apparent, and a complete loss of external rotation may be observed. This loss has been claimed to be pathognomonic of the disorder²⁹⁴. Diagnosis of plantar fasciitis and tennis elbow requires exclusion of a number of other disorders, particularly neuropathy^{285, 347}, but is not described as problematic in the literature. Ultrasound has been shown of value in diagnosing all three disorders³⁴⁸⁻³⁵²

Prognostic uncertainty is a barrier to creating homogeneous treatment and control groups and to making meaningful comparisons of their healing rates. This is a problem for all three of the disorders, but perhaps particularly so for frozen shoulder, because of the lack of relevant evidence. A factor that could be especially significant for tennis elbow and plantar fasciitis is aggravation by continued stress of the injured site. Since cumulative microtrauma is implicated in these two disorders^{285, 302, 335, 347}, aggravation should ideally be controlled in any clinical trial. This may be impossible because the movements causing the trauma can be hard to avoid. The argument does not arise for frozen shoulder because it appears not to be a repetitive strain injury.

Trials of the efficacy of various treatments for these disorders have employed a raft of outcome measures. Validated functional and quality of life measures that have been used include the Foot Health Status Questionnaire for plantar fasciitis³⁵³, the Shoulder Pain and Disability index for frozen shoulder^{321, 354}, and the Patient-Rated Forearm Evaluation Questionnaire for tennis elbow³⁵⁵. Algometry, dynamometry and goniometry can provide objective or semi-objective measures of clinical outcomes. To gauge the impact of treatments in the anatomical and pathophysiological domains, tissue biopsies give structural and histological information; haematology can indicate the presence of chemical mediators of inflammation and healing; and MRI, radiology and ultrasound imaging can evaluate structure and – in the case of sonography – blood flow. The advantage of these measures is that they may provide direct evidence about healing processes, whereas the clinical and functional tools offer only indirect evidence. Thermography has been proposed as an additional tool for assessing and monitoring changes in tennis elbow³⁵⁶, through quantification and mapping of superficial tissue temperature. However, a correlation of this variable with deeper structural and physiological changes has not been established. Biopsies, haematology and MRI were beyond the resources available to this investigation, whereas diagnostic ultrasound was not. This imaging modality has been used successfully to demonstrate anatomical and physiological changes accompanying treatment for including tennis elbow^{357, 358} and, to a lesser extent, plantar fasciitis³⁵⁹. Sonography has been used for imaging of tissue in frozen shoulder³⁶⁰, but no reference to its use for monitoring change could be found.

4.5 DRAWING THE EVIDENCE TOGETHER

Having gathered information from the literature and the survey of clinicians, a clearer rationale for the choice of disorder to treat was available. There remain areas of uncertainty and ignorance, and arguments can be made about how the data should be weighted. These factors meant there was an arbitrary element to the choice, although a new and effective treatment would be of significant benefit in the management of any of the top three disorders.

If the decision were to be taken purely on the basis of the survey, frozen shoulder would be the disorder of choice to treat in this study: it is seen commonly in clinic, can be extremely painful in its early stages, may take several years to resolve, leaving significant residual symptoms, and is often resistant to conservative treatments currently available. The disorder scores highly both from the clinicians' point of view and using evidence from the literature.

On the other hand there is no compelling evidence that it might benefit from microcurrent therapy, and there are several significant problems in developing a robust experimental protocol for its treatment. Prospectively identifying a group with similar prognoses for progression of the disorder is not possible. If some shoulders take three or more years to 'thaw' left to themselves, treatment effects might not be apparent within the timescale of this investigation. Recruitment might be easier if treatment were offered in the painful stage, but differential diagnosis on purely clinical criteria can be unreliable; once pain has subsided diagnosis is easier, but disability is not so severe and motivation to participate might diminish. Finally, the available outcome measures would not provide direct evidence of healing at a tissue level, which is a central concern of this investigation. Therefore practical issues could compromise the chances of a successful study.

Plantar fasciitis also scores highly as a problematic disorder according to both the survey and the literature, but choosing it would give rise to several theoretical and practical problems. There is very limited and poor quality trial evidence that it might respond to microcurrent. Obtaining a viable sample would present a significant practical challenge. Reliable prevalence figures are not available for plantar fasciitis and, although its frequency total score in the survey was higher than that of tennis elbow, its average score across 30 respondents was significantly lower. All interviewees said they encountered it rarely. Hence, it was deemed inappropriate for inclusions in the trial.

Tennis elbow did not score as highly as frozen shoulder and plantar fasciitis in the survey, but it ranked third in the list of 20 disorders. There is a considerable body of evidence already available to suggest that pathological tendinous tissue may respond to microcurrent therapy. The direct evidence regarding tendinopathies such as tennis elbow is limited, but the experimental literature relates more directly to tendons than to the tissues affected in the frozen shoulder and plantar fasciitis. Studying the effects of microcurrent on tennis elbow may well have relevance to other tendinopathies - such as rotator cuff, patellar tendon and Achilles tendon lesions, which were all high scorers in the survey. Many therapies for tendinopathy treat the symptoms, and it has been suggested that effective treatment strategies that stimulate a healing response in the diseased tendon need to be developed³⁶¹. Choosing tennis elbow also has several practical advantages: pain is an ongoing feature of the disorder, which might encourage recruitment of participants; compared to the other disorders, it is somewhat easier for the layperson to identify when reading recruitment literature; and diagnosis and monitoring of tissue changes has already been demonstrated as viable using sonography. The potential disadvantage of choosing tennis elbow is the chance

of re-injury during treatment, although monitoring participant activities would allow this factor to be investigated, if not controlled.

Tennis elbow was therefore chosen as the disorder for investigation in a clinical trial of MCT. The next steps in developing a protocol for the study were the definition of a trial population, the choice of treatment parameters, and the selection of appropriate outcome measures. These issues are addressed in the chapters that follow.

Chapter 5

Experimental Design Issues

5.1 INTRODUCTION

Having established an argument for subjecting microcurrent treatment of chronic tennis elbow to a clinical trial, the next step in this investigation was to plan one. Systematic reviews of treatments for tennis elbow consistently comment on the poor methodological and reporting quality of studies^{305, 334, 362}. So it was judged essential to give detailed consideration to the various elements of a trial protocol. This chapter addresses some of the key elements in that process: defining the disorder to be treated, choosing an experimental design, and selecting the form of treatment to employ and the outcomes to measure. Other methodological issues - such as eligibility criteria and methods of data analysis - could only be addressed once these fundamentals had been considered. Published clinical trials and other investigations of tennis elbow were used as source material for the discussion that follows. Approaches commonly employed in trials were assessed against criteria drawn up specifically for this investigation.

The chapter commences with development of an operational definition of tennis elbow. This is necessary to identify those components that might respond to MCT and which should therefore be measured in a trial. It was also used later when eligibility criteria were drawn up. The focus then moves to selection of an appropriate trial methodology, given the questions and requirements for further evidence identified in the systematic review. This is followed by consideration of the treatment parameters to be employed in the trial, and a report of the evaluation of several MCT devices to see which might be able to deliver the required form of microcurrent. Finally, the range of outcomes that might be measured in the trial is described, and several are assessed for suitability to the requirements of this investigation. The chapter concludes with a selection of the trial design, the form of treatment to be used, and a set of potentially appropriate outcome measures, some of which are identified as requiring further evaluation.

5.2 DEFINING THE DISORDER

Defining tennis elbow is not straightforward, and there is continued debate about its essential components. This is reflected in the variety of names that have been proffered as alternatives to the non-specific title, which derives from 'lawn tennis arm', first described in 1882³⁶³. Since it may afflict people who are entirely unacquainted with a tennis racquet, the term is clearly a misnomer, but it has been retained in both general and clinical use for the lack of a satisfactory alternative. 'Lateral epicondylalgia' has been suggested as preferable because it focuses on the main clinical feature – pain – without making any assumptions about the underlying pathology^{364, 365}. However, this investigation is particularly concerned with healing of tendon tissue damage, and lateral elbow pain may exist in its absence, for instance secondary to radial neuropathy, radiohumeral arthropathy or as referred pain from cervical spondylopathy^{308, 366}. The pain of tennis elbow may have many sources but the epicondyle itself is rarely reported as one of them, so the term offers little in terms of specificity to the disorder of interest. 'Lateral epicondylitis' has been (and still is) commonly employed^{367, 368}, although the term has been discredited by histological studies finding little evidence of inflammation in the affected tissue when the disorder has become chronic^{369, 370}. The title 'lateral elbow tendinopathy' is preferable because it identifies the element of the disorder of particular interest here, namely tendon tissue damage³⁷¹. Also, it is general enough term to encompass the range of tendon pathologies that might present in tennis elbow, such as damage to the tendon proper or the paratenon, and including cumulative micro-damage, calcification and tears. However, the term has the disadvantage of being primarily a histological entity, which may or may not have clinical correlates in a particular case. The common extensor tendon may show signs of pathology and yet cause no symptoms – this has been a finding of both histological and imaging studies^{348, 372, 373}. Equally, clinically significant changes may occur in presentations of tennis elbow whilst many tendinopathic features remain^{374, 375}. Thus, if tennis elbow is described only in terms of pathological change to the tissue, the essential concerns of clinical features and clinical change may remain unaddressed. Hence the term "tendinopathy" is also unsatisfactory in the context of an investigation concerned with therapeutic benefits. For these reasons, the alternative titles were rejected for use in this report, and the archaic term 'tennis elbow' was retained.

Tennis elbow has been defined as 'a painful condition affecting the tendinous tissue of the origins of the wrist extensor muscles at the lateral epicondyle of the humerus, leading to a loss of function of the affected limb [which can have] a major impact on the patient's social and professional life'³⁷⁶. This description identifies several significant elements of the

disorder: the symptoms it provokes, its impact on the individual, and the structure that is the source of the problem. It does not specify the nature of the tissue damage, however. Imaging of the affected tendon in tennis elbow has revealed many forms of structural change in tennis elbow, including disruption of the normal fibrillar pattern, calcific deposits, fluid accumulation, thickening of the tendon body or the peritendinous lining, tendon tears, and hyperaemia that may be due to increased blood flow in existing blood vessels or formation of new ones^{349, 357, 372}. Histological studies have confirmed that chronic tennis elbow is associated with cellular and extracellular changes, including increases fibroblast numbers and activity, disorganised and immature collagen formation, angiogenesis with associated neural ingrowth^{364, 377, 378}. The tendinopathy of tennis elbow could be regarded as any combination of these features, although some authors have attempted to restrict the meaning of this generic term to a specific form of damage - a result of failed healing following repetitive microtrauma^{285, 379}. This would exclude frank tears and calcific deposits, which are not in themselves examples of failed healing, and yet could be the main source of symptoms in some presentations of tennis elbow. Adjacent structures such as the radio-humeral ligament and joint capsule may be damaged and contribute to symptoms. Differentiating between these different forms of structural change and damage is important because it may be that microcurrent can affect some of them but not others. Indeed, this may be true of other forms of treatment, a possibility that has received little attention in the trial literature to date. This issue is further addressed in Chapter 9.

The pain of chronic tennis elbow has been associated, not only with nociceptive stimulation by biochemicals released by inflammatory cells, but also with peripheral neuropathy and central sensitisation mechanisms³⁸⁰. Local neurones may increase in number and sensitivity and themselves release noxious biochemicals, and neuroplastic change in the central nervous system may maintain a pain response even if damaged tissue has healed³⁸¹. The functional loss seen in the disorder is likely a consequence of both the pain experienced and a variety of motor deficits, including loss of muscle strength and control³⁸². A model of tennis elbow integrating these inter-related elements has been proposed³⁸¹. It conceptualises the disorder as a syndrome comprising local tendon pathology, changes in the pain system (both local and central) and sensori-motor system impairments (such as strength and proprioception). These may co-exist and interact to different extents in each case. In this investigation, tissue pathology and pain are of particular concern because it is these elements that MCT targets; nevertheless, if they improve, complex interactions between the systems might also reduce motor deficits and improve function.

The following working definition was therefore adopted.

Tennis elbow is a disorder characterised by damage to the common extensor tendon in the lateral elbow, local pain and motor deficits in the affected arm, which may affect the performance of work or recreational activities.

This definition was used in the formulation of diagnostic and eligibility criteria for the trials, which are discussed in Chapter 7.

5.3 METHODOLOGY

A randomised controlled trial (RCT) is the design of choice to explore the effectiveness of MCT in the treatment of chronic tennis elbow, because RCTs can provide the best evidence of whether an intervention causes an outcome²¹⁶. For the evaluation of MCT, the optimum format is a placebo-controlled trial with microcurrent or sham microcurrent applied in combination with another form of therapy. Combination therapy is appropriate for two reasons. First, MCT has been shown to be most effective in other tissue lesions when used as an adjunct treatment; for example with wound dressings in cutaneous ulcers or with instrumentation following spinal fusion surgery. Second, there is evidence that controlled mechanical loading is necessary to drive effective remodelling during tendon repair, and MCT cannot provide this.

There are several forms of RCT that could be employed. The most informative design in this context would be a three-armed trial. In many cases, tennis elbow is a self-limiting disorder that resolves in time whether or not it is treated^{366, 383}. However, symptoms may persist for several years, and the course is not necessarily predictable^{308, 337}. For a treatment to be judged worthwhile, it should lead to better outcomes than a wait-and see approach. A trial that includes a minimal intervention arm can be used to test this. This would be ethically acceptable because no single treatment has been found efficacious in all cases, and spontaneous healing is the expected outcome in most cases. A sham-MCT group is also desirable because treatment with microcurrent may produce a placebo effect. Hence, the most robust trial design would have a real MCT, a sham MCT and a “wait-and-see” group, with both treatment groups also receiving an exercise programme to provide mechanical stimulation.

Because part of the rationale for MCT is that it promotes tissue healing, a cross-over trial would not be appropriate. If MCT “kick starts” a healing process that was dysfunctional, outcomes using a sequence of treatment A → washout period → treatment B would be difficult to interpret since healing might continue through the washout period. A parallel arm trial should facilitate unambiguous attribution of causality. Many of the clinical trials cited in Chapter 2 used the case series design, sometimes justified on the basis that subjects acted as their own controls because their signs and symptoms had been stable for some time before the intervention commenced. This approach might be acceptable if used prospectively, with baseline assessment on all measures conducted at a defined time - at least several weeks - before treatment commenced. However, it would still not be the optimum design for a trial involving chronic tennis elbow because symptoms may not be stable. The parallel arm trial remains preferable.

As the systematic review of clinical trials reported earlier revealed, there is substantial uncertainty regarding the optimum MCT parameters to use in a trial. Also, because no trials so far conducted have measured the effects of MCT on tissue healing in tennis elbow, it is difficult even to make an educated guess about the potential effect size. This means that the minimum sample size required to produce a statistically significant result is unknown. Inadequate sample sizes reduce the power of a study to detect a real difference in outcomes, and so undermine the quality of evidence, a deficiency commonly noted in systematic reviews of tennis elbow trials³⁸⁴⁻³⁸⁶. For these reasons, proceeding directly to a full clinical trial was judged inappropriate and unethical. In the few published trials that have been conducted with the soft connective tissues, the selection of MCT parameters is not justified and, possibly as a consequence of using less-effective forms of microcurrent, their small samples and effect sizes lead to unconvincing conclusions. In order to avoid these pitfalls, it was decided to conduct preliminary studies to investigate whether certain parameters are key to the effectiveness of the therapy. These were not designed to evaluate the effectiveness of MCT compared to another type of treatment, or to no treatment, but to compare different parameter combinations using the same experimental protocol. Therefore, all participants would receive some form of MCT. This design is analogous to a phase II pharmacological clinical trial, in which dose/response relationships are investigated³⁸⁷. Its disadvantage is that it cannot prove whether MCT produces a better outcome than another management strategy (including “wait and see”). However, a comparative study such as this can provide a rationale for the choice of MCT parameters to be employed in a controlled clinical trial. It can also serve several other purposes: evaluation of outcome measures specifically related to tissue healing, which have rarely been used in trials of MCT; gathering data on adverse

events and patient acceptability; and gaining methodological experience that could inform the controlled trial protocol. The trial would therefore be exploratory, with the intention of providing preliminary data upon which a full RCT could be based.

Thus, a parallel-arm clinical trial in which the effects of different forms of MCT were compared, was selected as the most appropriate study design for this stage of investigation.

5.4 FORM OF MICROCURRENT TREATMENT

In theory, it would have been preferable to design and build a device capable of providing control over all the parameters considered in the review. In practice, doing so would have required resources beyond the capacity of this investigation. Instead, the variety of proprietary devices available for the delivery of therapeutic microcurrent was considered, and several of these were assessed in detail for possible use in the trial. As well as the capacity to deliver current with parameters within the therapeutic window delineated by the reviews, several other characteristics were considered:

- **Portability:** to achieve total treatment times of many hours, the device should be small enough to be carried around and not interfere unduly with normal activities
- **Ease of use:** repeated and long duration treatment is best carried out by the patient, and so the device should be simple to use and durable
- **Safety:** possessing a CE mark confirming that it meets European Union health, safety and environmental requirements
- **Cost and availability:** since multiple devices would be required, those that could be acquired at lower cost or on loan would be preferred
- **Existing evidence of benefit of treatment provided by the device.**

Devices were identified from published trials, existing contacts within the industry, and an internet search. Information on their characteristics was obtained from manufacturers' websites and data-sheets. A comparison of the devices using the selection criteria is summarised in Table 5.1.

Table 5.1: Characteristics of microcurrent devices evaluated (CR = current regulated)

Device name & supplier	Parameters	Portability	Ease of use	Available evidence	Suitable
Accu-o-matic Electro-Therapeutic Devices, Ontario, Canada	20-600µA 0.8-320 Hz Pulsed mono or biphasic	Mains operated Not easily portable	Requires therapist to apply manually via probes		✘
Alpha-stim 100 Electromedical Products Mineral Wells, USA	10-600µA Pulsed 0.5, 1.5, 100Hz 10s on 2s off Biphasic balanced rectangular waveform 10,20, 60 minutes or continuous.	Hand-held Battery operated	Adjustable but no markings to show parameters. Application by probes or small electrode pads	Weak evidence of benefit with musculoskeletal and post-operative pain ^{243, 245}	?
Electro-Myopulse & electro-acuscope Thorp Institute, Encinitas, USA	0-600µA rms 0.5-320Hz Amplitude and frequency-modulated square wave, alternating polarity every 2s	Mains operated Not easily portable	Requires many parameters to be adjusted. Small electrode pads on affected area.	Weak evidence of benefit in Radiation-induced fibrosis ²⁵⁰ , non-specific pain ¹⁰² and tennis elbow ²⁵⁴	✘
Elxoma Medic Redplane Zug, Switzerland	0-1500µA CR Up to 99 minutes	Hand-held Battery operated	Simple programming. Small electrode pads on affected area.	No published trials	?
Intellect Chattanooga Group Hixson, USA	0-1000µA CR Monophasic or biphasic Waveform not specified 0.1 – 1000 Hz 1 – 60 minutes	Mains operated Not easily portable	Delivers many programs including MCT. Requires therapist to operate. Small electrode pads or probes on affected area.	No published trials using microcurrent parameters	✘
Micro Plus Biomedical Life Systems Vista, USA	0 - 1000µA States output voltage 2.5V peak-to-peak so cannot be CR. Biphasic symmetrical square wave Pulsed 5 -120 Hz Carrier Frequency: 14,000 Hz Polarity: Positive, negative or bipolar with 1, 2, or 3 second adjustment within each range	Hand-held Battery operated	Similar to TENS device with dial controls. Markings do not allow accurate control of parameters.	Evidence of tendon healing in rats ¹⁴⁵	?
Microace MSL Medical London, UK	1-600µA	Hand-held Battery operated	3 pre-programmed settings Small electrode pads on affected area.	No published trials found	?
Microdoctor Micromed Technology Cranleigh, UKK6 HND	Microcurrent but otherwise unknown	Hand-held Battery operated	Simple programming Small electrode pads on affected area.	No published trials Predecessor of "Tendonworks"- see below.	✘

Device name & supplier	Parameters	Portability	Ease of use	Available evidence	Suitable
Pain-away / Pain Ease <i>Newmark Inc, Cheshire, USA</i>	Nominal 10-25µA Not CR DC or 0.5Hz monophasic square wave Continuous application for 5 days.		Circuit embedded in adhesive electrode. Very simple to apply.	Weak evidence of benefit with chronic low back pain ²⁴⁷ Authors state f=71.5kHz but manufacturer says 0.5Hz for that version.	?
Precision Micro Precision Electronics <i>Montclair, USA</i>	10 – 600µA 0.1-990Hz Monophasic Square wave 50% duty cycle Treatment for few minutes in total	Mains operated Not easily portable	Applied by therapist via probes	Found ineffective in a tennis elbow study ³⁸⁸	✘
Rebox <i>Unable to trace. May be unavailable</i>	0-300µA 200-5000Hz Pulsed monophasic square wave ¹⁹⁹	Unknown	Requires therapist to apply manually via probes	Trial gave limited support for use with tennis elbow ²⁵⁶ .	✘
Tendonworks Synapse Microcurrent <i>Canterbury, UK</i>	40-500µA CR 3 stage program, mainly 40µA monophasic square wave Current regulated 30 minutes	Hand-held Battery operated	Single button operation Automatic shut-off Small electrode pads on affected area.	Parameters based on published study for Achilles tendinopathy ²⁵¹	?
Wewo Thom Wewothom gmbh <i>Bad Saarow, Germany</i>	Nominal 25µA 8 -12 kHz Biphasic square wave Not CR 6 hours	Hand-held Battery operated	Single button operation. Small electrode pads on affected area.	No trials published in English but several summarised at http://hightonetherapy.com/studies.html	?

Those devices marked with a query in the table appeared capable of delivering microcurrent within the therapeutic window and meeting the criteria of portability and ease of use. Enquiries were made to the suppliers and several of the devices identified were made available for further evaluation: the Elexoma Medic, Painaway patch, Tendonworks and WeWo Thom. All of these devices have CE marks. Because of commercial sensitivities, some suppliers were unwilling to provide a full description of the microcurrent their device delivered and so laboratory measurement of their outputs was conducted.

5.4.1 Laboratory testing of microcurrent devices

The purpose of this study was to assess the suitability of the MCT devices for inclusion in a clinical trial with chronic tennis elbow. This was based on investigation of their electrical characteristics, and suitability for home-based, patient-controlled treatment, which would facilitate maximal treatment times. The specific aims were to:

- Obtain a full description of the current output
- Establish whether the output current intensity is regulated
- Gauge the level of parameter control available
- Assess for durability and ease of use

Current regulation is the variation of output voltage to compensate for changes in body circuit impedance that may occur during treatment. Without current regulation, the actual intensity and waveform may differ significantly from nominal values.

Methods and materials

All work was conducted by the author. The devices evaluated were: Elexoma Medic, Painaway Patch, Tendonworks and WeWo Thom (illustrated in Figure 5.1). Each device was subject to a electrical testing and simulated therapeutic use, following the instructions provided by the suppliers. To standardise the measurement and description of outputs of therapeutic devices, the currents reported in technical specifications are normally those it produces in a standard resistor, typically of 500 Ω or 1 k Ω . In this case, to inspect the waveform and confirm the nominal current intensity, each device was connected to a standard 980 Ω resistor and the voltage waveform across the resistor was displayed using a digital oscilloscope (TDS1002B, Tektronix UK Ltd, Bracknell). Sample waveforms were stored and their data transferred to a spreadsheet, enabling peak and average current values to be calculated.

To evaluate current regulation, readings were repeated with a 14 k Ω resistance, arbitrarily chosen to assess how the device responded to an order of magnitude increase in resistance. Finally, to observe electrical performance in clinical application, measurements were made with the device connected to the investigator's elbow using the adherent electrodes supplied. Robustness, ease of use and user-control were assessed by inspection of supporting documentation, handling of the device and simulating its use for treatment of tennis elbow. The skin was prepared by shaving and cleaning with an alcohol wipe, and the electrodes

were applied over the lateral epicondyle and the posterior elbow, just proximal to the olecranon.

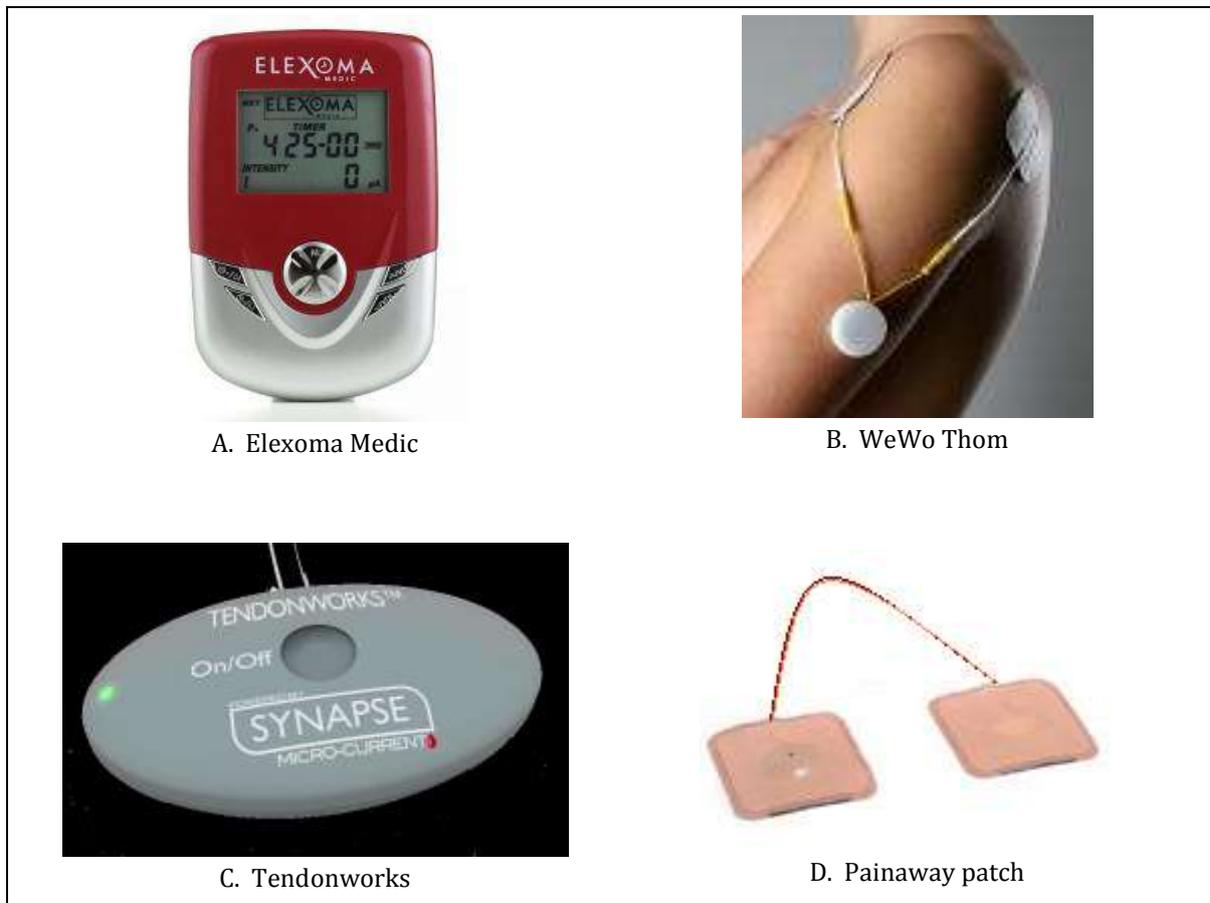


Figure 5.1: MCT devices evaluated in laboratory

Each device was used in accordance with the supplied manual, using nominal settings within the defined therapeutic window where possible. A diagram of the circuit used for electrical investigation is provided in Figure 5.2. Instantaneous current values were calculated by substituting the known resistance and measured voltages into Ohm's law (voltage = current \times resistance). Peak and time-averaged values were calculated using the data recorded from several cycles of each waveform. Because of the varying impedance of the body, calculation of the currents driven into the tissue by each devices was not possible.

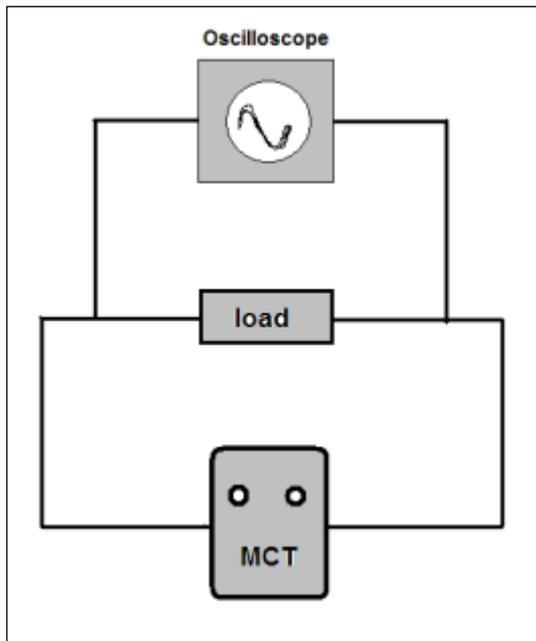


Figure 5.2: Circuit diagram for MCT device electrical testing

Results

The physical and control characteristics of each device were as follows:

- A. Elexoma Medic: about the size of a portable CD player, of sturdy construction, supplied in a rigid carry case, used 4 rechargeable batteries. LCD screen showing operational parameters and a series of push buttons on the front face for programming. These allow a choice of waveforms, current intensity and treatment duration up to a maximum of 99 minutes. Adherent electrodes are provided, and connect to the device via wires plugged into a socket at the top. Two sockets are available, allowing up to four electrodes to be connected. The device shuts off automatically once programmed treatment is complete. There is an audible “circuit broken” alarm but this does not function below currents of about $100\mu\text{A}$. A belt mounted carry-case is available. A user manual suggests which program to use for a particular application, electrode placement and numbers of treatments.
- B. WeWo Thom: disc-shaped device about 3cm diameter and less than 1 cm thick. A small recessed button is pressed for several seconds to activate the program, and a flashing LED indicates whether the program is running. No parameter adjustment is possible and the program runs for 6 hours before shutting off automatically; early shut-down can be forced by holding down the button. Supplied with adherent electrodes that connect to two sockets at the end of short wires emerging from the

side of the device. It can hang freely as it is very light, but may also be held in place with tape or a dressing. The battery is not rechargeable, but the manufacturers estimate its lifetime as 500 hours. Brief instructions for use are provided.

- C.** Synapse Tendonworks: a plastic ovoid of approximate dimensions 4x3x1 cm, with a recessed power button and a dim LED indicator within the casing that flashes every two seconds during operation. The treatment program runs for a preset 30 minutes before switching off, but can be interrupted by holding down the button. The LED flashes more quickly if the circuit is broken but there is no audible alarm. Adherent electrodes are provided and connect to the device via sockets on 50 cm-long wires emerging from its side. The device is designed for single use, the battery reported by the suppliers to be able to provide up to 50 treatments. User instructions are provided, and the suppliers suggest a complex treatment regime involving varying numbers of treatments each day and week for three weeks.
- D.** Pain-away patch: also known as the “Pain-ease” and by several other names. Takes the form of two adherent dressings approximately 5 cm square with waterproof backing, connected together by a conducting lead. Each dressing contains an integrated circuit and battery, claimed by the manufacturer to last up to 500 hours, and designed to be used continuously for 3 – 5 days.

A reliable electrical measurement process for use with the Painaway device could not be developed, because of the integration of its circuitry into its adherent electrodes. Therefore it was excluded from the evaluation. Both the Tendonworks and WeWo Thom delivered a fixed program that could not be adjusted by the user; the Elexoma Medic had 8 programs delivering a variety of waveforms. One program that provided a monophasic low frequency current was selected for evaluation.

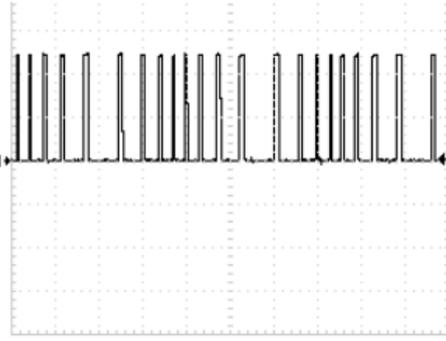
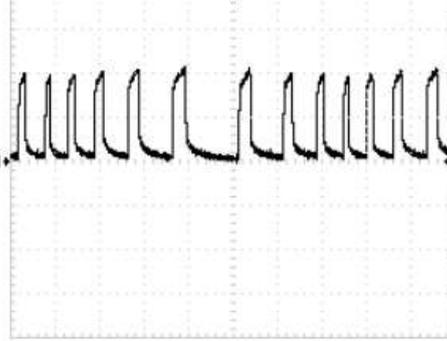
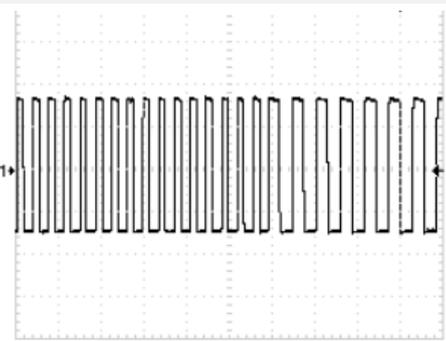
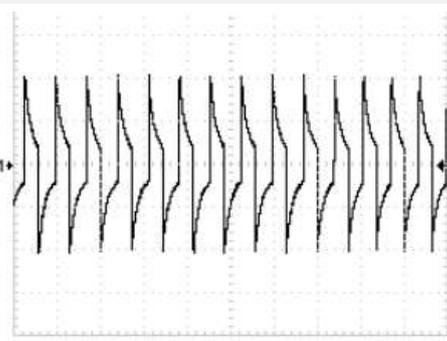
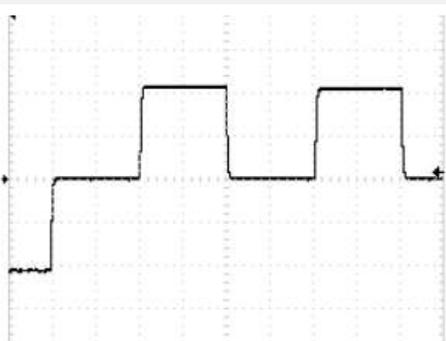
Table 5.2 provides exemplar waveforms recorded when the devices were attached to the standard resistance. The specific details of each device output were as follows:

- Device A produced a square wave of fixed amplitude (controlled by the operator) and frequency modulated in the range 75 – 160 Hz. Groups of pulses of approximate total duration 90 ms were seen, with individual square pulses varying stepwise between 1 and 3 ms and inter-pulse periods of 5-10 ms. The nominal current selected by the operator was seen to represent the peak rather than average current delivered, which was calculated to be approximately 80% of the peak value. When the fixed resistance was raised to 14 k Ω , the output current was controlled to within 10% of the nominal value.

- Device B produced a fixed amplitude alternating polarity square wave of frequency 8 - 12 kHz, and with pulses of duration varying between 70 and 110 μs , with inter-pulse periods about 20% longer than the preceding pulse. The device produced a peak current of approximately 80 μA and an average current of approximately 50 μA when applied to the standard resistor. These values dropped substantially when the larger resistance was used, demonstrating that the device was not current controlled. The manufacturers estimate that an average current of 25 μA is produced when the device is applied to body tissue.
- Device C's output was only measured for the first few minutes of its program, assuming that it remained constant throughout. However, the manufacturer later provided a technical specification sheet showing that this was not the case. In fact the output varied across a program period of just under 30 minutes, comprising three stages with different waveforms and durations. The illustration is taken from the first stage, in which an 0.1 second alternating polarity square waveform, amplitude- and frequency-modulated in 20 steps, is generated for six minutes; this is followed by a 20-minute duration 10 Hz, 40 μA peak, 20 μA average monophasic square wave; the program finishes with a repeat of the first stage waveform but for a slightly shorter time. During the first and last stages, the current amplitude varies between 40 and 500 μA , and the frequency between 10 and 900 Hz. Substitution of the higher resistance did not vary the peak current by more than 10%.

Although all three devices produced a square waveform in the standard resistor, the wave shape was altered when the device was applied to the body. Exponential rises and falls between pulses were seen with all three devices.

Table 5.2: Current waveforms recorded when MCT devices were attached across standard resistance and across elbow. Different scales are used to provide clearest presentation in each case

980 Ω resistor	elbow
A Elexoma Medic	
	
1 division = 25ms	1 division = 10ms
B WeWo Thom	
	
1 division = 0.25ms	1 division = 0.25ms
C Tendonworks	
	
1 division = 2.5ms	1 division = 0.25ms

Discussion

None of the devices was ideal in all respects, because none allowed complete control of the current output, which would enable a fixed amplitude and frequency current output to be selected. In the absence of evidence to the contrary, it would be preferable to use a constant waveform, but the devices most closely matching the criteria all used some form of amplitude and/or frequency modulation. No justification for these features was provided either in the accompanying literature or in the form of experimental data provided by the suppliers. In subsequent correspondence, the supplier of one device claimed that the modulation was necessary to prevent neural adaptation but, since MCT is often sub-sensory, this explanation is unsatisfactory. The supplier of another device, which used a three-stage program with quite different waveforms in each, claimed that the first phase “prepared the cells” to respond to the subsequent stimulation, but presented no supporting evidence.

Ideally, a bespoke device would have been developed that could deliver the required waveform, but the requirements of designing, engineering and obtaining safety approval for such a device were beyond the scope of this investigation. The device most closely matching the criteria was the Elexoma Medic. It could deliver a current-regulated stable, low frequency monophasic square waveform of adjustable average current intensity in the required range, with a maximum treatment time of 99 minutes before automatic switch-off. It was also robust, portable and reasonably simple to use. The other devices, the Tendonworks and the WeWo Thom, were also judged possible for use. They were particularly portable and simple to use, although the Tendonworks had a complicated output program with current intensity varying between 40 and 500 μA , and the WeWo produced a high frequency balanced biphasic current of nominal but unregulated average intensity 25 μA . The suppliers of all these devices were willing to loan them in sufficient numbers for a viable study.

5.5 OUTCOMES

Clinical trials of treatments and other studies of tennis elbow have measured a wide variety of variables, often using instruments that lack validity and reliability data, which threatens the credibility of their findings. As yet, there is no consensus on whether any of them should always be employed. Table 5.3 lists those that have been used most commonly, classified to reflect the different elements of the disorder that were identified in the definition given in section 5.2. Measures relevant both to tissue healing and to signs and symptoms were required for this study, and these are now considered.

Table 5.3 : Outcome variables and measurement instruments used in tennis elbow studies

Outcome variables	variable	Measures used
PAIN		
At rest ¹⁻¹⁷		
On movement of wrist ^{389, 390}		
On gripping ^{256, 391-393}		
On pinching ^{394, 395}		Dichotomous (yes/no) ^{418, 453}
During activities of daily living ^{392, 396-406}		Visual Analogue Scale (VAS) ³⁸⁹
On specific test		Numerical rating scale (NRS) ⁴²¹
Chair test / lifting test ^{256, 407-411}		Part of questionnaire
Stretch of extensors (Mills' test) ⁴¹²⁻⁴¹⁴		Patient-Rated Tennis Elbow Evaluation
Resisted wrist extension ^{396, 400, 406, 408, 411, 412, 415-417}		Questionnaire / Patient-Rated Forearm Evaluation Questionnaire ^{355, 415, 417, 429, 442, 443, 454-460}
Resisted finger extension ^{411, 412, 416-420}		Nirschl score ³⁹⁷
Resisted supination/pronation ^{406, 409, 411, 412, 418-420}		Roles & Maudesley scale ^{419, 461-463}
Palpation ^{396, 400, 412, 415-418, 421}		Choice of pre-set words in McGill Pain Questionnaire ^{423, 427, 464, 465}
Pressure pain threshold ^{253, 332, 401, 406, 418, 422-424}		Pain diary ⁴⁶⁵
Thermal pain threshold ^{422, 424-427}		Drawing on body diagram ^{418, 423, 438, 439}
Trigger points ⁴²⁸		Pressure algometry ^{332, 401, 418, 422-424}
Averaged over 24 hours / previous week / during day / night ^{332, 401, 406, 429-437}		Thermal algometry ^{424, 427}
Pain descriptors ^{423, 427}		
Location / extent ^{418, 423, 438-440}		
Unspecified ^{397, 398, 400, 416, 441-452}		
FUNCTION		
Maximum grip strength ^{332, 389, 390, 392, 393, 396, 402-404, 410, 411, 416, 418, 423, 429, 431, 434-436, 443-445, 447, 449, 451, 454, 459, 466-474}		Isokinetic dynamometry ^{411, 413, 439, 467, 480, 483}
Pain-free grip strength ^{253, 332, 333, 338, 391, 398, 401, 412, 415, 417, 422, 424, 427, 430, 431, 433, 436, 442-445, 468-470, 473, 475-479}		Isometric dynamometry ^{421, 426, 454}
Max middle finger extensor strength ^{466 421}		Squeezing sphygmomanometer ³⁹⁶
Pinch strength ^{394, 395}		Maximum weight lifted by wrist extension with forward supported on table ³⁹⁶
Wrist extensor strength ^{421, 423, 436, 439, 454, 466, 472, 480}		Performance on forearm exercise device ⁴⁴⁸
Wrist flexor /supinator / pronator peak torque ⁴³⁹		ORI-TETS (device for controlled simulation of chair pick-up test) ⁴²¹
Wrist extensor strength (Weight test) ^{396, 403, 412, 415, 447, 449, 471, 481}		Goniometry ^{414, 449, 466, 482}
Pain-free forearm exercise ⁴⁴⁸		Subjective rating of loss of grip strength ⁴¹⁶
Grip Endurance ⁴⁵⁴		Clinician subjective rating ⁴⁸⁴⁻⁴⁸⁶
Wrist extensor / flexor work done ^{411, 413, 439, 467, 480}		
Range of movement at wrist ^{414, 449, 466} or elbow ^{440, 482}		
Wrist proprioception ⁴¹³		

Outcome variables	variable	Measures used
IMPACT		
<p>Activities of daily living^{355, 415, 429, 442, 443, 454-460}</p> <p>Physical / psychological well-being^{442, 455, 485, 487, 488}</p> <p>Healthcare costs⁴⁸⁹</p> <p>Cost-effectiveness^{489, 490}</p> <p>Loss of workdays^{414, 416, 454, 489, 491}</p>		<p>Patient-Rated Tennis Elbow Evaluation^{355, 403, 415, 429, 442, 443, 454-460}</p> <p>Patient-Rated Wrist Evaluation Questionnaire⁴⁵⁵</p> <p>Disabilities of the Arm, Shoulder & Hand Questionnaire^{399, 433, 442, 455, 488, 492-497}</p> <p>Pain-Free Function Questionnaire^{332, 338, 431, 444, 479, 497}</p> <p>Patient-Specific Functional Scale (PSFS)^{417, 434}</p> <p>Nirschl Tennis Elbow Score⁴⁸⁴</p> <p>Mayo Clinical Elbow Performance Index^{405, 451, 452, 485, 498}</p> <p>Elbow Functional Assessment⁴⁵⁰</p> <p>American Shoulder & Elbow Surgeons (ASES) elbow form^{484-486, 498}</p> <p>Own questionnaire⁴⁸⁰</p> <p>Quality of Life Scales (SF36/SF12)^{417, 442, 485, 487, 488, 496, 497}</p> <p>Euroqol^{490, 499}</p> <p>Hospital Anxiety & Depression Scale⁴⁵⁵</p> <p>Cost of treatment⁴⁸⁹</p> <p>Days of absence from work/sick leave /resumption of work^{414, 416, 454, 489, 491}</p>
ANATOMY & PHYSIOLOGY		
<p>Joint swelling⁴⁴⁶</p> <p>Radial head mobility⁵⁰⁰</p> <p>Adverse neural dynamics^{401, 425, 501}</p> <p>Muscle balance⁵⁰²</p> <p>Tissue changes - Visual appearance^{285, 503}</p> <p>Tendon thickening^{357, 480}</p> <p>Fibroblast activity³²⁰</p> <p>Collagen changes^{320, 504}</p> <p>Neovascularity^{505, 506}</p> <p>Bone exostoses</p> <p>Calcification^{480, 507}</p> <p>Muscle morphology changes⁵⁰⁸</p> <p>Presence of pain neuromodulators^{509, 510}</p> <p>Sympathetic ns indicators (skin temperature & conductance, blood flow, heart rate, blood pressure)⁴²²</p> <p>Wrist extensor stretch reflex⁴¹³</p> <p>UL reaction time / motor performance^{382, 483, 511, 512}</p> <p>Trigger points⁵⁰¹</p>		<p>Physical examination^{446, 500}</p> <p>Visual inspection on surgery^{285, 446, 503}</p> <p>MRI^{349, 513 349, 513}</p> <p>Ultrasound^{348, 349, 357, 372, 389, 392, 397, 402, 410, 480, 505, 514-516}</p> <p>X-ray⁵¹⁷</p> <p>Isotopic bone scanning⁵¹⁸</p> <p>Thermography^{356, 396, 451, 518}</p> <p>Tissue analysis</p> <p>Histology^{504, 519, 520}</p> <p>Immunohistochemistry⁵⁰⁹</p> <p>Microdialysis⁵¹⁰</p> <p>Biopsy^{508 504, 519, 520}</p> <p>Electromyography^{483, 502}</p> <p>Upper Limb tension Test 2B^{401, 425, 427, 501}</p> <p>Physiological data collection devices⁴²²</p>

Outcome variables	variable	Measures used
OTHER FEATURES		
Severity of main complaint ^{332, 430, 490, 515} Tolerability ^{446, 446} Patient-rated global status / satisfaction / success-failure ^{332, 333, 338, 389, 390, 402-405, 408, 416, 429, 441, 442, 449, 471, 484, 521-523} Clinician-rated global improvement / change in severity ^{332, 333, 338, 468, 490, 515} Patient identification and rating of problems they would most like to see resolved ⁴⁹⁷		Numerical rating scale ^{332, 333, 338, 389, 405, 408, 416, 429, 441, 442, 449, 471, 521, 522} Verhaar tennis elbow score ^{484, 524} American shoulder & elbow surgeons (ASES) elbow form ^{484-486, 498} Roles & Maudesley scale ^{419, 420, 435, 461-463} Own questionnaire ^{411, 418, 431, 438, 439, 467, 480, 493} Problem Elicitation Technique (PET) ⁴⁹⁷

5.5.1 Pain

Pain comprises sensory, cognitive, affective and behavioural elements, and there is no fixed relationship between them⁵²⁵, so it is necessary to decide which are most significant in the evaluation of pain in each context. In a study of the different aspects of pain experienced in tennis elbow⁴²⁷, various measures were used to map it, including visual analogue scales of pain intensity over several time frames, quantitative sensory tests such as pressure and thermal algometry, and the McGill Pain Questionnaire, which asks responders to select words that describe the quality of the pain. The different measures were poorly correlated, suggesting that the pain of tennis elbow is multidimensional.

Pain intensity is a quantitative estimate of the severity of pain, and is commonly measured by verbal rating, visual analogue or numerical rating scales⁵²⁶. Assessing the construct validity of such scales is problematic because there is no accepted gold standard of what is essentially a subjectively measured variable⁵²⁷. Therefore validity is commonly assessed by looking for and comparing change, when change would be expected, in several pain measures⁵²⁸. Composite measures have been shown to be the most valid and reliable measures of chronic pain, since they reflect its multidimensionality^{528, 529}. Several questionnaires are available that assess multiple aspects of pain. The Patient-Rated Tennis Elbow Evaluation (PRTEE) has a pain sub-section, and has been increasingly adopted because of its specificity and a growing body of evidence regarding its measurement properties. It employs numerical scales to rate pain intensity over the previous week on several dimensions, including least, worst and with particular activities. Such features have been shown to increase the reliability and content validity of chronic pain rating scales⁵²⁸. The PRTEE Pain subscale correlates well with a Numerical Rating Scale of Pain for resisted wrist extension⁴⁵⁸. Its use of numerical rating scales (NRS) enables a broad range of statistical tests to be applied to collected data, although

such scales may not be as sensitive to treatment effects as visual analogue scales⁵²⁶. The PRTEE does not consider pain location, extent and quality, or other sensory changes that may occur in tennis elbow. Several of these variables can be assessed using a standard body chart during the examination, however.

Another expression of pain commonly used in the assessment of tennis elbow is tenderness. Tenderness to palpation at the lateral epicondyle is a common diagnostic criterion for the disorder⁵³⁰. This may be indicated dichotomously using a yes/no response, but can also be quantified by pressure algometry. Using algometry, tenderness is expressed by the pressure pain threshold (PPT), defined as the minimum pressure that induces pain or discomfort⁵³¹. In a study of unilateral chronic tennis elbow in 45 subjects, Pienimaki and colleagues found that PPT correlated with pain on palpation, common extensor stretch and perceived pain under load, the common diagnostic criteria for the disorder⁴¹⁸. They also found significant differences between PPT in the involved and uninvolved arms, and in pre- and post-treatment values, suggesting that it can be used as a sensitive measure of change. Sensitivity is indicated by a low p-value in a t-test of differences between means^{528, 532}, and the test for pre- and post- treatment PPT values in the Pienimaki study gave $p < 0.001$, as well as a 56% difference between values for involved and healthy arms⁴¹⁸. Only one study could be found that investigated the reliability of pressure algometry for tennis elbow measurement: it found that inter-rater reliability was reasonable, but only measured test-retest reliability within a single session⁴⁶⁸. Pressure pain thresholds have been found to vary diurnally and across the menstrual cycle^{533, 534} and so the inter-test interval may influence reliability.

5.5 2 Function

In this context, function is defined as a capacity or body characteristic, such as strength or range of joint movement. Comparisons of function between contralateral limbs, or between affected and unaffected individuals, allow the extent of an abnormality to be determined. Grip strength reductions are commonly reported in tennis elbow and this variable is one of the most widely measured in clinical trials for the disorder. Two measures have been adopted most frequently - maximum grip strength (MGS)^{332, 389, 396, 411, 416, 418, 423, 429, 431, 443-445, 447, 449, 454, 459, 466-469, 471, 478} and pain-free grip strength (PFGS)^{391, 401, 442, 445}. The wrist extensors, some of which attach to the lateral epicondyle via the common extensor tendon, stabilise the wrist during gripping activities^{395, 535}. So gripping can stress the damaged tendon and generate pain. Grip strength is normally measured with a hand dynamometer. For MGS, the subject squeezes the dynamometer trigger as tightly as possible; for PFGS, the trigger is gripped increasingly tightly until the pain threshold in the elbow is just reached.

The construct validity, reliability and responsiveness of hand dynamometry for the assessment of tennis elbow have been established in several studies^{431, 439, 444, 468, 469, 478}, and PFGS appears to be the superior measure. Validity has been investigated by correlation with pain intensity and difficulty scores for the performance of tasks often affected by the disorder, such as carrying objects and opening doors. In an early study, PFGS was found to correlate moderately well with the other measures, whereas MGS was not⁴³¹. Pienimäki and colleagues⁴⁶⁷ found that PFGS correlated better with disability than with pain, indicating that it is measuring something different from (or additional to) pain, which supports its use in the battery of outcome measures employed. MGS can improve when other data indicate that the disorder is stable or has deteriorated⁴⁴⁴, which suggests that MGS is not responsive to change in severity. Several other studies have corroborated these findings^{398, 418, 444, 478}. PFGS has been shown to have equal or superior reliability to MGS when used to assess tennis elbow^{431, 468}. The reliability of grip strength measurements has been found to be dependent on time of day, body and limb position, and numbers of readings taken, although studies have drawn different conclusions about their impact⁵³⁶. Therefore these variables should be controlled or at least noted during measurement. Because normal grip strength varies substantially depending on factors such as age and sex⁵³⁷, raw PFGS values cannot be used to compare symptom severity between individuals. Small absolute reductions in grip strength are likely to be more significant to individuals who have a low grip strength to start with. Expressing PFGS as a ratio of MGS on the unaffected side has therefore been recommended as a way of normalising PFGS and so allowing comparisons of deficits between individuals and groups⁴³¹.

Isokinetic dynamometry, in which dynamic strength or work done during elbow extension or forearm rotation is measured, has also been used in some tennis elbow trials^{480, 483}, although the technique is time consuming and expensive⁴⁸³. Range of movement at the elbow and wrist joints have also been assessed, as they may be reduced in tennis elbow^{440, 466, 482}. The use of all of these measures in tennis elbow trials is uncommon, however, and their validity and reliability for the purpose have not been established. Hence, PFGS (expressed as a ratio of MGS on the unaffected side) was selected as the most appropriate measure for use in this investigation.

5.5.3 Disability and participation

The pain and reduced strength associated with tennis elbow can cause difficulties in many activities of daily living, such as lifting bags, turning door handles and gripping petrol pump triggers. Pain can be exacerbated by repetitive activities involved in work or recreation. In more severe presentations, the affected individual may have to change jobs or cease sporting

involvement. These types of consequences are explored in the various patient-rated questionnaires that have been used in tennis elbow trials. The PRTEE, mentioned earlier for its inclusion of a pain subsection, has two sections relating to disability. Using an 11-point numerical rating scale, the respondent estimates the difficulty experienced in carrying out named activities over the previous week. The questionnaire was developed specifically for assessment of the impact of tennis elbow, and its validity and reliability for the purpose have been established in several studies^{355, 456, 458}. Its specificity confers an advantage over more generic measures: greater responsiveness to relevant change^{457, 538}. A manual is available for the administration of the PRTEE⁵³⁹, which can help ensure consistency in its administration. It is also reported as uncomplicated and easy to use^{355, 455}.

Several other elbow-specific questionnaires have been used to assess disability and other features of tennis elbow. The Nirschl tennis elbow score was designed specifically for the purpose; other instruments, such as the Mayo Clinical Elbow Performance Index⁴⁸⁶ and the Liverpool Elbow Score⁴⁹³, are also available. Whilst some of these scales have been validated, their measurement properties for use with tennis elbow have received very little scrutiny. Where they have, the PRTEE has been shown to be equal or superior, although it is not without limitations. Whilst some other scales incorporate clinician opinion^{486, 493}, the PRTEE depends entirely on rating by the patient, and so lacks an element of objectivity. Its wording is rather specific to a North American population, and its questions limit assessment to a number of specific activities that may not be the main indicators of disability for a given respondent. Compensation for these limitations is possible. Objective measures can be added to the assessment protocol, and comprehension by another population may be assisted by minor modifications of wording. The problem of inflexibility due to standardisation can be addressed by use of another form of functional rating, the Patient Specific Functional Scale (PSFS). This enables respondents to identify and rate the activities that they find most problematic, so augmenting the data derived from a more condition-specific measure^{540, 541}.

Other related variables, such as absence from work and economic costs, may require sophisticated, resource-intensive and intrusive techniques to measure reliably. Qualitative information on these possible consequences of the disorder can be obtained during the subjective assessment, but it was decided not to attempt to collect quantitative data on these variables.

5.5.4 Global assessment

Whilst questionnaires and specific measurements may capture important elements of the disorder, an indicator of global status or change is often used to ensure that the totality of its effects is also evaluated. Tennis elbow trials have used a variety of patient- and clinician-rated scales including satisfaction with results of treatment⁴⁴², patient-rating of current overall status⁴²⁹ and assessor severity rating³³². Patient-rated Likert scales of change are commonly used, and a six-point scale varying between -2 (much worse) and +3 (completely recovered) provides a reasonable balance between sensitivity to change and descriptors that signify meaningful levels of change to the respondent. These scales have been criticised for failing adequately to incorporate the prior condition (i.e. their baseline status), and may give more information about current status, but they provide reliable assessment of health transition in people with musculoskeletal disorders⁵⁴².

5.5.5 Tissue changes

Pain, function and disability may be related to tissue damage, but measuring them does not provide any direct information about tissue status. Several methods of gathering relevant data have been adopted in trials. The most direct forms of assessment are histological analysis of tissue samples^{504, 543} and microdialysis of biochemicals present in the site of interest⁵¹⁰. These can confirm the presence and concentrations of cells and chemical mediators involved in inflammatory and healing processes, and identify structural changes. Biochemical markers of inflammation and repair may also be assayed through blood tests. For instance the erythrocyte sedimentation rate may be elevated in acute tendinitis^{544 ch20}; however no markers are currently available that are specific to chronic tendinopathy. All these procedures are invasive and require specialist skills and knowledge which were beyond the scope of the present study.

An alternative approach is tissue imaging, including radiography, magnetic resonance imaging (MRI), bone scanning, thermography and sonography^{349, 357, 513, 517, 518, 520, 545}. Correlational studies comparing image analyses with histological findings have established that MRI and grey-scale sonography can identify structural changes typical of tendinopathy in general^{513, 546-550} and tennis elbow in particular^{349, 513, 520}. Tendon thickening and tears, collagen fibre disruption, increases in ground substance volume, calcific deposits and spur formations on the epicondyle can be identified by both modalities^{348, 357, 551, 552}; they also enable quantification of tendon thickness⁵⁵³, and Power Doppler (PD) sonography can be used to quantify hyperaemia^{506, 545}. Unlike MRI, ultrasound cannot be used to image intra-

articular structures, but its superior spatial resolution means that it is better able to depict focal areas of degeneration³⁷² that are characteristic of tendinopathy. Sonography is also more portable and less expensive than MRI⁵⁵⁴.

Despite the growing use of sonography in clinical trials, there is little data available on its reliability for the purpose. This is particularly true of the various scales that have been adopted to grade the severity of tendinopathy in the disorder⁵⁵⁵. However, its reliability in the identification of pathological features and diagnosis of the disorder have been investigated. Studies in which particular grey-scale features were identified by several assessors have found only poor to moderate correlation between raters and between successive assessments on most features^{348, 349}. These studies used assessment of stored static images; live scanning or using recorded movie images might improve reliability. PD imaging of tennis elbow has been subject to limited evaluation. A study comparing sonographic findings with a clinical diagnosis provided by an experienced musculoskeletal physician found that Power-Doppler sonography was 98% specific, and a combination of power-Doppler and grey-scale imaging were 97% sensitive, in diagnosing chronic tennis elbow⁵⁰⁶. It concluded that the absence of a Doppler signal and grey-scale image changes could be used reliably in the differential diagnosis of tennis elbow, suggesting that some cause of symptoms other than tendinopathy should be sought. These figures compare with respective specificity and sensitivity ranges of 72-100% and 36-82% found in other studies, none of which used PD imaging^{348, 349, 515}.

The reliability of all forms of imaging is dependent on the operator and the assessor, but tendon sonography has been seen as particularly problematic in this regard^{348, 547, 556}. Partial tears may be indistinguishable from areas of degeneration³⁷², and ultrasound reflection may cause image anisotropy, an artefact that may be mistaken for a hypoechoic area^{557, 558}. Slight variations in probe positioning can make tendon thickness appear very different⁵⁵³. The advent of improved image processing software and higher frequency probes in recent years has offset some of the potential difficulties^{546, 547, 557}, but reliability studies to confirm this are lacking. Despite these limitations, sonography was judged the most appropriate outcome measure relating to tissue healing feasible in this investigation, though it was clear that attention to its reliability would be required.

5.5.6 Other variables

As noted in the earlier review, side effects using surface-mounted electrodes are rare and usually mild. In broader surveys of “electrical stimulation” that include this modality, the

most commonly reported adverse incidents are skin irritation, burns and local pain^{559, 560} ; more general effects such as nausea and fainting have also been observed, although it is difficult to attribute these to the therapy in such cases⁵⁶⁰. Given the novel application of treatment in this study, collection of information about any adverse incidents was included in the assessment protocol.

Acceptability and ease of use are key considerations in the adoption of any new therapy. The devices assessed in the laboratory for use in this study were all straightforward to operate, but evaluation in the context of a course of treatment is also required. Structured questioning of study participants was planned for this purpose.

5.6 CONCLUSIONS

In this chapter, a working definition of chronic tennis elbow has been produced, a clinical trial design selected, and several suitable microcurrent devices identified. A review of available outcome variables and measurement instruments has enabled a battery of outcome measures to be drawn up, capable of evaluating both tissue healing and clinical signs and symptoms of tennis elbow. The use of patient-rated and objective or semi-objective instruments enables triangulation of findings based on different measures of related variables, and employing both specific and global measures provides a rich account of any changes that may occur. The variables initially identified as potentially suitable for use in this investigation were:

1. Tendon tissue structure and blood flow, by sonographic assessment
2. Pain-free grip strength, using isometric dynamometry
3. Pressure pain threshold at the lateral epicondyle, using pressure algometry
4. Pain and disability, using the Patient-rated Tennis Elbow Evaluation Questionnaire
5. Disability, using the Patient-Specific Functional Scale
6. Overall change from baseline, using a patient-rated global change score (GCS)
7. Adverse events, by patient report
8. Acceptability and ease of use, by patient report

These may be supplemented by qualitative information gathered in the subjective assessment. Unfortunately, little or no evidence is available on the reliability and responsiveness of some of these measures for use in the assessment of tennis elbow. In any case, since reliability is affected by contextual factors such as operator skill and the measurement protocol, it is necessary to evaluate it in the specific circumstances of this investigation⁵⁶¹. Experimental work was conducted to enhance and measure the reliability of several of the selected outcome measures, and this is the subject of the next chapter.

Chapter 6

Development and evaluation of outcome measures

6.1 INTRODUCTION

The reliability of a measurement process is an indicator of its consistency when used by different operators, or by the same operator at different times. It depends on the skills of the operator, the measurement protocol employed, and the population with which it used^{562(ch5)}. Where change over time is measured by a single investigator, test-retest reliability must be established⁵⁶¹. Consistency between measurements taken at two points in time, between which the variable of interest is not expected to change significantly, is essential if real changes are to be reliably detected. Clinical trials sometimes use reliability data gathered from other studies to support their use of particular measures (e.g. ^{454, 563}). This is only valid if the same instruments are used in the same way with the same population, which may be difficult to establish with confidence. Particularly where previous reliability studies have reached inconsistent conclusions about an instrument, or where there is evidence of operator-dependence, it is important to evaluate reliability before using any instrument in a trial.

This chapter provides a report of work to enhance and evaluate the reliable use of algometry, dynamometry and sonography for use in the clinical trial. Ideally, all of the outcome measures selected would have been subject to reliability-testing, but these measures were prioritised for investigation because their reliability has been found to vary with device, operator and measurement protocol^{349, 537, 564-567}. The PRTEE and the PSFS have standard protocols for use^{539, 540} and have been found reliable by a range of studies, as indicated in the previous chapter; and the global change score is often used as a gold standard for assessing the validity and reliability of other measures⁵⁶⁸⁻⁵⁷⁰.

Work was first conducted to develop the investigator's skills in the use of algometry, hand grip dynamometry and sonography of the elbow, and this was followed by a series of tests to evaluate their reliability when used to assess normal individuals and those affected by tennis elbow. This chapter describes that work. It begins with a report of training and practice in the

use of the instruments. This is followed by an account of a study conducted with a sample of healthy people with no signs or symptoms of tennis elbow. The primary purpose of the study was to gain experience using the instruments, but it also provided an opportunity to develop measurement protocols and to test their reliability. The chapter ends with an account of a further study which evaluated the reliability of measurements using a sample of people with symptomatic tennis elbow. These studies provided reliability data that informed the final choice of outcome measures to be used in the clinical trial, as well as information on their capacity to register changes in the variables of interest.

6.2 DEVELOPMENT OF MEASUREMENT SKILLS AND PROTOCOLS

6.2.1 Algometry and dynamometry

Pressure algometry involves the application of increasing pressure to a spot on the body surface, via a rubber-tipped probe, until pain is first reported. Tenderness is quantified as the pressure applied at this pain threshold, which is displayed by the device. The technique had been used by the investigator in a previous study, in which the pressure pain thresholds (PPT) over superficial abdominal lesions were measured⁵⁷¹. The device used in that study has also been employed in several tennis elbow studies^{422, 423, 475, 476, 572}, although protocols vary among them. For instance, pressure may be applied to a specific point over the lateral epicondyle and/or extensor muscle belly⁴²³, or over the most tender point identified by the patient⁴⁷⁵. For the purposes of this investigation, a protocol shown to have reasonable inter-rater reliability⁴⁶⁸ was adopted.

Grip strength measurements in tennis elbow studies commonly employ isometric dynamometry (e.g. ^{421, 426, 454}). Typically, a Jamar-type device is used: this has a hand grip that is squeezed against hydraulic pressure, the applied force being registered on an integral display dial. The Jamar dynamometer has been found to have excellent inter-rater reliability in the measurement of both MGS and PFGS in people with tennis elbow⁴⁶⁸, although its test-retest reliability with this population has not been reported. Studies have reached conflicting conclusions about the most reliable measurement technique for grip strength dynamometry. A standard protocol, suggested by the American Association of Hand Therapists⁵⁷³, is commonly adopted, but several of its elements - such as the number of trials and body positioning - may be less suited to use with a symptomatic population⁵⁷⁴⁻⁵⁷⁷. The protocol was

adapted for the current study by changing the testing position: the subject was required to stand with the arm by the side and the elbow extended, rather than seated with the elbow flexed. Gripping with an extended elbow results in greater stress on the common extensor tendon than with the elbow flexed and so is a more sensitive indicator of PFGS in tennis elbow⁵⁷⁴.

Calibration of the dynamometer was checked using a series of standard weights between 10 and 50 kg, which were suspended from the device via a leather strap of 5cm width looped around the grip. The mean of four readings was taken for each weight. These checks were carried out on a monthly basis throughout this and subsequent studies.

6.2.3 Sonography

In most studies where sonography is used to assess tennis elbow, the operator is either a sonographer or a radiologist with several years of experience of musculoskeletal imaging. In fact, experience is often the only guarantor of reliability proffered by authors^{506, 578, 579}. Although inexperienced operators have been found to be less reliable in identifying some features of tendinopathy⁵⁸⁰, several studies have concluded that even very experienced radiologists can differ significantly in their interpretation of sonographic images^{567, 580, 581}. On the other hand, evaluations following short focussed courses in specific applications of sonography have shown that novices can be trained to reliably produce and interpret images of both normal and pathological tissue, including tendons⁵⁸²⁻⁵⁸⁴.

Efforts to secure the services of an experienced musculoskeletal imager for the clinical trial were unsuccessful, and so a training package was created to develop the investigator's skills in sonography specific to tennis elbow. This built on previous experience gained in a study that involved imaging of subcutaneous nodules⁵⁷¹. The training package consisted of (i) attendance of short courses in general and musculoskeletal sonography (totalling 12 hours), (ii) study of on-line and other educational materials⁵⁸⁵⁻⁵⁸⁷, and (iii) six hours of one-to-one training and supervision with a radiologist with eight years of clinical experience in musculoskeletal sonography. Supplementary guidance was also obtained from another radiologist with several years' experience using sonography in tennis elbow studies and trials. Imaging of the lateral elbow was the main focus of the practical work, initially with healthy volunteers, and later with people diagnosed with tennis elbow. During this process, terms used for the sonographic description of tendinopathy in published tennis elbow studies were employed⁵⁵⁵, and a quantitative measure of several types tissue changes was developed for use in the clinical trial.

6.3 MEASUREMENTS USING HEALTHY SUBJECTS

The aims of this initial laboratory work were to develop the investigator's skills employing algometry, dynamometry and sonography for the measurement of outcomes selected for use in the trial, and to assess the test-retest reliability of grip strength and PPT measurement protocols. The study also provided an opportunity to practise using a structured assessment process with participants that would be employed later with symptomatic individuals. Approval for the study was obtained from the investigator's institutional ethics committee, a copy of which is provided in Appendix 4.

6.3.1 Study materials and methods

Participants

A convenience sample of apparently healthy individuals, recruited from the staff and students of the investigator's institution, was recruited. Those eligible to participate were over 18 years old, with no current elbow pain or other upper quadrant symptoms that might affect PPT and grip strength measurements, and no current clinical signs or symptoms of tennis elbow. Participants were recruited by posters and emailing; an information sheet sent to those registering interest and followed up two weeks later if no response was received. Informed written consent was obtained at initial assessment. Based on an assumption that a reliability coefficient of at least 0.7 would be obtained for each measure, a minimum sample size of 20 was required^{431, 588}. In fact, a greater number was sought to maximise experience in using the various instruments.

Assessment

A subjective assessment was conducted initially, during which relevant medical history and demographic data was obtained. Several standard clinical tests for tennis elbow were then conducted: pain on palpation at the lateral epicondyle, on resisted extension of the wrist, on resisted extension of the middle finger, or on passive flexion of the wrist (Mills' test)^{530, 589}. Any participant with signs or symptoms of tennis elbow was excluded from this study but invited to take part in the subsequent study which would involve symptomatic subjects. Participants were asked not to take any analgesia in the 24 hours prior to each assessment.

PPT measurements were made using a Somedic Pressure Algometer (Somedic AB, Hörby, Sweden) with a 1cm² rubber tip. A patient-operated switch, which froze the pressure display reading when operated, was attached to the algometer via a cable. The participant sat with the shoulder abducted to about 60°, elbow in 90° flexion, forearm pronated, horizontal and

supported on an examination table. The other hand held the display freeze control. The investigator demonstrated the principle of PPT measurement on the dorsum of the participant's hand, with an instruction to 'press the freeze switch and say "now" as soon as the pressure sensation changes to discomfort'. The elbow was palpated to locate the lateral epicondyle and radial head, and a small cross was drawn midway between these landmarks. The algometer was applied to the mark with its barrel perpendicular to the skin surface, and pressure was applied and increased at 40 kPa/s according to display until the participant said "now". Three PPT measurements were taken on each side, with a minimum 20 s interval between readings.

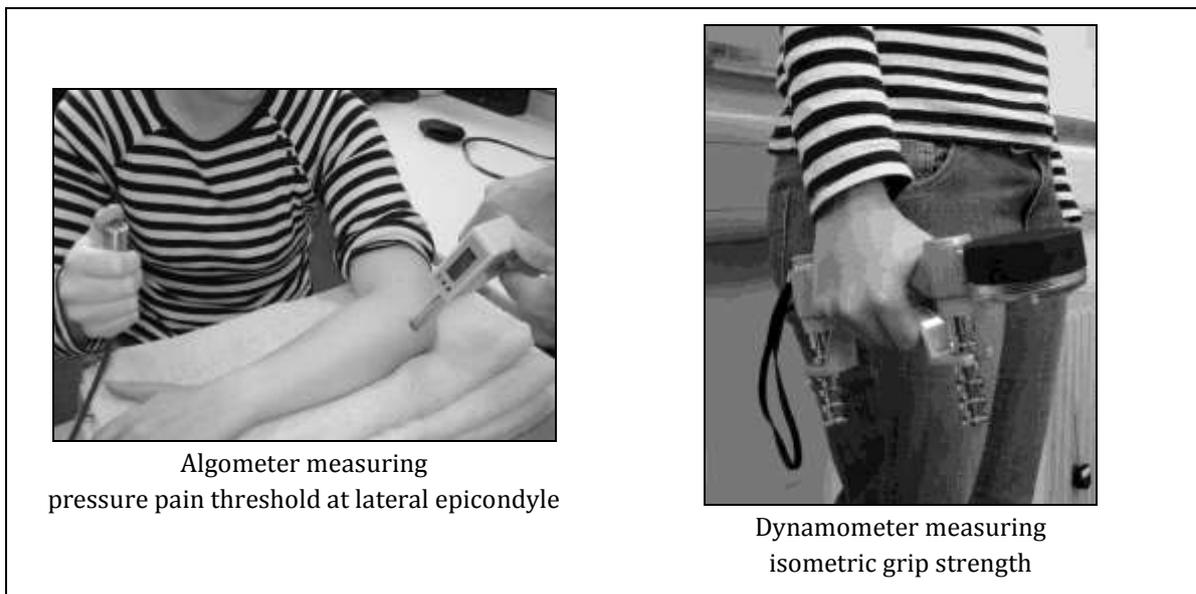


Figure 6.1: Measurements of tenderness and grip strength

Grip strength was measured using a Baseline hydraulic hand dynamometer (Fabrication Enterprises Ltd, White Plains, USA). This device is of the Jamar-design and has excellent levels of inter-instrument agreement with the standard Jamar device for grip strength measurements with a non-symptomatic population⁵⁹⁰. The participant stood with arms by side, forearm and wrist neutral, lightly gripping the dynamometer, whose handle was in position 2. After an initial practice, the participant was instructed as follows: 'When I say, squeeze the handle as tightly as you can... Now! Squeeze, squeeze.' After a few seconds the participant was told to stop squeezing. Three readings were taken on each side alternately, starting with the non-dominant limb, and ensuring a minimum 20 s interval between readings on the same side. The rate of squeezing was not controlled. Figure 6.1 illustrates the instruments and technique used for measurement of tenderness and grip strength.

Sonography was conducted using an Esaote MyLab 25 ultrasound scanner with an 18 - 12 MHz linear array probe (Esaote, Genova, Italy). The shoulder was abducted to about 60°, the elbow flexed to about 60°, the forearm pronated and supported by an examination table. Longitudinal and transverse greyscale and Power Doppler scans of the common extensor tendon and adjacent structures were conducted bilaterally, and representative static images and movie clips were recorded for subsequent examination. Figure 6.2 illustrates the positioning used for sonographic assessment. For greyscale imaging, scans were made at 15 MHz and 70% gain; PD scanning used a pulse repetition frequency of 0.7 kHz and gain was adjusted between 70 – 90% to balance sensitivity with noise minimisation. Other parameters were set according to the manufacturer's recommendations for musculoskeletal imaging. Notes of any abnormal findings were made whilst reviewing the movie clips shortly after the assessment, but no formal attempts were made to assess reliability of assessment in this study. Rather, findings were discussed with the radiologist as part of the supervised skills acquisition process. A copy of the assessment form used in this study is provided in Appendix 4.



Figure 6.2: Sonographic assessment positioning

There appears to be no agreed interval between assessments for the evaluation of test-retest reliability. They vary between a day and three months in other studies considering grip strength and PPT measurements with non-symptomatic populations^{564, 576, 591}. For this study, a period of 2-3 weeks was selected. Participants were asked at follow-up if anything might have happened that could affect the measurements, for example upper limb injury or taking heavy exercise or use of analgesia in the previous 24 hours.

Data Analysis

Mean and maximum values were calculated for each set of three readings of PPT and MGS. Descriptive statistics, including graphical plots and tests for normal distributions of data, were obtained and inspected. Estimates of test-retest reliability were calculated using the Intraclass Correlation Coefficient (ICC) to indicate the level of absolute agreement between baseline and follow-up test values^{592, 593}. To establish whether three readings of each variable were necessary, ICC values for first reading, maximum reading and mean of three readings were calculated. The ICC selected was for single or average measures, depending on whether a single reading or mean of three was being used. All statistical tests were conducted with SPSS 17, setting test significance at $p < 0.05$, and 95% Confidence intervals were obtained for each test result.

6.3.2 Results

Between June and September 2008, 46 people were assessed for inclusion in the study. Ten had symptoms or clinical signs of tennis elbow and so were excluded from the analysis, but were invited to participate in the later study of symptomatic individuals. Two of those remaining were unable to attend second assessment, leaving data from 34 participants available for the reliability analysis. Although attempts were made to conduct the follow-up assessments within the defined period, this was not always possible, and in ten cases there was a longer or slightly shorter inter-assessment period (minimum 3 days, maximum 31 days). Most follow-up assessments happened at a similar time of day to the baseline readings, and in only four cases did the time differ by more than 4 hours. One participant reported the development of minor forearm pain between assessments; no other changes that might affect readings were reported. Participant histories and clinical tests did not always match: of those with current symptoms of tennis elbow, few demonstrated a positive response to Mills' test – passive extension of the wrist; one person with no other signs, symptoms or history of tennis elbow had a strong positive reaction to resisted middle finger extension.

Visual inspection of distribution curves suggested that grip strength and PPT measurements were approximately normal, but the Shapiro-Wilk test – recommended for sample sizes smaller than about 50⁵⁹⁴ – indicated otherwise: although all PPT measures (first, maximum and mean) were normally distributed, most grip strength measurements were not. Levene's test for homogeneity of variance indicated no significant difference between variances of baseline and follow-up measures for each variable. Given the ICC's robustness to violations of parametric assumptions^{562 ch26}, the test was employed with both PPT and grip strength data.

Baseline characteristics for included participants are given in Table 6.1 and summary measurement data for the two assessments are given in Table 6.2.

Table 6.1: Baseline characteristics of participants included in reliability analysis. MGS and PPT values are means (95% CI)

Age (range) / yr	46 (23 – 68)
Sex	25 Male; 9 Female
Hand dominance	26 Right; 3 Left; 5 Ambidextrous
MGS / kg	35 (32-39) Right; 33 (29-36) Left
PPT / kPa	127 (112 - 143) Right; 128 (109 – 146) Left

Table 6.2: Summary measurement data for repeated assessments of healthy subjects

Variable	First Assessment		Second Assessment	
	n ₁	mean±S.D (range)	n ₂	mean±S.D (range)
Maximum Grip Strength / kg				
Left	34	31±10 (13 - 55)	34	33±10 (17 - 53)
Right	34	33±10 (14 - 52)	34	34±10 (18 - 53)
Pressure Pain Threshold / kPa				
Left	22	129±34 (61 - 197)	19	150±35 (89 - 204)
Right	22	127±39 (57 - 213)	19	137±33 (75 - 204)

During the study it became apparent that, for many participants, it was unfeasible to measure a PPT at the lateral epicondyle. If pressures greater than 250 kPa were applied, there appeared to be risk of skin damage, and so measurement was stopped at that value. Only 18 participants reported thresholds below 250 kPa, and so the analysis for PPT is based on data from these cases. Scatter-plots for dynamometer and algometer measurements are presented in Figures 6.3 and 6.4 respectively. ICC values calculated for PPT and MGS measurements are presented in Table 6.3.

Table 6.3: Intraclass Correlation Coefficients (95% CI) for numerical data obtained in elbow assessments.

Variable	First value		Maximum value		Mean of 3 values	
	Left	Right	Left	Right	Left	Right
Maximum Grip Strength	0.93 (0.83 – 0.97)	0.92 (0.85 – 0.96)	0.95 (0.88 – 0.98)	0.97 (0.94 – 0.98)	0.98 (0.95 – 0.99)	0.98 (0.97 – 0.99)
Pressure Pain Threshold	0.25 (-0.20 – 0.65)	0.45 (-0.01 – 0.76)	0.21 (-0.18 – 0.58)	0.38 (-0.08 – 0.71)	0.33 (-0.08 - 0.67)	0.60 (-0.23 - 0.85)

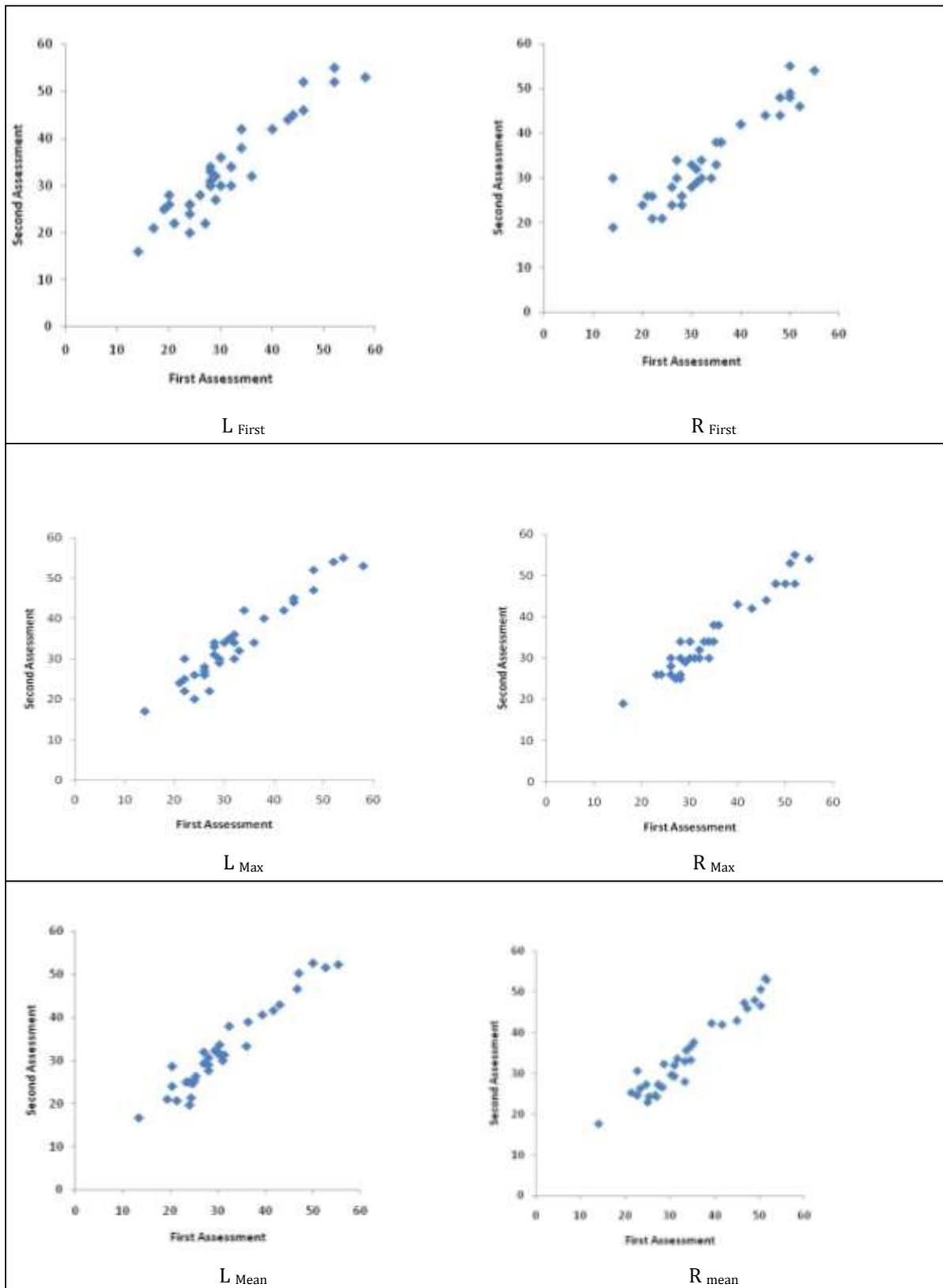


Figure 6.3: Scatter plot of repeated measurements of Maximum Grip Strength (MGS, all in kg) with normal subjects.

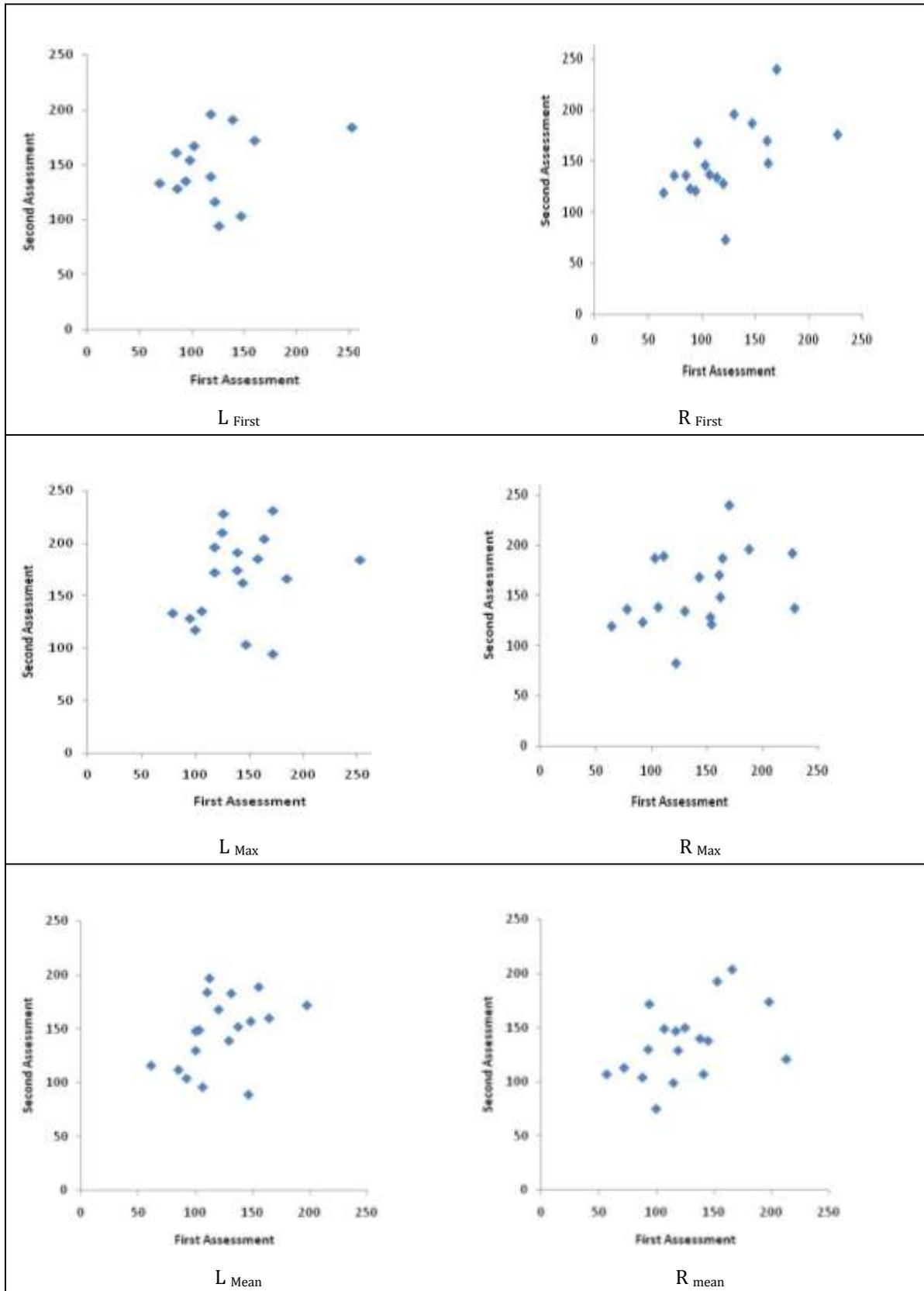


Figure 6.4: Scatter plot of repeated measurements of Pressure Pain Threshold (all in kPa) at lateral epicondyle with normal subjects.

Maximum grip strength measurements had ICC values in excess of 0.9 for all variables, with the highest values (and narrowest confidence intervals) for the mean of three readings. PPT values were much lower, and all had very broad confidence intervals. These findings are reflected in the scatter plots. Grip strength data points (Figure 6.3) are reasonably tightly distributed about a 45° line, suggesting a close correlation between assessments. Scatter is least for the mean of three measurements at each assessment. PPT data points for all three data presentations (Figure 6.4) are widely scattered and so provide little evidence of anything other than a positive correlation.

The primary purpose of the sonographic assessment was to obtain experience in using the apparatus and knowledge of the variety of presentations seen in images of the lateral elbow. Although none of the participants had symptoms of tennis elbow, abnormalities in the common extensor tendon and adjacent structures were identified in several of them. No quantitative analysis of these was attempted, but findings were discussed with the supervising radiologist, and a number of assessments were conducted jointly. Feedback from the supervising radiologist suggested that the investigator was capable of conducting competent assessments of the lateral elbow and identifying at least some abnormalities. The sonographic apparatus did not have as sophisticated image-processing specifications as mainframe devices that are used in many reported trials. Nevertheless, it was found capable of identifying typical features of tendinopathy and to register hyperaemia by Power Doppler imaging. However, its limitations were demonstrated by the fact that rather high gains had to be applied to visualise all structures, and this produced noisy images in some cases.

6.3.3 Discussion

The study provided a number of useful insights and conclusions about the assessment protocol and the outcome measures themselves. The process of subjective and objective assessment shared elements with a typical physiotherapeutic clinical assessment, and appeared satisfactory overall.

The interpretation of ICC values depends on the intended application of the scale⁵⁹², but a value greater than 0.75 has been suggested as indicative of good reliability^{562(ch26)}. By this standard, measurements of maximum grip strength using all three methods had good reliability, but the highest ICC value (and the narrowest confidence interval) was obtained when the mean of three readings were taken. The ICC values are consistent with – in fact somewhat better than – those of other test-retest reliability studies, which used the American Association of Hand Therapists protocol^{576, 595}. Since this study only involved asymptomatic

individuals, maximum rather than pain-free grip strength was measured. The reliability data is still valuable because, in trials with symptomatic individuals, MGS of the unaffected arm is measured and used to normalise PFGS values^{332, 333, 466, 478, 500}. Nevertheless, it remained necessary to assess the reliability of PFGS measurements with symptomatic individuals.

PPT measurements were much less consistent, and levels of agreement varied significantly depending on whether single or mean values were used. The mean of three readings gave a moderate ICC value but with very wide confidence intervals, and the other methods were altogether unreliable. This may have been a result of several factors: slight variations in placement and angulation of the instrument were reported by participants as producing very different sensations, and many had difficulty identifying a distinct cross-over point from pressure to pain. Ceiling effects were often observed, with no threshold being reached even at pressures that appeared in danger of causing superficial tissue damage. This highlights a limitation of testing reliability with an asymptomatic population: the test site is not naturally" tender. Test-retest reliability has not previously been reported using healthy elbows, but inter-rater reliability has. In a study assessing several outcome measurements used with tennis elbow, PPT measurements on the uninvolved arm were found to have an inter-rater reliability of 0.72 (CI:0.55-0.83), better than in this study but still with a rather wide confidence interval⁴⁶⁸. Assessments in that study were both carried out on the same day and memory effects may have aided consistency between measurements. Good test-retest reliability has been established for PPT measurements on other parts of the body, for example over shoulder muscle bellies in healthy individuals⁵⁹¹, but the results of the present study suggests that reliability differs with site of application. This may reflect differences in the sensitivity of different parts of the body. Kosek and colleagues⁵⁷² found that pressure pain thresholds over bony areas were considerably higher than over muscle bellies, and the lack of sensitivity over the lateral epicondyle reported by several participants may reflect a relatively low number density of nociceptors in the normal common extensor tendon⁵⁹⁶. In any case, the findings here suggested that this measurement process required further evaluation in a symptomatic population before use in the trial.

The focussed training in sonographic assessment of the lateral elbow provided relevant experience and increased the confidence of the investigator in this skill. The fact that abnormalities were identified in several tendons, and were confirmed by the radiologist in some cases suggested that, after assessing up to 70 elbows, a capacity for pattern-spotting was being developed. However, there was a risk of false positives in identifying abnormalities, and this would require investigation in the study with a symptomatic sample. The supervising radiologist judged the sonographic apparatus capable of providing the level

of detail required for this investigation, but suggested further discussion with the manufacturers to optimise image processing for this application.

The study had a number of limitations. One was the lack of formal training in algometry and dynamometry. Although the instruments appear straightforward to use, errors in technique may have gone undetected and uncorrected because nobody with relevant expertise was available to guide and monitor performance. This may have been a factor in the difficulties experienced using the algometer and the poor reliability of PPT measurements. Training and supervision in sonography was obtained, but the supervising radiologist admitted to limited experience in assessing the lateral elbow – in the clinical context, sonography is usually only used for this purpose if surgery is being considered. Published guidance from expert panels and the additional advice received from another radiologist, who had substantial experience in sonography of tennis elbow, compensated for this to some degree.

The study served two purposes: obtaining experience and assessing reliability. Since there was likely to be an initial steep learning curve in processes of measurement, incorporating data from early assessments into the analysis may have depressed reliability scores. Ideally, a separate period of learning and practice would have preceded data collection for a reliability analysis.

6.3.4 Conclusion

Despite these drawbacks, experience using the assessment process with asymptomatic subjects was generally encouraging. The test-retest reliability of maximum grip strength measurement by dynamometry was excellent, and the sonographic skills development process appeared to provide a reasonable foundation for further work and testing. The manufacturers of the apparatus were approached to discuss the best settings for tendon imaging, and they supplied a software update for enhanced image processing. The reliability of PPT measurement was a cause for concern, but further testing with symptomatic subjects was necessary before deciding whether to retain PPT as an outcome variable, since it might prove more reliable when used with that population.

6.4 RELIABILITY OF OUTCOME MEASURES IN ASSESSMENT OF TENNIS ELBOW

Following the study using healthy subjects, further laboratory work was undertaken to assess reliability with a symptomatic population. PPT at the lateral epicondyle and pain-free grip strength are more meaningful variables where subjects are symptomatic, and a broader spectrum of tendinopathic changes would be expected in sonography in such cases. As before, test-retest reliability was investigated, but a shorter inter-test period of 1 – 2 weeks was selected to provide a balance between learning or memory effects and the potential for change in the disorder. Additional reliability testing was deemed appropriate to evaluate the investigator's sonographic imaging and measurement skills. Inter-rater reliability was investigated by comparing assessments conducted independently by the investigator and a radiologist experienced in musculoskeletal sonography.

Estimates of reliability can also be used to calculate the responsiveness of a measurement process, which determines the minimum detectable change (MDC) it can resolve. This is the smallest measured change in a variable that cannot reasonably be attributed to random error, and so can confidently be interpreted as “real” change⁵⁹⁷. No studies establishing MDC values for any of the instruments under test could be found, so, as well being necessary for the present investigation, this study could provide data of value to the broader research community. The aims of the study were to establish:

- the test-retest reliability and MDC values for PFGS, PPT and sonographic measurements, and
- the inter-rater reliability of sonographic rating of tendinopathy

in a sample of people with symptomatic tennis elbow.

Approval for the study was obtained from the investigator's institutional ethics committee and all recruits provided written informed consent before participation (See Appendix 5).

6.4.1 Study materials and methods

Participants

A sample of people with tennis elbow was recruited by advertising to staff within the investigator's institution and several local sports centres. Included participants were over 18 years of age with a current diagnosis of tennis elbow. Diagnosis was made on the basis of a

history of lateral elbow pain exacerbated by gripping movements, and lateral elbow pain provoked by at least one of the following tests^{530, 589}:

- palpation over the common extensor tendon
- resisted middle finger extension with elbow extended
- resisted wrist extension with elbow extended
- passive wrist flexion with elbow extended

Diagnosis in other studies typically requires a positive response to more than one of these tests^{345, 506, 598}. However, since this study was primarily concerned with the reliability of measurement processes, a less restrictive case definition was used. In addition, tenderness over the radial tunnel and pain on resisted supination were tested for, as these have been suggested as differential diagnostic criteria for radial tunnel syndrome⁵⁹⁹. As in the previous study, and for the same reasons, a minimum sample size of 20 was sought.

Assessment

The subjective assessment followed a similar format to that used in the previous study, but with additional questioning about the disorder. It began by recording demographic and medical data, and collecting a history of the complaint, which included initial cause (if known), symptom duration and any treatment received. This was followed by the clinical tests for tennis elbow, which formed part of a standard bilateral physical examination of the upper quadrant with particular attention to the elbow^{589, 600}. This consisted of visual inspection of the upper limb, palpation of the lateral elbow, subjective assessment of active range of motion of neck, shoulder and elbow, and of the strength of major upper limb muscle groups, overpressure to elbow extension and application of valgus and varus forces to assess joint stability, and compression and rotation of the radio-humeral joint as a check for osteoarthritis⁵³⁰. Possible cervical involvement was checked by a clearance test, consisting of compression and passive extension, side flexion and ipsilateral rotation of the neck⁶⁰⁰. A full cervical assessment was not conducted, and neurological examination was limited to myotome testing. An Upper Limb Tension Test for the radial nerve (ULTT2B) was used to assess for its involvement⁶⁰¹. Because it was expected that some assessments in the later trial might take place at the participant's home, tests were conducted in standing or sitting, rather than supine. Figure 6.5 demonstrates the positioning used for the radial nerve stress tests. If tensioning produced lateral elbow pain, the subject was asked to laterally flex the neck towards the affected side to desensitise the nerve and confirm its involvement. Although

testing in sitting is unorthodox, it was thought the most feasible option given the uncertainty about the test venue.



Figure 6.5: Positioning and movements used for upper limb tension test 2B.

Algometry was used in the same manner as the previous study to measure the PPT at the lateral epicondyle. Grip strength measurement differed, however. After the participant practised by squeezing the dynamometer lightly on the unaffected side, maximum grip strength was measured on that side using the same protocol as in the previous study; then pain-free grip strength was measured on the symptomatic side by asking the participant to increase the squeeze until pain first became apparent at the lateral elbow or adjacent forearm. Readings were alternated between sides to provide a minimum 20 s rest between measurements, and no verbal encouragement was given during the each trial. If a participant was symptomatic bilaterally, PFGS was measured for both arms.

Sonography was conducted as before, and movie clips of longitudinal and transverse scans were recorded during each assessment. In addition, rating scales were developed to enable numerical grading of the severity of tissue abnormalities. These were intended to provide a measure of tendinopathic severity at baseline, and to monitor any tissue changes occurring over time. The scales were constructed on the basis of those used in other tennis elbow studies. These were evaluated in a literature review conducted by the investigator, which has been published⁵⁵⁵ and is reproduced in Appendix 7. Although some studies have used computer-assisted measurement of certain features, most rely on subjective assessment by a clinician. Some have used scales with up to 11 grades^{374, 397}, but it is more common to employ three or four^{375, 402, 480}, and the more conservative approach was adopted here. Greyscale

images were used to grade tendon thickening, hypoechoic areas, fibrillar disruption and calcification, and PD images were used to grade hyperaemia. Ratings were based on subjective estimation of the physical extent of the abnormality. The greyscale ratings were not precisely defined at this point, but agreed to equate to normal, mild, moderate and severe presentations. The hyperaemia scale was defined, however, using the scheme presented in Table 6.4. Examples of sonographic images obtained, and gradings assigned, are given in Figure 6.6.

Table 6.4: Sonographic grading scales for greyscale abnormality and hyperaemia

Grade	Greyscale feature	Power Doppler signal
0	Normal	No signal
1	Mild	Single small signal
2	Moderate	Several signals in less than 33% of visible field
3	Severe	Multiple signals in 33-67% of visible field
4	n/a	Multiple signals in more than 67% of visible field

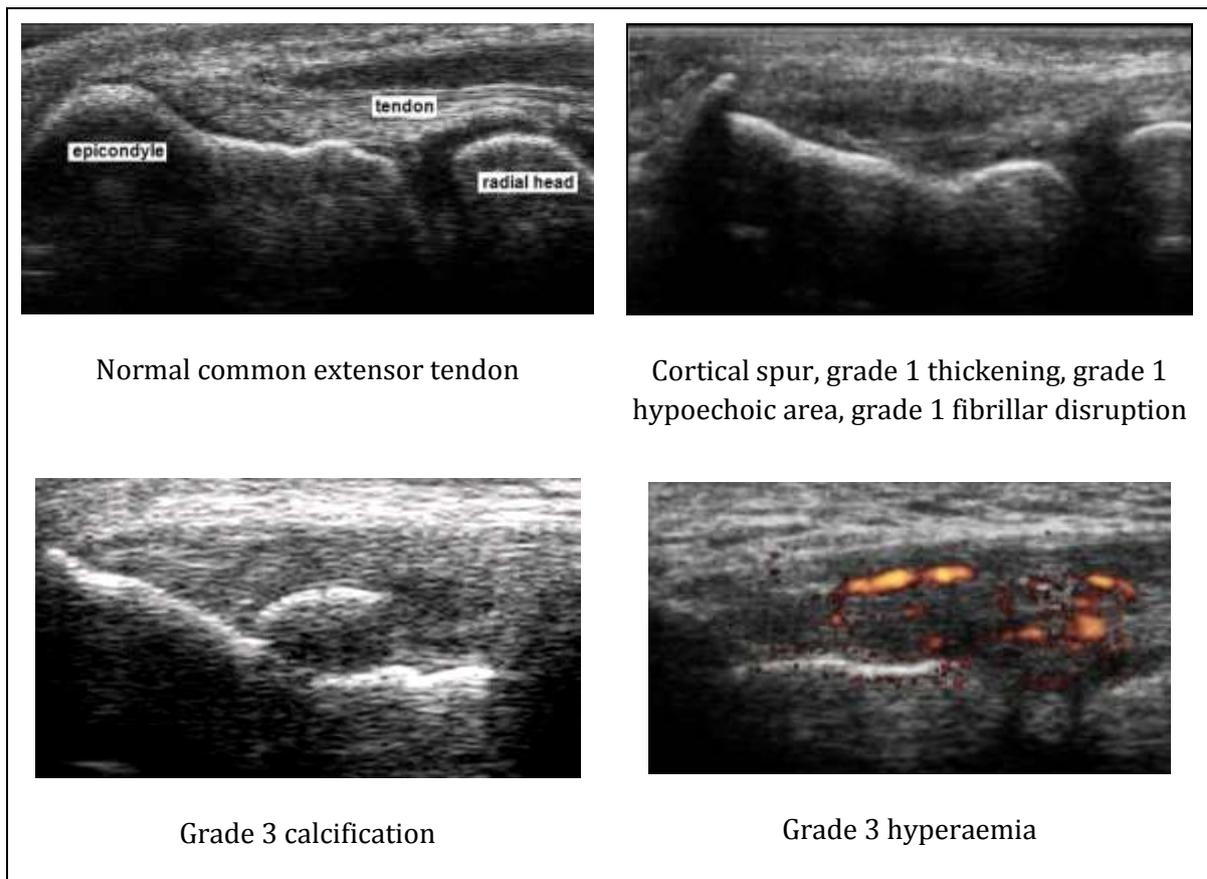


Figure 6.6: Greyscale image of common extensor tendon, demonstrating grading of greyscale abnormalities and hyperaemia

An aggregate greyscale pathological severity score was obtained by summing the scores for the individual elements, giving a maximum possible score of 12 points. Since hyperaemia may be part of the normal physiological response to tissue damage, it was not assumed to be pathological in itself and its score was not combined with those of the greyscale features. Scores were assigned by the investigator whilst viewing the move clips recorded at each assessment.

Assessment of PPT, PFGS and tissue abnormality was repeated at a follow-up assessment. As in the previous study, participants were asked not to take any analgesia in the 24 hours prior to each assessment. At follow-up, they were asked whether they had complied with this request, and if anything else had happened that might affect measurements, such as heavy upper limb stress, treatment for their tennis elbow, or changes in symptoms.

Additional evaluation of reliability of sonographic assessment

Because of the relative inexperience of the investigator in musculoskeletal sonography, and the novelty of the sonographic scoring system, an inter-rater reliability study was also conducted. This evaluated the consistency in scoring the same images by the investigator and a radiologist with 10 years' experience of musculoskeletal sonography. (This was not the supervising radiologist who had been involved in the initial skills acquisition work.) For this study, the investigator selected from each baseline sonographic assessment a one-minute duration movie clip of the longitudinal greyscale scan, and a static PD image in which the maximum signal was visible. Movie clips were used for greyscale images to enable identification of the variety of features that might be seen in different parts of the tendon, and to help distinguish hypoechoic areas from anisotropy. In other studies, PD signals are typically graded according to the maximum signal visible^{506, 602}, and so this convention was adopted here by using a single static image. The investigator analysed these recorded images after the assessment, and they were also sent to the radiologist for assessment using the same grading scheme.

Analysis

Mean PPT and grip strength values were calculated for each arm using the three measurements taken in each case, and tests for normality and homogeneity of variance were applied. PFGS was analysed as an absolute value and as a percentage of MGS on the unaffected side, which provided a normalised value for each person⁴³¹. Grip strength data from those with bilateral symptoms – for whom this ratio could not be calculated – was not included in the reliability analysis. Test-retest reliability for parametric data was assessed using the ICC, as before. Correlation coefficients for measurements of PPT and grip strengths

were calculated separately for symptomatic and non-symptomatic limbs. The ICC for each measure was then used to estimate its minimum detectable change (MDC) using the formula

$$\text{MDC} = 1.96 * \text{SD} * \sqrt{2(1 - \text{ICC})}$$

where SD is the standard deviation of the baseline measurements for the sample^{592, 597}.

The ICC is only recommended for use with such data when the intervals between levels can be considered as equivalent^{562 ch26}, which may not be true for the sonographic scales used in this study. Therefore Kendall's tau-b, which measures levels of association between ordered datasets^{562 ch25}, was calculated in addition to the ICC. All statistical analysis was performed using SPSS 17, significance was set at $p \leq 0.05$ and 95% confidence intervals were calculated where appropriate.

6.4.2 Results

Of 27 participants screened, one did not have current signs or symptoms of tennis elbow, four reported symptom changes between assessments, and one was unable to attend the second assessment. Of the 21 individuals remaining, 13 were male and 8 were female. The mean age was 49 (range 20 – 71) years and the median duration of symptoms was 3 (range 1 – 240) months. Nineteen were right hand dominant, two were left hand dominant. Six were symptomatic on the non-dominant side and one was symptomatic on both sides. The upper limb tension test suggested radial nerve sensitisation in two thirds of those assessed and produced lateral elbow pain in a third. Inter-assessment periods were between 1 and 2 weeks in all but three cases (4, 6 and 15 days respectively).

All participants responded to at least one of the diagnostic tests used, with the exception of passive wrist extension (Mills' test) which was never positive. Several of those positive to the resisted movement tests, and who also had sonographic evidence of tendinopathy, did not have any noticeable tenderness on palpation over the lateral epicondyle. Summary data for measurements taken at each assessment are presented in Table 6.5, and the corresponding scatter plots are given in figures 6.7-6.9.

Table 6.5: Summary measurements data for repeated assessments with symptomatic subjects

Variable	First Assessment		Second Assessment	
	n ₁	mean±S.D (range)	n ₂	mean±S.D (range)
Maximum Grip Strength / kg (unaffected limb)	17	38±12 (16 – 56)	16	40±11 (16 – 53)
Pain-free Grip Strength / kg (affected limb)	17	34±13 (12 – 55)	16	35±14 (11-58)
Sonographic scores				
Greyscale abnormality /12 (aggregate)	34	1.7±1.7 (0 – 6)	34	1.7±1.5 (0 – 6)
Hyperaemia / 4	30	0.8±1.0 (0 – 3)	31	0.7±0.9 (0 – 3)

Grip strength

Several participants reported hand pain when using the dynamometer. In three cases, this pain rather than lateral elbow pain was reported to be the limiting factor for PFGS assessment, one because of osteoarthritis in the hands. Four people refused to use the device on at least one assessment because of fear of exacerbation of symptoms. This meant that reliability data was only available from 17 people. One of these had bilateral symptoms and so PFGS/MGS ratios were not calculated for them. The Shapiro-Wilk test for normal distribution, and Levene's test for homogeneity of variance, showed that grip strength data could be analysed parametrically. The baseline mean PFGS/MGS ratio was 94% (SD 24%; range 33 – 130%). Table 6.6 presents calculated ICC values for this group, and Table 6.7 provides the corresponding MDC values. Scatter plots of the data are given in Figure 6.7.

Table 6.6: ICC (95%CI) for grip strength measurements with symptomatic subjects

Variable	First reading	Maximum of 3 readings	Mean of 3 readings
PFGS (affected limb)	0.95 (0.86 – 0.98)	0.96 (0.90 – 0.99)	0.98 (0.94 – 0.99)
MGS (unaffected limb)	0.92 (0.72 – 0.97)	0.94 (0.82 – 0.98)	0.95 (0.86 – 0.98)
PFGS / MGS	0.77 (0.46 – 0.91)	0.78 (0.47 – 0.92)	0.84 (0.54 – 0.94)

Table 6.7: Minimal detectable changes for single, maximum and mean of three grip strength measurements with symptomatic subjects (kg unless specified)

Variable	First reading	Maximum of 3 readings	Mean of 3 readings
PFGS (affected limb)	8.1	7.8	5.1
PFGS / MGS	17%	10%	9%

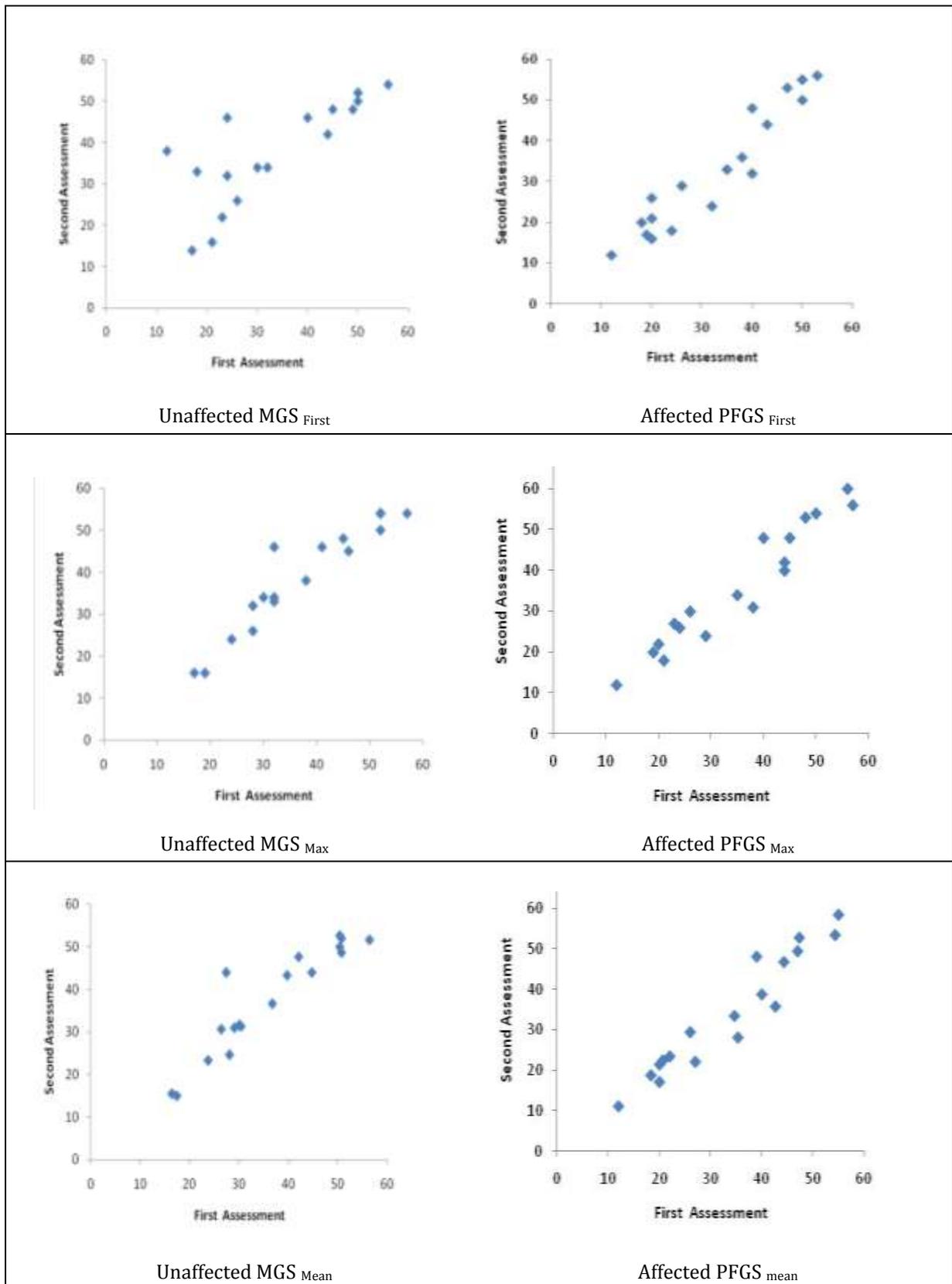


Figure 6.7: Scatter plot of repeated measurements of grip strength measurements (all in kg) with symptomatic subjects

Pressure Pain Threshold

PPT measurements using the algometer were problematic. The pain threshold could not safely be reached with seven participants and three others refused measurement, fearing an exacerbation of their irritable symptoms. With nearly all other participants there was substantial variation between intra-session PPT readings, and no pattern of decrease or increase across successive readings suggestive of sensitisation or desensitisation could be discerned. Calculated ICC values using the remaining viable data indicated poor to moderate levels of agreement for all variables, but with very wide confidence intervals: lower limits were less than zero in most cases. As in the previous study, several participants found it impossible to identify a specific pain threshold. Scatter plots are provided in Figure 6.8.

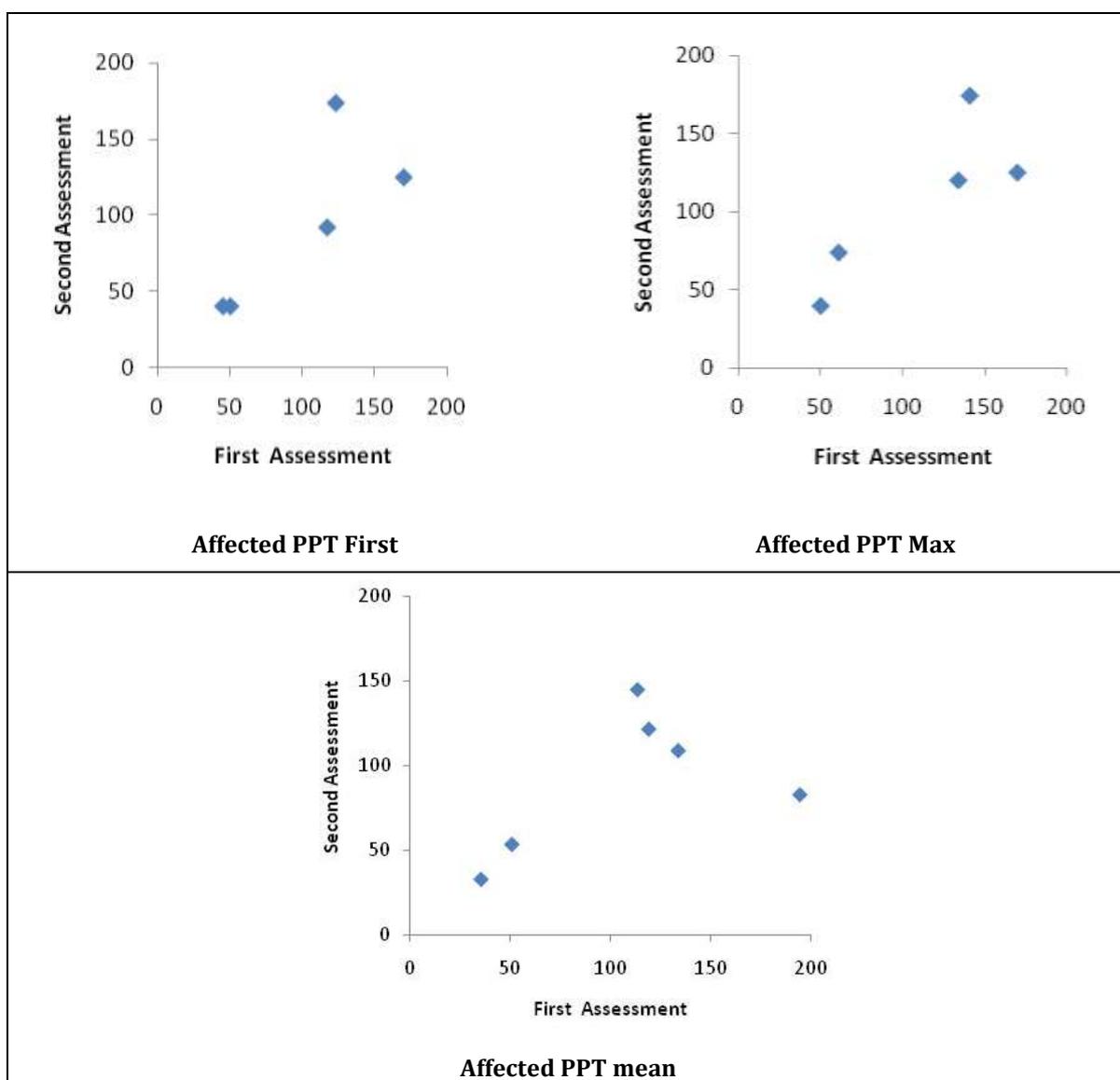


Figure 6.8: Scatter plot of repeated measurements of pressure pain threshold (all in kPa) at lateral epicondyle with symptomatic subjects

Sonography

One set of follow-up sonographic images were lost and two sets were judged of too poor quality for analysis, so 17 (34 left and right images) were available for test-retest reliability analysis. On first assessment by the investigator, all 17 affected limbs had greyscale abnormalities but only 14 showed signs of hyperaemia. Of the 17 unaffected limbs, greyscale changes were visible in nine and hyperaemia in three. The majority of presentations had low overall greyscale scores, with none higher than 6/12.

Table 6.8 provides ICC and Kendall's tau-b values for test-retest reliability of sonographic scoring by the investigator, using recorded images from baseline and follow-up assessments, and Figure 6.9 provides scatter plots of test-retest measurement of the aggregate greyscale and hyperaemia scores. The ICC values indicate moderate to good consistency in rating scores on all features, although confidence intervals for tendon thickening and fibrillar disruption are wide. Kendall's tau-b scores were of similar magnitude. Using the ICC values and baseline standard deviations, MDC values were calculated as 2.0 for the aggregate greyscale score and 1.1 for the PD score. Changes of at least these magnitudes would be required in the means of group values to be confident that they are not attributable to random error alone. The scatter plots illustrate the positive correlations between assessments, and suggest that the high ICC values may be influenced by the numbers of data points with low greyscale scores and zero hyperaemia scores.

Table 6.8: Test-retest reliability of sonographic scoring of tendinopathy

Feature	ICC (95% CI)	Kendal's Tau-b
Tendon thickening	0.70 (0.48 – 0.84)	0.72
Hypoechoic area	0.77 (0.59 – 0.88)	0.77
Fibrillar disruption	0.71 (0.49 – 0.84)	0.73
Calcification	0.86 (0.73 – 0.93)	0.84
Greyscale abnormality (aggregate)	0.82 (0.66 – 0.90)	0.74
Hyperaemia	0.78 (0.58 – 0.89)	0.73

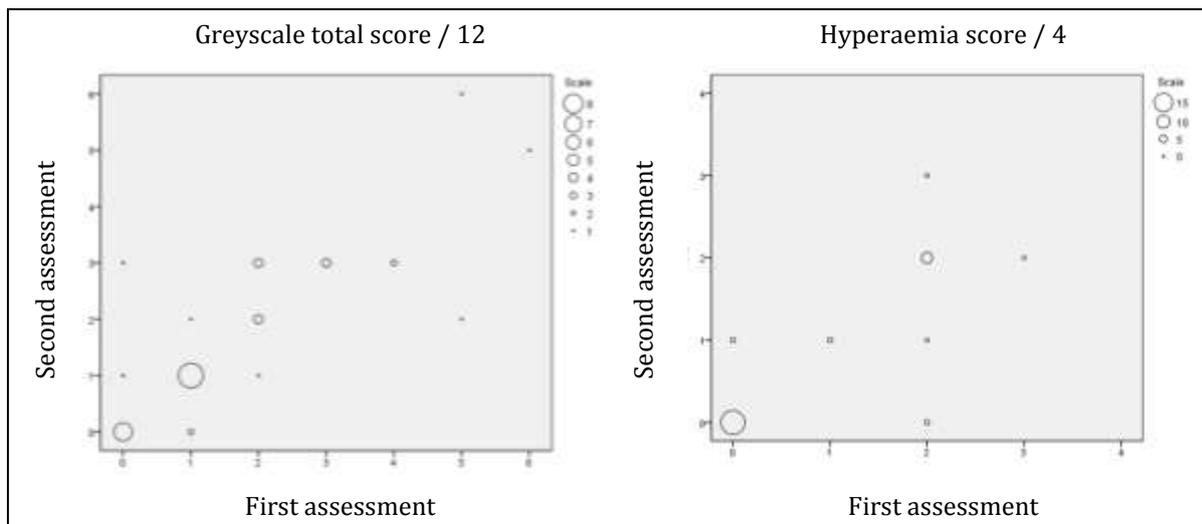


Figure 6.9: Scatter plots of test-retest aggregate greyscale and hyperaemia scores in symptomatic subjects. The size of the marker indicates the number of data points at that coordinate.

By the time the radiologist who agreed to collaborate in the inter-rater reliability study was available for the work, the clinical trial had already begun and baseline assessment data was available from a number of participants. Some of the earlier scans recorded in the test-retest study were of poor quality and so, on the assumption that the investigator's scanning and assessment skills would have improved with practice and supervision, it was decided to use only the second half of the scans from that study, and supplement these with the first tranche of baseline scans conducted in the trial. This provided a sample of 19 participants, all with symptomatic tennis elbow, and it is the data from their assessments that was analysed. Ratings for both arms are used, since many of the unaffected limbs had signs of tendinopathy. ICC values and Kendall's tau-b values, showing the levels of agreement between the investigator and the radiologist in sonographic ratings, are presented in Table 6.9.

Table 6.9: Inter-rater reliability in sonographic scoring of tendinopathy

Feature	ICC (95% confidence interval)	Kendall's Tau-b
Tendon thickening	0.46 (0.16 - 0.68)	0.43
Hypoechoic area	0.72 (0.52 - 0.85)	0.72
Fibrillar disruption	0.35 (0.05 - 0.60)	0.36
Calcification	0.76 (0.58 - 0.87)	0.60
Greyscale abnormality (aggregate)	0.77 (0.55 - 0.88)	0.60
Hyperaemia	0.89 (0.79 - 0.95)	0.90

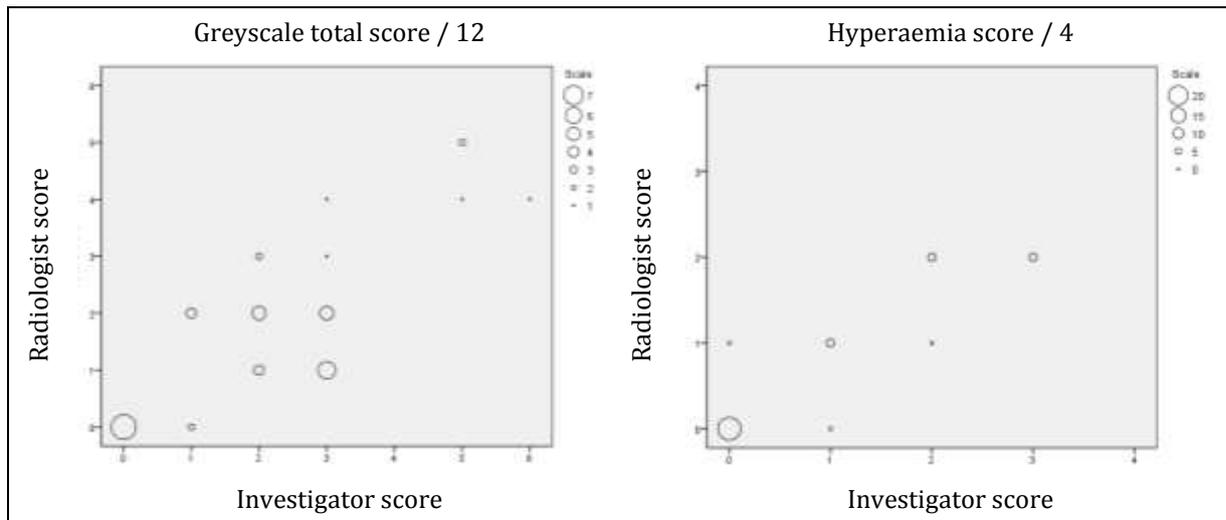


Figure 6.10: Scatter plots of aggregate greyscale and hyperaemia scores assigned by investigator and radiologist to symptomatic subjects. The size of the marker indicates the number of data points at that coordinate.

ICC values for tendon thickening and fibrillar disruption were low with wide confidence intervals. Kendall's Tau was also low for these variables. Correlation coefficients for rating of hypochoic areas, calcification, aggregate greyscale score and hyperaemia were considerably better, but Kendall's Tau for calcification and aggregate greyscale showed only moderate agreement between raters. Scatter plots of the data, provided in Figure 6.10, illustrate the large number of cases with low scores on both scales. Particularly for the hyperaemia score, these will have contributed to the high ICC value. In both plots, data points are reasonably tightly scattered about the 45° line, however, supporting a good correlation between assessments.

6.4.3 Discussion

A reasonably-sized sample of participants was obtained through the promotion and recruitment and most elements of the assessments proceeded satisfactorily. Although a formal evaluation of the diagnostic tests was not conducted, using several of them in combination with the subjective history increased confidence in the clinical diagnosis. Despite its common use in other studies, Mills' test was never positive, even with the more severe presentations, and so it was decided to eliminate this test from the assessment. To provide a more provocative test for milder cases of tennis elbow, it was decided to add the chair lift test (lifting a chair by its back with the elbow extended and forearm pronated)⁵⁸⁹ to the assessment protocol for the clinical trial. Although several provocative tests are available

as clinical signs of tennis elbow, their diagnostic reliability appears to be rather poor, as is inter-rater reliability in their use⁶⁰³. The addition of sonographic signs of tendinopathy may increase confidence in a clinical diagnosis, although symptoms of tennis elbow do not necessarily accord with signs of tendinopathy. In any case, validating one set of diagnostic criteria by correlation with another risks reliance on a circular chain of reasoning. Thus, for the purposes of a clinical trial, it may be more appropriate to apply a case definition based on patient history, clinical tests and sonographic findings. This issue is further addressed section 7.7.2.

Dynamometry

The test-retest reliability of grip strength measurements, including the PFGS/MGS ratio, were excellent, and highest for the mean of three readings. The MDC value was also lowest for this ratio, meaning that a smaller change in this variable could confidently be interpreted as “real”, i.e. not due to random error. Some studies with normal populations have concluded that a single reading of MGS is as reliable as a mean of three^{575, 604}, but if MDCs are calculated, the benefits of using the mean of three over a single measurement become apparent. MDC values for PFGS measurements in tennis elbow have not previously been reported. The scatter plots (Figure 6.7) confirm the good correlation between assessments with minimal scatter for all but first MGS value for the unaffected limb.

Comparable data from other studies is unavailable. Smidt and colleagues found excellent inter-rater reliability in the measurement of PFGS using a Jamar dynamometer with patients with tennis elbow⁴⁶⁸, but patients were assessed by both raters in a single session, so test-retest reliability was not assessed. Based on an ICC of 0.97, they calculated an minimum detectable difference of 1.4 kg, considerably less than in this study. However, they appear to have made an error in their calculation: instead of substituting the pooled standard deviation of the two datasets as is required⁵⁶⁹, they used the much smaller standard deviation of the difference between the two group assessments. When the appropriate data are used, minimum detectable difference value is 5.8 kg, somewhat higher than the MDC value obtained here. This is more consistent with an expectation that repeated readings by the same assessor (as in this study) would be more reliable than readings by two different raters (as in theirs).

Stratford and colleagues concluded that pain-free grip strength measurements had excellent test-retest reliability over a period of up to a week when used to assess tennis elbow^{431, 444, 469, 474}. However the instrument used was specified in only one of these⁴⁶⁹ studies: it was a

Smedley dynamometer, which is quite different in design to Jamar-type devices and cannot be assumed to have the same measurement properties.

Several methodological features may have influenced dynamometry reliability in the present study. Although the rest-period used in multiple measurement protocols has been found to affect reliability only marginally in a normal population⁶⁰⁵, this may not be the case with symptomatic groups. The presence of tennis elbow may lead to more rapid fatigue in the gripping musculature⁶⁰⁶, and a 20 second rest period may be insufficient for recovery between readings. However, inspection of the raw data showed that, within a single measurement session, strength readings increased in some cases and decreased in others; so any fatiguing effect may have been balanced by other factors such as learning effects. The speed of grip build-up was not controlled and this may have influenced the point at which participants stopped squeezing when PFGS was measured. In particular, a rapid build-up may lead to PFGS “overshoot” as the individual passes the pain threshold before releasing. Recorded values were not hidden from participants and this may have affected their effort levels in subsequent testing^{607, 608}.

Three participants refused to use the dynamometer after initial trial because their condition was so irritable. The measurement process may therefore be limited by a floor effect where symptoms are particularly severe. Reports received of hand pain on gripping the dynamometer were observed in another study, using asymptomatic individuals⁵⁷⁵. This may result from the design of the device, which has an un-cushioned metal handle with no discernible “give”, which ensures that the measurement is isometric. Despite the limitations of the device and measurement protocol, the reliability data and practical experience of use suggested that they were suitable for use in a trial.

Algometry

Pressure pain threshold algometry was unsatisfactory, which is unfortunate because it can provide a semi-objective pain measure and has been shown to be reliable in other applications^{591, 609}. The scatter plots illustrate the paucity of usable data: even though the first and maximum readings might conceivably match a positive linear correlation, inspection of individual data coordinates shows that readings usually differ significantly between assessments. Few studies have considered the reliability of algometry for use with tennis elbow. One investigated inter-rater reliability, and concluded that differences between ratings of PPT were such that algometry could not be recommended⁴¹⁸. Another assessed “intra-examiner repeatability” of three readings taken in a single session and reported values of 0.90 - 0.92, although the authors did not specify the statistical test used⁴²⁸. In any case,

such a short inter-test period allows no extrapolation to reproducibility over several days or weeks.

It might be expected that measurements conducted by the same examiner would be more consistent, but this was not found to be so in the present study. This suggests that variations in response by the same individual may be the more significant factor. Another approach to measuring tenderness has been used: a pre-defined pressure is applied with the algometer and the subject gives a numerical rating of pain at that pressure³⁹⁰. This method may provide greater consistency but was not assessed in the present study so cannot be substituted with confidence. In consequence, PPT measurement was deemed unsuitable for inclusion in the trial protocol. However, other measures intended for use in the trial address various aspects of pain and its consequences. The Patient-rated Tennis Elbow Evaluation has several items rating pain, and PFGS provides an indication of pain irritability. Therefore the loss of PPT as an outcome variable was not felt to compromise the outcomes assessment battery too severely.

Sonography

The study investigated two aspects of the reliability of sonographic assessment of tennis elbow. First, test-retest reliability to indicate consistency in scoring of images made at two time points by the same rater. This was necessary to evaluate the fitness of the scale for a longitudinal study. It also enabled the calculation of MDC values that would be needed for the interpretation of trial data. Second, inter-rater reliability, which gauged the extent of operator-dependence in obtaining images and interpreting them. In the absence of a gold standard for comparison, and notwithstanding the earlier comment that experience does not guarantee reliability, reasonable agreement between the investigator and a more experienced imager would increase confidence in the investigator's use of this measure.

The results for test-retest reliability were mixed. Ratings of hypoechoic areas, calcification, overall greyscale abnormality and hyperaemia all demonstrated good consistency between assessments. ICC values for tendon thickening and fibrillar disruption fell short of the benchmark but by a small margin. Kendall's tau-b values were largely in accord with the ICC. These results suggest that this system of aggregate greyscale and hyperaemia scoring could be used reliably to monitor tissue status in longitudinal studies of tennis elbow. The corresponding MDC values suggest that an appropriate number of levels was chosen for each of these two scales: if more levels had been added, they may have been redundant because the MDC would have spanned several of them. This argument only applies to the investigator's use of the scales: a more experienced imager may have been able to discern

smaller gradations reliably, and so a scale with more levels and a smaller MDC might be feasible.

The findings of the inter-rater study follow a similar pattern, but the levels of agreement were lower. ICC values for consistency between raters was poor for tendon thickening and fibrillar disruption, but better for all the other features. There was good agreement between the investigator and the radiologist in scores for calcification, overall greyscale abnormality and hyperaemia, and scoring of hypoechoic areas fell just short of the benchmark. For all variables, confidence intervals were wider and ICC values lower than in the test-retest study, with the exception of hyperaemia. Repeated ratings by a single assessor are usually better than those conducted by two different assessors, but it appears that – at least in the case of hyperaemia – enhanced experience may have improved the investigator's reliability. Indeed, a comparison with ICC values calculated using only data from the earlier scans (not reproduced here) confirmed that inter-rater reliability was better using the later scans. The low ICC value for rating of fibrillar disruption may have been because the raters interpreted the term differently, as either a disappearance of the fibrils in hypoechoic or indistinct areas, or an obvious discontinuity in their parallel arrangement. Poor agreement on the presence of tendon thickening may have been a consequence of ambiguous tendon boundaries in some cases, and paratenon thickening being registered as tendon thickening in others.

Where there is a discrepancy between Kendall's tau-b and ICC, the former test should be preferred because of uncertainty over whether the intervals in the sonographic scale are equivalent. This guideline was applied to test values for calcification and aggregate greyscale scores, where agreement appears moderate rather than good. This might be attributable to the different levels of experience of the raters. Comparable studies that could help judge this issue are not available, since none has considered the reliability of sonographic rating scales for tennis elbow. One study used the ICC to express levels of agreement between several well-experienced imagers in identifying (but not rating) sonographic abnormalities, and found that the ICC for individual greyscale features was 0.49 at best³⁴⁸. Another study, also using well-experienced imagers, found moderate levels of test-retest reliability in identifying greyscale features³⁴⁹. These studies demonstrate that general musculoskeletal sonographic experience and training does not guarantee interpretation reliability in a specific application.

In that context, the results of this study are encouraging. This may be a result of several of its methodological features. Movie clips were used for greyscale image assessment, in contrast to the static images used for assessment in the other studies. Throughout the recording the transducer was moved back and forth across the area of interest, so each part of the tendon

could be seen repeatedly from a slightly different point of view, enabling an initial impression to be verified or amended. Also, images were identified by number and side for each participant, enabling comparison of left and right. This could assist interpretation, since the sonographic appearance of normal tendons varies between individuals. Such left and right pairing is used in some studies³⁴⁹ but not others³⁴⁸. These factors may have enhanced reliability. On the other hand, the investigator's relative lack of experience is likely to have diminished it. Moreover, preliminary discussion between assessors of the definitions and rating of greyscale abnormalities was limited, and the radiologist had no practice in the use of the rating scales. Such preparatory work, has been shown to improve inter-rater reliability⁶¹⁰. The scanning apparatus may also have limited reliability because it is a portable device with less sophisticated imaging software than used in mainframe devices.

In this study, five sonographic features that are commonly reported in sonographic studies of tennis elbow^{349, 357, 372, 506} were rated. Other features, such as tears, sub-tendinous fluid and cortical irregularities have also been reported^{349, 357}, but were not included. All the greyscale features selected have been associated with pathological changes observed during surgery or histological analysis^{349, 372}, but the aggregation of their scores is somewhat arbitrary. Doppler ratings were not combined with other scores because hyperaemia may be a pathological feature or an indicator of healing, depending upon the stage of damage and repair^{611, 612}. The relative contribution of these different elements to the overall status of the tendon is unknown, and none appears to be present in every case of tennis elbow^{348, 349, 372}. Moreover, grading features only by their physical extent may be inappropriate. For instance, does a small but highly hypoechoic area represent more advanced pathology than a larger, less hypoechoic one? Validation of the scoring system would require histological analysis for comparison but, since tissue samples are normally obtained only during surgery on tendons with advanced tendinopathy, this would be problematic.

The images assigned low ratings could represent pre-clinical signs of damage, or age-related degeneration rather than pathological change. In any case, the scales may best be interpreted as representing a spectrum of abnormality. Greyscale and Doppler changes have been proposed as signifying a progressive continuum of symptomatic tendinopathy in the patellar tendon⁶¹³, and the same may be true for the common extensor tendon.

Study limitations

Relatively mild presentations of the disorder seemed to predominate in this study. Although some participants were severely affected by tennis elbow, the group mean PFGS ratio of 93% is considerably higher than seen in several other tennis elbow studies (e.g. ^{332, 333}), and the

sonographic rating scale was suggestive of fairly mild tendinopathy in most cases. This may be due to people with more severe presentations being unwilling to participate in a study that offered no treatment. Nevertheless, the limited spread of data means that reliability was not proven for more severe cases. Indeed, the refusal of some participants with irritable symptoms to use the dynamometer illustrates the potential limitations of the device in this respect. On the other hand, the sonographic scale could be judged as having “spare capacity” to rate more severe cases that might be seen in the trial.

The inter-assessment duration of 1-2 weeks used in the test-retest reliability study may have been too long. Although most of the participants had been symptomatic for at least three months, several reported a history of labile symptoms. Even in chronic tennis elbow, there is normally a gradual improvement in signs and symptoms and, although participants reporting significant changes between baseline and follow-up assessments were not included in the analysis, this could have impacted upon the data. The decision to use only part of the available data from symptomatic individuals, and its post-hoc supplementation with data from the trial, could be challenged as “cherry picking” to obtain favourable results. Statistical analysis is most rigorous when used as planned, with prospectively-acquired data. In this case the amalgamation of data was judged legitimate because of the on-going skills development that could be expected with novice-use of sonography. Even so, the reliability of the assessment protocol used might have been enhanced in a number of ways. The greyscale grading system was neither objective nor adequately defined, and it was not piloted before use in the reliability study. This is likely to have particularly impacted upon inter-rater reliability. More specific definitions for each grade, initial agreement on terminology between raters, and shared practice using the scales, would have facilitated similar implementation of the grading systems by raters. Interpretation whilst scanning, rather than when viewing recordings, would have enabled more control and checking of provisional interpretations, although this would not have been possible in the inter-rater study because of constraints on the radiologist’s time. Although the use of a single representative Doppler image was reliable, a movie of a dynamic scan across the tendon would have produced a more comprehensive representation of the extent of hyperaemia.

Although more than 20 people were recruited for the study, various factors identified earlier reduced the sample available for analysis to 17 participants. Statistical tests lose some of their power as the sample size falls, and so some measure of caution must be applied in interpreting the test results obtained. Finally, the minimum detectable changes calculated for the grip strength and sonographic measurements are useful quantities for interpretation of trial data. However, they are not the same as the minimum clinically significant difference

(MCSD) - the minimum change that would be considered important by the patient and/or clinician⁶¹⁴. The latter measure is of greater clinical import, but could not be calculated within this study. It is addressed in the next chapter, however.

Revised sonographic grading

To address some of the limitations identified in the sonographic assessment process, a number of changes were implemented. Specific definitions of the greyscale abnormality grades were drawn up – these are presented in Table 6.10. Also, in order to more accurately represent the location and extent of any abnormalities, a template was created to provide a visual representation of the tendon and adjacent structures. This allowed abnormalities across the full width of the tendon to be recorded in a two-dimensional image, and could provide qualitative as well as quantitative information, such as the presence of tears and the location of bony spurs (which sometimes appeared in relationship with tendon lesions). Completing a template at every assessment allowed longitudinal changes to be pictured more easily. An example, including the symbols used, is provided in Figure 6.11.

Table 6.10: Revised grading system for sonographic greyscale abnormalities

Grade	Hypoechoic area or fibrillar disruption	Tendon thickening	Calcification
0	Normal	Normal	None
1	Only just apparent	Only just apparent	One or more punctate calcifications
2	Present in less than half of the tendon between the enthesis and the radial head	Thickened by less than 50% of normal	Deposit up to 1cm long
3	Present in more than half of the tendon between the enthesis and the radial head	Thickened by more than 50% of normal	One or more deposits longer than 1cm

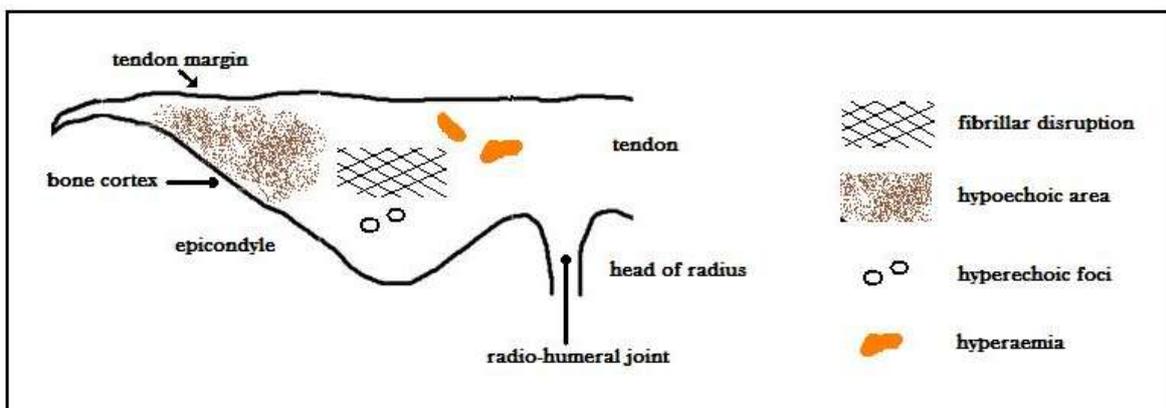


Figure 6.11: Sonographic assessment template with examples of abnormalities

6.4.4 CONCLUSIONS

Taken together, these reliability studies proved valuable in providing data and experience essential to the planning of the clinical trial. As a result of them, several changes were made to the assessment process and data collection form to be used in the trial. These included a change in the battery of tests used to diagnose the disorder, the rejection of PPT as an outcome variable, more detailed instructions in dynamometry to control the speed of gripping, more precisely-defined greyscale rating levels, and further adjustment of some of the ultrasound scanner settings to enhance imaging. Signs of radial nerve sensitisation were observed so regularly that using this as an exclusion criterion, as some studies do⁴⁸⁰, could significantly limit enrolment to a trial. Since the primary focus of the trial would be tendon healing, it was reasoned that radial nerve sensitivity should not be used to exclude participation in the trial.

Although the diagnostic tests for tennis elbow used in this study are commonly employed, none has been validated for identification of tendinopathy. However, this study indicates that sonography can be used for the purpose. Using a combination of subjective history, clinical assessment and sonography increases confidence in a diagnosis of tendinopathic tennis elbow and so can be used to formulate eligibility criteria for the trial.

This study provided evidence on a number of methodological issues that have as yet not been reported in the literature: the test-retest reliability of PFGS measurement using a Jamar-type dynamometer with a symptomatic population; the minimum detectable change for PFGS measurements; the test-retest reliability of a sonographic scale to rate tendinopathy in tennis elbow; and the capacity of a relatively inexperienced operator to use such a scale in a longitudinal study. Having conducted this assessment of potential outcome measures, it was possible to move on to develop the remaining elements of the trial protocol and then conduct the trial. This is the subject matter of the next chapter.

Chapter 7

Clinical evaluation of microcurrent treatment

7.1 INTRODUCTION

The preceding chapters addressed some of the key issues in drawing up a reliable protocol for a clinical trial of MCT with tennis elbow. This chapter is concerned with the experimental work itself. Before this could commence, further aspects of the protocol required development. These included trial objectives, eligibility criteria, a comprehensive description of the intervention, and methods of data analysis. The first part of this chapter addresses these issues and the trial protocol that was developed. The revised CONSORT statement, which provides guidelines for the conduct and reporting of clinical trials involving non-pharmacological interventions²³⁶, was used to provide a framework for this process. As in previous chapters, reports of trials of other treatments for tennis elbow were used as source material. This section of the chapter constitutes the methods section of the trial report.

The second part of the chapter provides the data analysis and discussion of the trial findings. This preliminary study was intended to establish whether there are reasonable grounds to conduct a full scale clinical trial and, if so, to inform decisions about what type of MCT and what experimental protocol it should use. Its main aims were to provide evidence of whether MCT can improve outcomes in chronic tennis elbow, and whether varying the intensity of the microcurrent affects the outcome. The reported data provides limited evidence that MCT may accelerate recovery in chronic tennis elbow, and that varying the current intensity affects outcome. Various problems encountered in the conduct of the trial are described, and the implications of the study for a full trial protocol are explored.

7.2 TRIAL PROTOCOL

In this section, the remaining elements of the trial protocol are addressed, using the structure suggested by the Consolidated Standards of Reporting Trials statement, which is an evidence-based, minimum set of recommendations for reporting RCTs²³⁶. The title of the study was:

A randomised clinical trial comparing the effectiveness of two forms of microcurrent treatment of chronic tennis elbow.

7.2.1 Objectives And Hypotheses

The objectives of the trial were to assess:

- Whether the effects of MCT depend on the intensity of the current applied;
- The patient experience of home-based treatment using MCT
- The suitability of a protocol for a full clinical trial of MCT for this disorder

The first objective was addressed by testing the hypotheses that treatment with microcurrent of intensity 50 μA and 500 μA would produce different outcomes in:

1. healing of associated tissue damage, particularly to the common extensor tendon
2. associated pain
3. associated functional deficit
4. overall improvement or resolution of the disorder from the point of view of the person affected

The trial did not compare MCT with other forms of management. However, data is available from trials that have included a minimal intervention group, and comparisons with their data were planned to provide an indication of whether – and to what extent - MCT could improve outcomes. The patient experience was addressed by collecting data on adverse events and patient attitude to the microcurrent device and the treatment process. Analysis of the data and the experience of conducting the study enabled a judgement to be made about the need for a full scale trial.

7.2.2 Eligibility Criteria

A diagnosis of tennis elbow

The primary criterion for entry to the study was a diagnosis of chronic tennis elbow, as defined earlier (see section 6.4.1). There is no agreed gold standard for diagnosis of tennis elbow⁶⁰³. Typically it is based on the individual's history and response to several clinical tests, including – but not limited to – those used in the reliability studies reported earlier^{530, 589, 615}. These tests have not been subject to extensive psychometric evaluation; indeed, their validity as indicators of tendinopathy is questionable because other disorders may give positive results using some of them. For instance, radial nerve entrapment at the elbow may produce pain on resisted middle finger extension⁵⁹⁹, and cervical radiculopathy can reduce grip strength⁵⁹⁵. Positive tests do not necessarily correlate with other signs and symptoms of tennis elbow^{418, 603}. Moreover, individual tests, such as pain on palpation or resisted wrist extension, have shown only moderate levels of inter-examiner agreement⁶¹⁶.

For these reasons none of the typical tests can be considered pathognomonic of tennis elbow. A clinical judgement is made, based on the balance of probabilities. The uncertainties inherent in this approach may partly account for poor outcomes in some trials. If the treatment under evaluation is for tendinopathy, but the familiar signs and symptoms are being produced by a different disorder in at least some of the participants, the power of the trial to detect a treatment effect may be diminished. Since the potential effectiveness of MCT is predicated on its capacity to influence tissue healing, the presence of tendinopathy was a key diagnostic consideration in this study. Sonographic evidence of tendon damage (indicated by a non-zero greyscale or hyperaemia score) was therefore included as a specific eligibility criterion, along with a clinical opinion based on the history of the complaint, current symptoms, and a positive response to two or more of the selected clinical tests: pain on palpation of the lateral epicondyle, resisted middle finger extension, resisted wrist extension and on the chair lift test^{530, 589}. The last test was added because it appeared likely to apply a greater stress to the common extensor tendon than the others, and so be sensitive to milder presentations of the disorder. It is one of the few tests with proven intra- and inter-rater reliability⁵⁸⁹. The combination of criteria was used to maximise confidence in the diagnosis, although it did not necessarily rule out co-morbidities.

The earlier review of MCT concluded that it appears to be most effective in cases of failed healing, so chronicity was selected as an additional inclusion criterion. Tendon healing is not naturally a rapid process but, under normal circumstances, might be expected to have moved into the remodelling phase within a few months of an acute injury⁶¹¹. Following bone and

skin damage, union or wound closure mark reasonably distinct transitions in the repair process, by which healing rates may be estimated and chronicity defined. Tendon healing does not have an equivalent milestone. Moreover, tendinopathy often has no identifiable moment of causation, so defining chronicity is rather arbitrary. Hence different symptom durations have been classified as indicating chronicity in tennis elbow studies - typically it is 3 months^{411, 412, 481}, and less often 6 months^{461, 617}, although some studies include durations as short as one month have been viewed as chronic^{422, 427}. A three-month threshold was used in this study.

Other criteria

A wide range of eligibility criteria have been applied in tennis elbow trials, summarised in Table 7.1. It is not common for these to be justified, and the different selections that appear in study protocols suggests that the choices are not always rational. Excluding those with bilateral symptoms is one example: unless there is a strong suspicion that this is secondary to a central neurological deficit, it is difficult to see why it should exclude participation. Tennis elbow may affect both limbs³¹⁰ and there is no reason to suppose that a treatment that is effective for one limb might not benefit the other. Calculating PFGS/MGS ratios is not possible in such cases, but this does not appear sufficient reason to exclude them. Excluding those with other upper quadrant disorders may be reasonable, because they could be the main source of symptoms or could present as co-morbidities and so confound the study by influencing outcomes. However, for the present study, it was decided for several reasons to apply as few of these exclusions as possible. The use of sonography would give confidence in a diagnosis of tennis elbow, by providing evidence of the presence of tendon damage and tissue changes, whether or not there were co-morbidities. It could also be used to detect and monitor some other forms of damage, such as a torn radio-humeral ligament, that might respond to MCT. If evidence of any upper quadrant disorders excluded participation, the available population could be significantly reduced. For instance, excluding those with other upper quadrant disorders resulted in the loss of more than half of otherwise eligible participants in one study³³³. Rejecting these exclusion criteria gives the trial a more pragmatic character, providing evidence regarding effectiveness in the typical clinical situation, rather than of efficacy in a more tightly controlled but less realistic one.

On the other hand, if any of these disorders were present, they might influence variables such as pain and function, and so disguise any effects of MCT on them. This is a significant disadvantage of the pragmatic approach but, since the primary focus of interest was tissue healing, it was deemed justified in order to maximise the chances of obtaining a viable sample size. So that some account could be taken of the potential impact of co-morbidities,

the initial assessment was designed to look for evidence of them. Although formal sub-group analysis would be inappropriate given the anticipated sample size, if there were large differentials between individuals in treatment response, data on co-morbidities could be used to make inferences on their potential as prognostic indicators.

Table 7.1: Eligibility criteria used in trials of treatments for tennis elbow

Inclusion
Diagnosis based on standard tests ^{411, 433, 478, 480, 618} (e.g., tenderness to palpation plus two others ⁶¹⁸)
Age 18-65 ⁴³³ , 18-70 ³³²
Not responding to other treatments ^{411, 480}
Capable of following instructions ⁴³³
symptom duration > 3w ⁴³³ , 6 weeks ^{332, 333} , 3 months ^{411, 412, 481} , 6 months ^{461, 617}
physician's diagnosis ^{433, 506}
ability to understand and complete a questionnaire ³³²
Exclusion
Bilateral symptoms ^{332, 441, 478, 480, 506, 618}
Cervical radiculopathy ^{332, 411}
Peripheral nerve involvement ⁴⁸⁰
Radial tunnel syndrome ^{411, 441, 480, 618}
Pain over the radio-humeral ligament ⁴⁸⁰
Sensory disturbance in affected arm ^{441, 480}
Exacerbation on movement of neck or with overpressure ⁴⁸⁰
Any other elbow pathology ^{480, 506} e.g. tendon rupture in last 12 months ³³² , Osteoarthritis ⁴¹¹
History of elbow fracture or dislocation ^{332, 411}
Congenital/acquired deformity of elbow ³³²
Cervical ⁴¹¹ , Shoulder, wrist, hand pathology ^{411, 441, 480}
Carpal tunnel syndrome ⁴¹¹
Rotator cuff tendinopathy ⁴¹¹
Upper quadrant pain (other than due to tennis elbow) requiring treatment or preventing full participation in normal work/recreation ⁵¹¹
Systemic / neurological disorders ^{332, 441, 506, 618}
Rheumatoid arthritis ⁴¹¹
Signs and symptoms suggestive of other causes of pain ³³²
Treatment by a health care professional for elbow pain in last 1 month ⁶¹⁸ , 6 months ⁵¹¹ , apart from oral/topical analgesia ⁵¹¹
Elbow injection (including cortisone) in last month ⁵⁰⁶ , 6 months ^{332, 478} , year ⁴⁴¹
Previous elbow surgery ^{332, 478, 506}
Previous treatment with trial intervention ⁵⁰⁶
Contraindications to trial interventions ^{332, 506}
Compensation / litigation ⁴⁴¹
Not first episode ⁴⁴¹

Several other exclusion criteria were applied, however. Participants must not have received any other active treatment (other than oral or topical analgesia) in the previous month, and must have experienced no significant improvement in symptoms over that time. This period

was selected to provide a washout period for any previous treatment. Participants were also required to be over 18 years old, though no upper age limit was set. The lower limit was chosen to avoid unnecessary assessments of individuals whose elbow pain would be unlikely to be due to tennis elbow, which is uncommon in this age group⁶¹⁹. See Appendix 6 for the relevant documentation.

7.2.3 Recruitment

Several sources of participants were used. Those who had taken part in the earlier reliability study using symptomatic subjects were invited to participate; promotional material was emailed to staff in the investigator's institution and to several local racquets clubs; and an account of the study with the investigator's contact details was submitted to a number of local newspapers, several of which published it either in print or on line. Expressions of interest were sought from people with typical symptoms of tennis elbow, present for at least three months. Those replying were sent a detailed information leaflet and a brief screening questionnaire, which they could return via email or with the supplied stamped addressed envelope. Reminders were despatched after about two weeks if necessary, after which no further contact was made with non-respondents. Those appearing to meet the eligibility criteria were invited to an initial assessment where they provided informed written consent to participate. If found eligible, they were enrolled into the trial and allocated to a treatment group.

7.2.4 Interventions

The CONSORT statement calls for descriptions of (a) the experimental treatment and comparator, (b) the different components of the interventions and, when applicable, of the procedure for tailoring the interventions to individual participants, (c) how the interventions are standardized, and (d) how adherence to the treatment protocol is assessed or enhanced²³⁶.

Experimental treatments

Based on the hypothesis that current intensity is the most significant variable, two substantially different values - 50 μ A and 500 μ A - were compared. The Elexoma Medic was the device selected to deliver the treatment because it allowed the current intensity to be set by the user. The portability and relative simplicity of the device also meant that it was suitable for home-based, patient-controlled treatment. This enabled substantial treatment durations to be employed with minimum inconvenience to the participant. Apart from current intensity, the treatment protocol was the same for both groups. All participants used

Program 5, which provided a low frequency monophasic square wave (described fully in Section 5.4.1). The device has an “active electrode” designated by the manufacturer. It corresponds to the cathode when used with monophasic programs, and this electrode (identified by colour) was attached over the tendon. Participants were instructed to apply the treatment continuously for 99 minutes, once a day for 21 consecutive days. The time of day was not specified, and there was no requirement to treat at the same time every day. For one group (A), the current intensity was 50 μA ; for the other (B) it was 500 μA . These are peak rather than average intensity values, which were calculated in the laboratory evaluation to be about 20% lower.

The total treatment period represented a compromise between competing considerations. The systematic review suggested that successful applications of MCT usually last between weeks and months. The literature provided by the device manufacturer suggested that treatment times of 2-4 weeks might be necessary, although they did not provide evidence to support this guideline. Increasing the duration of treatment beyond three weeks might enhance the chances of success, but also risked reducing participant adherence to the protocol since daily self-treatment was required. Three weeks of daily treatment, with total exposure times in the tens of hours, is considerably longer than typically used with other electrotherapeutic modalities that are claimed to assist healing in tennis elbow (such as extracorporeal shockwave therapy⁶²⁰ and low intensity pulsed ultrasound⁴²⁹), and so was felt to be a reasonable compromise.

The skin areas where electrodes were to be placed - over the common extensor tendon and just proximal to the olecranon - were shaved if hairy and cleaned with an alcohol wipe to aid adherence of the electrodes. The lateral elbow was palpated to identify the epicondyle, and a short line was drawn from it, extending distally to indicate the position of the common extensor tendon. This was used during the practice session as a guide for placement of one electrode so as to cover the area over the tendon. The other electrode was then placed - with less precision - just proximal to the olecranon. This configuration (illustrated in Figure 7.1) was thought likely to ensure that the microcurrent had both transverse and longitudinal components through the tendon, although the actual current path was unknown. The electrodes were standard 5x5cm reusable adherent flexible conducting pads with integrated short leads. Two sets were provided but further supplies were available if adhesion diminished. During treatment, patients could carry move about by carrying the device in their pocket or in a supplied case that attached to a belt.



Figure 7.1: Positioning of electrodes for treatment

Other components of the intervention

The literature review concluded that MCT appears most effective in promoting tissue healing when it is accompanied by other interventions. Were a full clinical trial to be conducted, exercise therapy would be an appropriate co-intervention since there is evidence that controlled mechanical stress can enhance the remodelling process⁶²¹. However, exercise therapy appears to be most effective when it is supervised; home-based exercise programmes are difficult to control and adherence may vary substantially between participants⁶²². A systematic review considering patient adherence to exercise programmes prescribed by musculoskeletal physiotherapists found that that depression and pain during exercise may reduce adherence⁶²³. Substantially higher levels of depression have been found amongst those with chronic tennis elbow than in the broader population⁴⁵⁵, and at least some forms of exercise recommended for the treatment of tennis elbow are painful⁶²⁴. Thus, maintaining a controlled level of exercise as part of a home-based treatment programme for chronic tennis elbow may be problematic. So, for the purposes of this comparative study, a formal exercise programme was not applied. Instead, a minimal intervention approach that has been used in several other studies^{333, 625} was adopted. This comprised education about the disorder and advice on activity modification to minimise stress on the affected tendon. Where participants were likely to engage in intense manual activity, either at work or in recreation, they were encouraged (and taught how) to use a tennis elbow brace. Although the evidence for such braces is mixed⁶²⁶, they may provide some protection against the stresses that can cause pain and re-injury of the tendon^{627, 628}. The use of a brace was not mandatory but was monitored by questioning the participant at assessments. Non-prescription analgesia was also allowed as needed, although participants were asked not to use any on assessment days, so as not to influence PFGS measurements.

Standardisation of intervention

In order to ensure that participants in each trial arm all received the same MCT, a number of measures were planned. Each person was trained in the use of the microcurrent device and observed rehearsing the process of applying the treatment; printed instructions were supplied along with a diary sheet to record every treatment and any departures from the protocol; and the positioning of electrodes was checked at the post-treatment assessment by asking the participant to indicate where they had been applied. If a participant missed a treatment for any reason, they were asked to indicate this on the diary, and add a treatment to the end of the schedule, so that the total treatment time would be maintained.

The advice given regarding activity modification and use of a brace depended on individual circumstances. Although this sacrificed one element of control in the trial, it is representative of a management strategy likely to be used in clinical practice. At the same time it sought to provide some measure of control over another potential confounder - the everyday stresses acting on the tendon, which may differ substantially according to individual circumstances. Exposure to such stresses may have a significant impact on outcome, but this is virtually impossible to standardise in any trial. Instead, enquiries were made at each assessment about activity levels in the preceding period.

7.2.5 Assessment

Assessments were conducted four times over the course of the trial. At the initial assessment, demographic data and medical histories were recorded, and baseline values for all outcome variables were measured. At subsequent assessments, the outcome variables were re-measured. These processes are now described in detail.

Data collected during the initial subjective assessment covered demographics, medical history and history of the disorder. They included information on factors that might influence response to treatment, and so act as confounders in the study. A wide variety of prognostic factors may influence outcomes after treatment for tennis elbow. They include age^{336, 383}, gender^{383, 629}, prior occurrence of the disorder⁴⁷⁴, baseline pain intensity^{336, 629}, involvement in manual work³³⁶, involvement of the dominant arm³³⁶ and duration of symptoms^{332, 383}. However, there is inconsistency in the findings of prognostic studies, which may reflect the fact that the trial data is for different forms of treatment or combinations of treatment, for which the prognostic factors may not be the same. Also, short and long term prognoses may differ for a particular factor – one analysis found that age was associated with worse outcomes in the short term, but had no influence in the longer term³⁸³. A systematic review of

studies concerned with prognostic factors for tennis elbow concluded that there was insufficient evidence to draw confident conclusions about the prognostic value of any factor⁶³⁰. Several studies published since that review have concluded that, for a range of conservative treatments there is evidence of a weak association between baseline pain intensity and worse short-term outcomes^{338, 383}, and between ongoing stress to the arm (e.g. by manual work or involvement in sports) and worse long term outcomes^{336, 338, 631}. Even though the evidence for other factors is inconclusive, it was decided to collect data on several of those that have at least face validity for influencing outcomes. These include age, diabetes and smoking, all of which may suppress tissue healing⁶³², as well as concomitant upper quadrant neural or musculoskeletal disorders, and previous episodes of tennis elbow.

It was also judged important to consider the potential influence of psychosocial factors on outcomes. For instance time taken off work may lead to depression and increase anxiety levels, which could increase pain perception and functional disability: scores on the DASH and PRTEEQ questionnaires have been found to correlate with depression and anxiety^{455, 633}. Depression can affect the memory of pain⁶³⁴ and so may influence responses. Involvement in litigation or compensation claims may also skew reporting of symptoms⁶³⁵, and fear-avoidance behaviour may be the cause of maladaptive neuromuscular changes and general deconditioning that can contribute to deterioration in soft tissue quality^{636, 637}. Questions were therefore included to assess whether the participant was taking off work or involved in litigation or a compensation claim because of the disorder. Alizadehkhayat and colleagues advocate the assessment of psychological status in people with tennis elbow⁴⁵⁵. They found that, in a sample of 16 patients with tennis elbow of more than 3 months duration, 55% were likely to be suffering from anxiety and 36% from depression, according to their Hospital Anxiety & Depression Scale scores⁴⁵⁵. These compare to scores of 0.7% and 2.6% respectively in the general population⁶³⁸. These rather alarming findings should be tempered by the fact that the sample was self-selected from a group of 46 patients enrolled in a broader study. Nevertheless they indicate that psychological status may be significantly compromised in people with tennis elbow, and so should be assessed. Hence, three screening questions were added to the subjective assessment. Two have 96% sensitivity for depression case-finding⁶³⁹; the third was of a similar format and enquired about levels of anxiety.

A physical examination of the upper quadrant (cervical spine, shoulder and upper limb) was then conducted, using the diagnostic tests specified above and the process described previously (see section 6.4.1).

Outcome Measures

Since tissue healing was the major focus of this investigation, the primary outcome variable was :

1. Local tissue status, measured using sonographic rating scales

and secondary variables were:

2. Pain-free grip strength expressed as a ratio of maximum grip strength on the unaffected side, measured by isometric dynamometry
3. Pain and functional limitation, quantified by the Patient-rated Tennis Elbow Evaluation questionnaire
4. Functional limitation, using the Patient Specific Functional Scale
5. Patient-rated global change, using a 6 point Likert scale
6. Adverse events, by patient report
7. Acceptability and ease of use, by patient report

The new rating system described in section 6.4.3 was adopted for sonographic assessments. The PRTEE was also modified by minor changes to the wording of some questions in order to make them more meaningful to British respondents. For example “pants” was changed to “trousers”, and “washcloth” to “wet cloth”. Although wording changes to questionnaires can threaten their validity, these were thought more likely to improve it by enhancing understanding. The other measures were used as described previously (see section 6.4.1).

Timing Of Assessments

MCT might result in changes in signs and symptoms during or immediately following treatment, and these may or may not be sustained. It might also promote tissue changes that take some time to become apparent. For this reason, several assessments were planned: at baseline, at the end of the course of treatment, and at three weeks and three months after treatment was completed. Whilst longer follow-up periods are desirable to establish whether any benefits are sustained, three months was judged the most feasible period within this investigation. Some trials using sonography as an outcome measure have conducted follow-up assessments from 6 months to two years after treatment^{374, 375, 397}, but grey scale changes following treatment have been observed within 9 weeks of treatment⁴⁸⁰, and PD changes in as little as 2 weeks post-treatment⁶⁰². Significant remodelling seems unlikely to be seen

within three months, but fibroplasia and neovascularity could certainly be expected to occur within that time^{640, 641}. It is also reasonable to expect that other outcome variables, such as pain and functional limitation, could change on that timescale.

Outcomes 1 – 5 were measured at all assessment points. At baseline, outcome 5 was defined as overall change in symptoms over the previous month. At other assessment points, outcome 5 was defined in relation to baseline status. Outcomes 6 and 7 were recorded at the first post-treatment assessment, but generic questioning at subsequent assessments allowed for participants to report any further adverse events. The data collection pro-forma used in the trials is reproduced in Appendix 6.

7.2.6 Sample Size

Because of the lack of high quality trial data on effect sizes of MCT with soft connective tissues, estimating the required sample size is problematic. This trial was a preliminary study rather than a formal pilot study because it did not include several elements likely to be included in a full RCT proposal, such as a co-intervention and a placebo control group. Nevertheless, in the absence of more specific published guidance, recommendations on pilot study sample sizes were obtained from the literature. Typically, they are in the range 10 - 15⁶⁴², and it has been suggested that 12 subjects per arm is sufficient to enable statistical inferences to be drawn about treatment effects⁶⁴³. Based on this guidance, and to compensate for potential drop outs, recruitment of 15 participants per arm was planned.

7.2.7 Randomisation And Allocation Concealment

Since participants would commence treatment as they were recruited, a block randomisation process was used to ensure random allocation to each treatment group. A computer-generated series of blocks was constructed, each comprising a random sequence of four letters – two As and two Bs. Each letter represented one treatment group. When a participant was enrolled, the next letter in the sequence determined their group allocation. The investigator generated the group allocation sequence list before the trial began and applied it as each participant was accepted into the study. The sequence was, therefore, not concealed from the investigator pre-allocation.

Blinding

The investigator provided participants with the MCT device and trained them how to use it. Participant knew that no placebo was being used and that they would therefore be receiving some form of active MCT. They were told what current intensity to use, but were unaware of

the intensity being used by the other group. Therefore the participants were blind to group allocation but the investigator was not.

All elements of the assessment process were conducted by the investigator, and no attempts were made to mask group allocation or which arm was symptomatic during assessment. However, sonographic ratings of recorded images were conducted several weeks after the clinical assessments and, at these times, the investigator was blinded to these factors. The investigator also conducted all aspects of data analysis, and was not blind to the form of MCT used with each group.

7.2.8 Methods Of Analysis

Quantitative data on baseline and outcome variables were analysed statistically where appropriate. Descriptive statistics were first obtained, and data were inspected for distributions and identification of outliers. The Shapiro Wilk test was employed to assess for normality of distributions, and homogeneity of variance between comparison groups was assessed using Levene's test. These tests were necessary to establish whether parametric statistics could be employed⁶⁴⁴ (ch3). For baseline comparisons, Chi-square was used for categorical variables, Mann Whitney for ordinal data and a two-tailed independent samples t-test for parametric data. Comparisons between groups at baseline can help establish whether there are significant differences between them in variables that might affect outcomes⁶⁴⁵.

Outcome variable data was tested for significant changes over time and significant differences between groups over time. A repeated measures analysis of covariance (ANCOVA) was used to examine the data, treating time as a main effect, MCT group as an interaction effect and the baseline value of the variable as a covariate. ANCOVA has several features making it suitable for use in this study. It offers enhanced power over the standard ANOVA for smaller samples⁶⁴⁶; it has been found to be robust to violations of parametric assumptions, to the extent that ordinal data with all but highly skewed distributions can be analysed⁶⁴⁷; any differences in variance between groups can be compensated for; finally, it allows the effects of variations in the baseline parameters within and between groups to be taken into account⁵⁶² (ch24). Because the baseline score was used as a covariate it was not included as a dependent variable in the ANCOVA. Therefore the analysis of main effects does not provide information across all four time points. Planned contrasts were made between subsequent time points, and a two-way related-samples t-test was used to test for significant changes between baseline and final assessment, for each group. The non-parametric

Wilcoxon's signed ranks test was used as an additional test for changes in ordinal variables over this period.

For all ANCOVAs, Mauchly's test of sphericity was applied. If significant departures were detected, the Greenhouse-Geisser correction was used where its ϵ value was less than 0.75, and Huynh-Feldt otherwise^{644 (p431)}. Significance was set to $p \leq 0.05$, and exact significance was calculated for non-parametric tests as the sample sizes were relatively small^{644 (p528)}.

Differences between treatment groups were further investigated by comparing the changes in scores between baseline and post-treatment assessments, and between baseline and final assessments. Two-tailed independent group t-tests were used for this purpose, with significance again set to $p \leq 0.01$ to compensate for multiple testing. The t-test has been shown to be reliable even with small group trials using 5-point ordinal scales⁶⁴⁸. Nevertheless the Mann-Whitney U test was employed as an additional test for differences between groups on ordinal scales.

The global change score (GCS) was used to create a binary measure of treatment success, defined as $GCS \geq 2$ ("much improved" or "completely recovered"), and success rates were calculated at each post-treatment assessment³³². Treatment groups were compared on this measure using the odds ratio^{644 (p694)}.

Differences over time and between groups were also quantified by the effect size for each variable. This is most meaningful for focussed comparisons made at single time points, rather than for multiple comparisons across several time points^{644 (p453)}. Therefore effect sizes were calculated using the formula^{562 (p648)}: $\text{Effect size} = (\text{group mean}_1 - \text{group mean}_2) / \text{pooled standard deviation}$. They were interpreted as 0.2-0.5 = small effect, 0.5-0.8 = medium effect, and >0.8 = large effect⁶⁴⁹. The effect size for changes over time was calculated for each group between baseline and final assessment; for differences between groups it was calculated for changes between baseline and second assessment, and baseline and final assessment.

Effect sizes based on non-parametric tests can be difficult to interpret⁶⁴⁷, but the odds ratio was used to signify effect size of the "treatment success" indicator^{644 (p693)}. Where statistical test results were non-significant, their power was calculated to gauge whether there was a likelihood of type II error having occurred. These calculations enabled estimation of the necessary sample size for a fully powered study, and were conducted using G-power⁶⁵⁰. SPSS 17 (SPSS Inc, Chicago, USA) was used to perform all other statistical analysis.

An intention-to-treat analysis was planned, with missing scores imputed for individuals by the last observation carried forward method, making a conservative assumption of no change over time^{562 (ch9)}. If an individual PRTEE questionnaire was not fully completed, any missing score was imputed using the rules provided by questionnaire originators⁵³⁹. Sub-group analysis of data from individual trials was deemed inappropriate because of their relatively small sample sizes⁶⁴⁵.

Approval for the study, a copy of which appears in Appendix 6, was provided by the investigator's institutional ethics committee, and the study was registered on www.clinicaltrials.gov, an international register (identifier: NCT00817232).

7.3 RESULTS

Between December 2008 and August 2009, thirty one eligible participants were randomly allocated into the two treatment groups. One member of group B withdrew from the trial after a single treatment because of an adverse event (see 7.3.3). The reported analysis is per-protocol, but an ITT analysis including this person's data was also conducted for the primary outcome variable (greyscale and hyperaemia scores) and on treatment success, and did not materially affect conclusions. Inspection of treatment diaries suggested that all participants completed the allotted number of treatments, apart from one who missed one treatment and one who added a treatment by mistake. There were eight instances in group A, and four in group B, of treatments being missed for a day or more during the three weeks. In these situations more treatments were added to the end of the course to bring the total up to the required 21. All courses of treatment were completed within 4 weeks. One person in group B was unable to attend one of the follow-up sessions and another from group A missed the final two assessments. Their missing data was imputed by using the last set of data collected for each individual. Seven people had either bilateral symptoms or other morbidity potentially affecting grip strength measurements and their data for this variable was excluded from the analysis. Figure 7.2 charts the flow of participants through the trial and the baseline characteristics for those included in the analysis are given in Table 7.2.

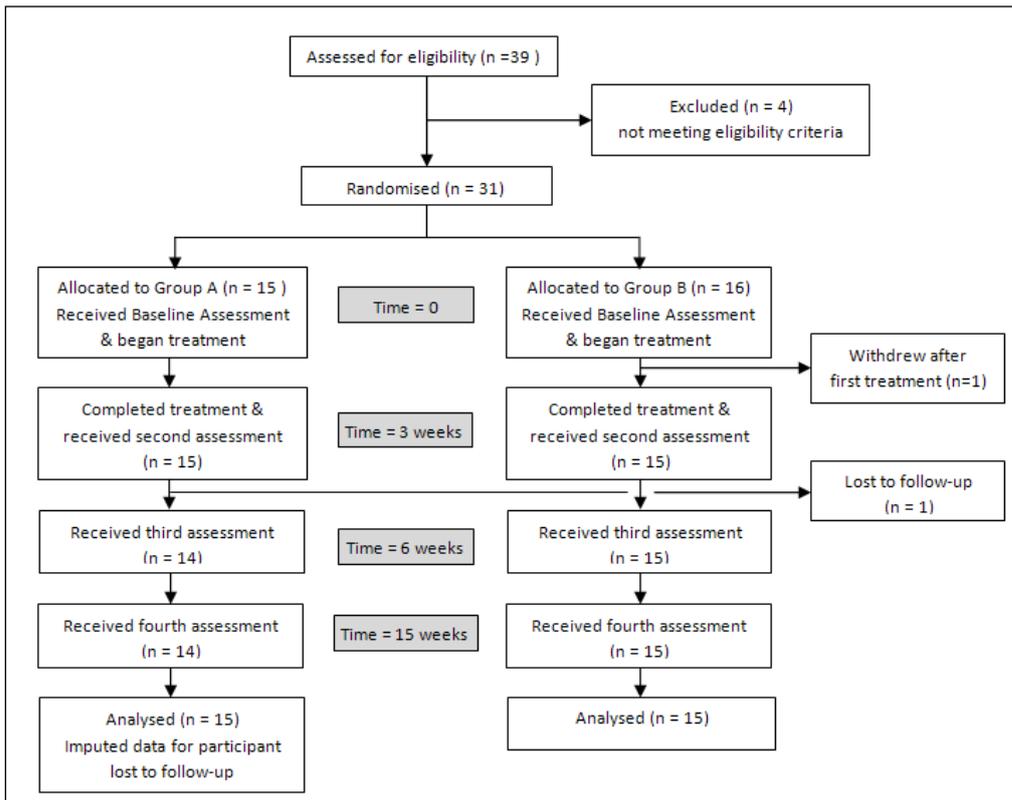


Figure 7.2: Flow chart of participants through trial

Ten people thought racquets sports were the main cause of the disorder; nine thought it was due to an unaccustomed load; four said it was work-related, and seven reported no obvious cause. Three people in the whole sample had taken sick leave as a result of the current episode (one in group A; two in B). Two people were experiencing symptoms bilaterally. Nine in group A and five in group B reported ongoing heavy upper limb use during the trial, either because of work activities or competitive sports (which they were unwilling to forego, despite advice to the contrary). All but one of these individuals in each group reported using a tennis elbow brace of some kind during the trial. On initial assessment, a third of the whole sample showed signs of radial nerve sensitisation by reporting abnormal sensation in the upper limb on ULTT2B. In most cases (see Table 7.2) the test produced pain at the lateral elbow.

The data set for PFGS was compromised by a leak of hydraulic fluid in the dynamometer during the trial. This was identified during one of the monthly calibration checks, and inspection of the raw data suggested that the dynamometer may have been underestimating grip strength for several weeks previously. A replacement device was obtained within a few days, and all suspect data was removed from the analysis and imputed by carrying forward

the last reading. This mishap led to the imputation of 18% of the dataset (12% from group A and 6% from group B).

Data analysis for the patient-specific functional scale proved problematic. A third of the participants were unable to identify an activity that caused them difficulty and which was not already listed in the PRTEE. Of those who were able, some could identify three whereas others could only identify one. In subsequent assessments several participants could not provide a rating for the activity because they had not done it in the intervening time. As a result, complete datasets were only available for eight participants. Therefore no statistical analysis was attempted, although the data were considered in evaluation of the study protocol.

Patterns of abnormality observed on sonographic assessments were similar to those seen in the reliability study. Hypoechoic areas were the most common finding in symptomatic tendons, being evident in 26/30 cases. Cortical spurring was also commonly observed (19/30), tendon thickening and fibrillar disruption less so (13/30 each). Where calcification was seen (in 12/30 symptomatic tendons) it was normally punctuate and sparse; in three cases there were large plaques. Almost all non-symptomatic tendons had sonographic signs of structural abnormality. Although these were normally mild (grade 1), two had calcific plaques (grades 2 and 3). A frank tear was only evident in one tendon at baseline. All but two of the symptomatic tendons, and ten of the non-symptomatic tendons, had signs of hyperaemia. The maximum Doppler signal was normally visible in the anterior portion of the tendon, but in several cases vessels were more prominent or only visible exterior to the tendon body, either just superficial or just proximal to it.

Table 7.2: Baseline characteristics of participants included in analysis

Group	A	B
n	15	15
Females (n)	9	7
Age mean \pm SD (range)	55 \pm 5 (48-63) years	52 \pm 7 (40-69) years
Arm dominance (n)	11 Right; 2 Left; 2 Ambidextrous	14 Right; 1 Left
Dominant arm affected (n)	11	14
Median duration current episode (range)	5 (3-18) months	8 (3-24) months
History of previous episodes (n)	4	6
Ongoing heavy upper limb use (n)	9	5
Positive to cervical tests (n)	8	10
ULTT2B caused lateral elbow pain (n)	4	5
Greyscale total score mean \pm SD (range)/12	3.3 \pm 1.0 (2-5)	2.5 \pm 1.2 (0-4)
Hyperaemia score mean \pm (range)/4	2.1 \pm 1.2 (0-4)	1.6 \pm 1.1 (0-3)
PRTEE pain score mean \pm SD (range)/100	36 \pm 18 (10-78)	40 \pm 18 (12-72)
PRTEE function score mean \pm SD (range)/100	36 \pm 22 (0-84)	38 \pm 22 (4-80)
PRTEE total score mean \pm SD (range)/100	36 \pm 20 (6-81)	39 \pm 20 (14-76)
PFGS/MGS mean \pm SD (range)	67 \pm 34 (15-114) %	66 \pm 36 (22-132) %

7.3.1 Baseline comparisons between groups

The Shapiro Wilk test showed that baseline values for participant age and PFGS ratios were distributed normally, but that duration of current episode and greyscale score for group A were not (see Table 7.3). The skewness of group A grey-scale score (0.5) and group B hyperaemia scores (-0.04) were not extreme. Levene's test suggested equality of variance between groups on age ($p=0.613$), sonographic greyscale score ($p=0.221$), sonographic hyperaemia score ($p=0.864$), PFGS ratio ($p=0.617$), and PRTEE pain, function and total scores ($p=0.992$, $p=0.986$, $p=0.809$ respectively) but non-equality of variance on duration of current episode ($p=0.025$). Inspection of box and whisker plots for baseline data indicated one outcome variable outlier: a participant in group B whose pain-free grip strength ratio was high (in other words, less severe) compared to the group mean.

Table 7.3: Shapiro Wilk test for normality of outcome variables

Variable	Group	statistic	df	sig
Age	A	0.907	15	0.120
	B	0.952	15	0.559
Duration current episode	A	0.831	15	0.009
	B	0.874	15	0.038
Sonographic greyscale score	A	0.872	15	0.037
	B	0.923	15	0.241
Sonographic hyperaemia score	A	0.931	15	0.278
	B	0.873	14	0.046
PRTEE (Pain)	A	0.941	15	0.396
	B	0.922	15	0.207
PRTEE (Function)	A	0.978	15	0.956
	B	0.954	15	0.594
PRTEE (total)	A	0.961	15	0.706
	B	0.967	15	0.809
PFGS ratio*	A	0.929	12	0.367
	B	0.911	11	0.249

* PFGS data for participants with bilateral symptoms or other disorders potentially affecting grip strength were excluded from this and all other analyses.

Tests were then applied to assess whether potentially significant baseline characteristics were equivalent between the trial groups. Independent groups t-tests indicated no significant differences on any of these variables (see Table 7.4), although the mean greyscale score for group A was higher (worse) than group B and the difference nearly reached significance. Mann Whitney was used as an additional check on symptom duration and sonographic greyscale scores because of their distributions, as well as the sonographic hyperaemia scores because this scale had only 5 points (Table 7.5). Pearson's Chi-square test was used to examine differences between groups on dichotomous variables that might influence outcome (see Table 7.6). No significant differences were found for any variable using any of these tests.

Table 7.4: Independent samples t-test for baseline differences between groups on continuous data

Variable	t	df	sig
Age	1.155	28	0.259
Duration current episode*	- 0.166	23.6	0.110
Sonographic greyscale score	1.805	28	0.082
Sonographic hyperaemia score	1.014	27	0.320
PRTEE (pain)	-0.513	28	0.612
PRTEE (function)	-0.221	28	0.827
PRTEE (total)	-0.373	28	0.712
PFGS ratio	0.053	21	0.958

* homogeneity of variance not assumed

Table 7.5: Mann Whitney test for baseline differences between groups on non-parametric data

Variable	U	sig
Duration current episode	79.5	0.174
Sonographic greyscale score	78.0	0.155
Sonographic hyperaemia score	84.0	0.338

Table 7.6: Pearson's Chi-square test for baseline differences between groups on dichotomous data

Variable	χ^2	sig
Females	0.536	0.464
Dominant arm affected	2.160	0.142
History of previous episodes	0.600	0.439
Ongoing heavy limb use	2.140	0.143
Use of brace in study	0.122	0.269
Positive to cervical tests	0.536	0.464
ULTT2B causes lateral elbow pain	0.159	0.690

7.3.2 Analysis of outcome variables

Summary outcomes data for the trial groups are given in Tables 7.7, and these are demonstrated graphically in Figures 7.3 and 7.4. Group means suggest improvements over time in most outcome measures with the exception of hyperaemia score, whose interpretation is discussed later. However, broad error bars indicate that the differences between groups and over time may not be significant and that statistical tests are required.

Table 7.7: Summary data for all outcomes at each assessment in Groups A and B

Variable	Mean score \pm s.d.	
	Group A	Group B
Greyscale Score / 12		
Baseline	3.3 \pm 1.0	2.5 \pm 1.2
3 weeks	3.3 \pm 1.1	2.5 \pm 1.2
6 weeks	2.7 \pm 0.7	2.3 \pm 1.3
15 weeks	2.4 \pm 1.1	2.7 \pm 1.2
Hyperaemia Score / 4		
Baseline	0.7 \pm 1.1	0.5 \pm 0.9
3 weeks	2.3 \pm 1.1	2.0 \pm 0.9
6 weeks	2.1 \pm 1.2	1.7 \pm 0.7
15 weeks	2.2 \pm 1.1	1.9 \pm 1.0
Pain-free Grip Strength ratio / %		
Baseline	0.66 \pm 0.34	0.69 \pm 0.34
3 weeks	0.74 \pm 0.35	0.74 \pm 0.29
6 weeks	0.79 \pm 0.33	0.69 \pm 0.34
15 weeks	0.96 \pm 0.29	0.87 \pm 0.29
PRTEE (pain) / 50		
Baseline	18 \pm 9	20 \pm 9
3 weeks	11 \pm 6	17 \pm 8
6 weeks	8 \pm 6	17 \pm 8
15 weeks	4 \pm 5	12 \pm 6
PRTEE (function) / 50		
Baseline	18 \pm 11	19 \pm 11
3 weeks	9 \pm 7	18 \pm 11
6 weeks	6 \pm 5	15 \pm 10
15 weeks	5 \pm 5	9 \pm 7
PRTEE (total) / 100		
Baseline	36 \pm 19	39 \pm 20
3 weeks	20 \pm 12	33 \pm 18
6 weeks	15 \pm 11	32 \pm 18
15 weeks	9 \pm 10	21 \pm 12
Treatment success / %		
3 weeks	40	13
6 weeks	67	7
15 weeks	93	47

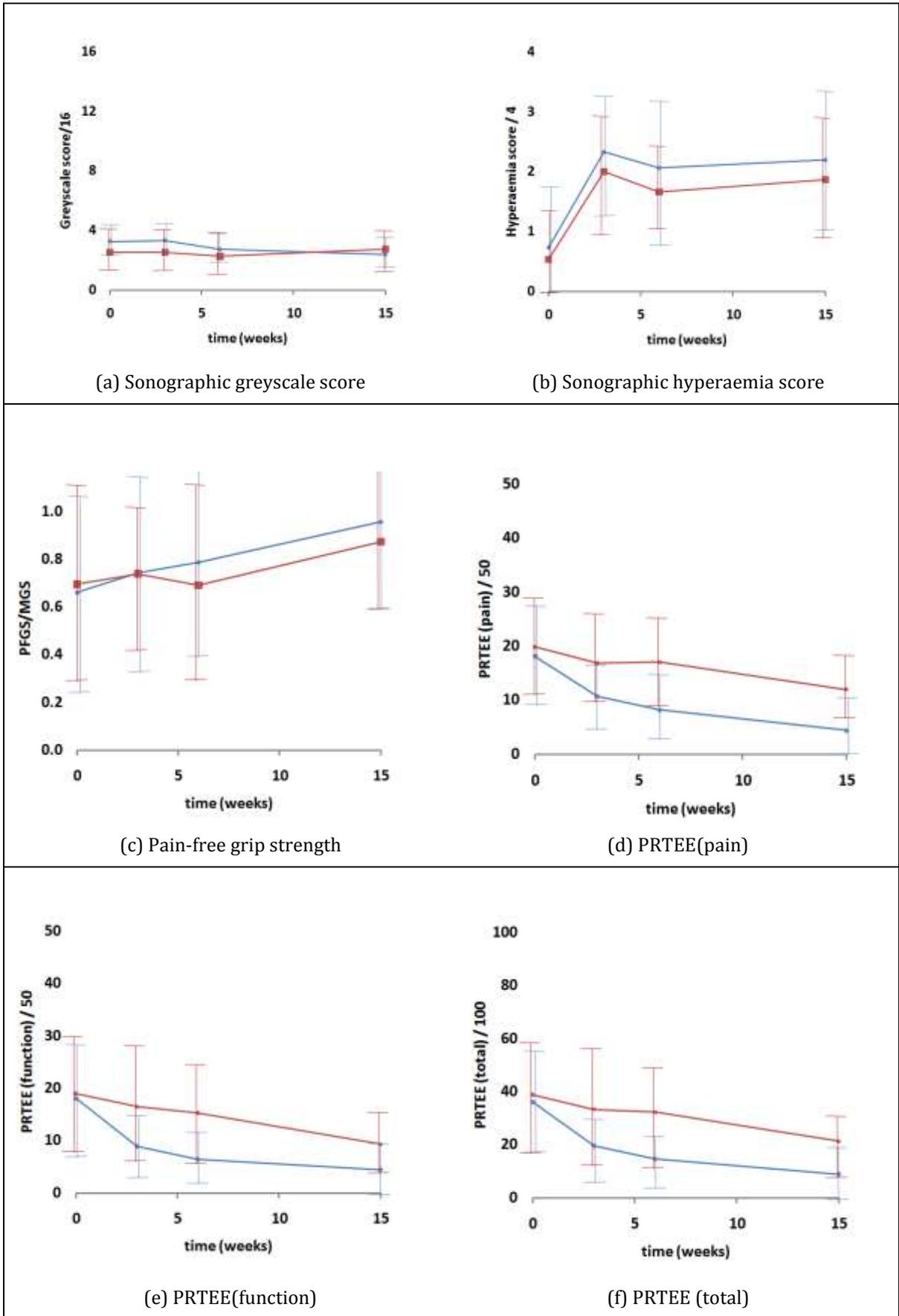


Figure 7.3: Variation of outcome measures in ◆ Group A ■ Group B

Analyses were conducted to establish whether there were significant changes in the outcome variables over time, and significant differences between group outcomes at follow-up assessments. Table 7.8 summarises the results of repeated measures ANCOVAs conducted with interval and ordinal scales, with time as the main effect and treatment group as an interaction effect. In this and subsequent tables, p values reaching the significance threshold are given in bold type. Mauchly's test indicated homogeneity of variance for every variable, and Levene's test of error variance showed no significant differences across assessments for any variable.

Table 7.8: Repeated measures ANCOVA for time*group interactions for groups A and B

variable	Within-subjects time*group interactions		
	df	F	p
Greyscale	2, 54	2.77	0.039
Hyperaemia	2, 52	0.06	0.942
PFGS	2, 40	0.33	0.724
PRTEE-Pain	2, 52	1.23	0.300
PRTEE-function	2, 52	1.33	0.273
PRTEE-Total	2, 52	0.90	0.415

Within subjects contrasts showed that the interaction between time and group was significant for greyscale score between times 3 and 4, where $F(1,27) = 5.39$, $p=0.03$. The results of independent samples t-tests, conducted on changes in variables at second and final assessments, are presented in tables 7.9 and 7.10 respectively.

Table 7.9: Independent samples t-test for differences between groups on change scores at second assessment

	df	t	p	Mean diff (99%CI)	effect size	power
Greyscale*	14	-1.0	0.334	-0.07 (-0.12,0.25)	0.38	0.17
Hyperaemia	27	-0.257	0.799	-0.09 (-1.1,0.88)	0.09	0.06
PFGS	21	0.226	0.793	0.01 (-0.12,0.14)	0.11	0.06
PRTEE-Pain	27	-1.61	0.120	-4.2 (-11.5,3.1)	0.59	0.34
PRTEE-function	27	-0.92	0.367	-3.6 (-14.6,7.3)	0.34	0.14
PRTEE-Total	27	-2.05	0.050	-10.5 (-24.8,3.7)	0.75	0.50

* equality of variance not assumed;

Table 7.10: Independent samples t-test for differences between groups on change scores at final assessment

	df	t	p	Mean diff (99%CI)	effect size	power
Greyscale*	28	-3.1	0.005	-1.1 (-2.1, -0.1)	1.1	0.84
Hyperaemia	27	-0.2	0.843	0.1 (-1.2, 1.1)	0.07	0.05
PFGS	21	0.63	0.534	0.1 (-0.3, 0.5)	0.25	0.09
PRTEE-Pain	27	-1.6	0.125	-5.6 (-15.5, 4.2)	0.59	0.33
PRTEE-function	27	-0.9	0.036	-6.3 (-14.1, 1.6)	0.81	0.56
PRTEE-Total	27	-1.3	0.197	-9.5 (-29.2, 10.3)	0.48	0.49

* equality of variance not assumed;

These tests confirmed that, for most variables, improvements in scores did not differ significantly between groups. The significant difference between groups in greyscale score improvements was in favour of group A. Calculations of effect size and associated power demonstrated that low power was an issue in all cases of non-significance, which means there was a significant risk of type II error, missing a significant difference when one existed. Because there were significant numbers of tied ranks between groups in the greyscale score changes, a contingency table was constructed and Kendall's tau-b calculated for the difference in improvements at final assessment. These indicated a significant association between group and level of improvement (see Table 7.11) in favour of group A, with Kendall's tau-b = 0.46, exact sig = 0.005, confirming the result of the t-test.

Table 7.11: Greyscale score change between baseline and final assessment in groups A and B

Group	Greyscale Score change					
	-3	-2	-1	0	1	2
A	1	4	3	6	1	0
B	0	0	1	12	0	2

Five cases had evidence of a frank tendon tear (an anechoic area), which was not accounted for in the greyscale score. In one case in group B, the tear was visible at baseline and did not change significantly over the duration of the study; in two cases (one in each group), a tear became apparent at third assessment but had resolved by the final assessment; and in two cases (one in each group), a new tear was apparent at the final assessment. These changes did not show any obvious correlation with pain or global change scores, except that the case with no change in the tear showed no change until the final assessment, when the pain score dropped and the GCS = +1. Most cases of calcification were grade 1, but in group A there was one grade 2, which resolved entirely, and one grade 3, which reduced to grade 2 by final

assessment. In group B there was one case with grade 2 calcification, which did not change over the course of the study. All three showed substantial improvement in symptoms by final assessment.

In order to calculate the effect size of the treatment between baseline and final assessment, a related samples t-test was conducted for each group at these time points. Results, along with effect sizes for each variable are presented in tables 7.12 and 7.13.

Table 7.12: Related samples t-test for differences in scores between baseline and final assessment for group A

	df	t	p	Mean diff (95%CI)	effect size
Greyscale	14	-2.98	0.01	-0.88 (-1.5, 0.2)	0.77
Hyperaemia	14	0.44	0.67	0.13 (-0.52, 0.79)	0.11
PFGS	11	2.67	0.02	0.31 (0.05, 0.57)	0.71
PRTEE-Pain	13	-4.99	<0.001	-13.5 (-19.3, -7.8)	1.34
PRTEE-function	13	-4.78	<0.001	-13.2 (-19.2, -7.3)	1.27
PRTEE-Total	13	-5.16	<0.001	-26.9 (-38.1, -15.6)	1.37

Table 7.13: Related samples t-test for differences in scores between baseline and final assessment for group B

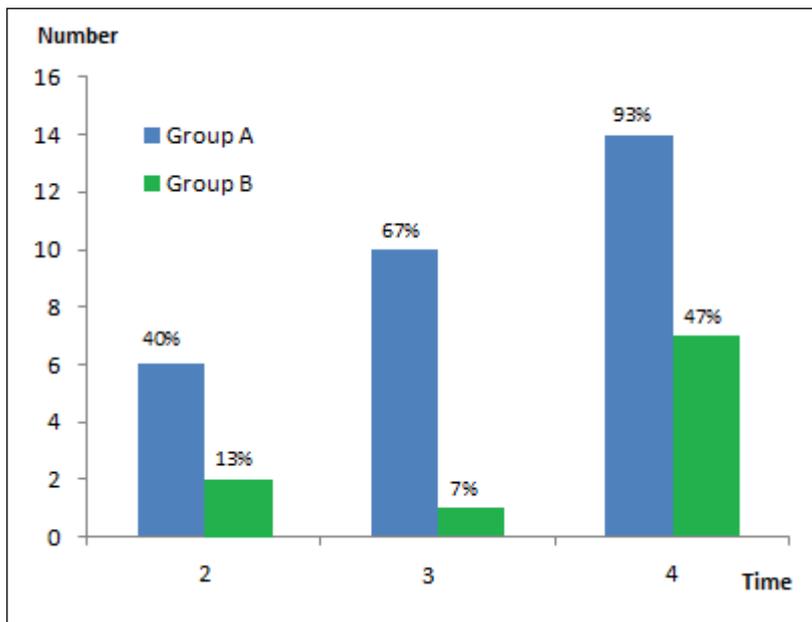
	df	t	p	Mean diff (95%CI)	effect size
Greyscale	14	1.00	0.334	0.20 (-0.23, 0.63)	0.26
Hyperaemia	13	0.82	0.426	0.21 (-0.35, 0.78)	0.23
PFGS	10	3.51	0.006	0.23 (0.08, 0.37)	1.06
PRTEE-Pain	14	3.68	0.005	-7.9 (-12.9, -2.9)	0.87
PRTEE-function	14	3.48	0.004	-9.7 (-15.6, -3.7)	0.90
PRTEE-Total	14	3.54	0.003	-17.4 (-17.9, -6.9)	0.91

Changes in all variables were significant, with the exception of hyperaemia for both groups and greyscale score for group B. The power of the tests in these cases was found to be less than 0.3. Wilcoxon's signed ranks, conducted with all the ordinal scales as an additional check for significant change over time (see Table 7.14), confirmed the findings of the related samples t-tests for each group.

Table 7.14: Wilcoxon's signed ranks for changes between baseline and final assessment in ordinal variables with groups A and B

Variable	Group A		Group B	
	Z	Exact Sig	Z	Exact Sig
Greyscale	-2.4	0.020	-1.1	0.500
Hyperaemia	-0.5	0.745	-0.8	0.594
PRTEE-Pain	-3.2	<0.001	-2.7	0.004
PRTEE-function	-2.8	<0.001	-2.9	0.002
PRTEE-Total	-3.3	<0.001	-3.0	0.001

The numbers of successful treatments in each group at each post-treatment assessment are plotted in Figure 7.4, along with the corresponding success rates. Group A performed considerably better than group B at all assessments. One member of each group saw deterioration in symptoms between second and third assessments, but improved again by final assessment.

**Figure 7.4: Number of successful treatments and success rates for groups A and B**

Chi square values and odds ratios calculated for each post-treatment assessment (see Table 7.15) show significant associations between group and success rates by assessments 3 and 4, and odds ratios in favour of group A at all time points. (The chi square test was underpowered at assessments 2 and 4 because cell counts were less than expected, but Fisher's Exact test reached the same conclusions.)

Table 7.15: Differences in success rates and odd ratios for success in groups A and B

Assessment	χ^2	Exact Sig	Odds ratio (95%CI)
2	2.7	0.215	0.23 (0.04, 1.4)
3	11.6	0.002	0.04 (0.004, 0.36)
4	7.8	0.014	0.06 (0.006,0.61)

7.3.3 Adverse events and side effects

Group A

Two people reported occasional tingling either in the forearm or little and ring fingers; one reported initial discomfort during the first few treatments, and another felt forearm muscle tightness and discomfort during and for a few minutes after treatment. One person handled the device with wet hands and reported receiving an electric shock, with arm ache for a few subsequent days. Another person reported receiving a mild pulsing shock when touching the USB cable socket.

Group B

Seven people reported tingling, usually for the initial few minutes of treatment; one of these said the feeling was stronger some days and that symptoms were stirred up on those days. Another reported three episodes of arm ache the morning after treatment. One person reported strong unpleasant bilateral leg tingling during the night after the first treatment and withdrew from the trial. Another person reported mild erythema under the cathode after treatment, which quickly disappeared.

7.3.4 Acceptability and ease of use

Generally, participants found the devices easy to use. Being able to choose a convenient treatment time was appreciated, and nobody said they found the programming necessary with this device difficult. The main practical problems reported were associated with the length of the electrode leads. These were found to catch on furniture if the wearer moved around, even when the device holder was used. If the holder was used, it was necessary to unplug and re-plug the leads after treatment is started, which might have led to inadvertent pushing of buttons. The holder also obscures the viewing screen. Although the device has an audible alarm to indicate whether the circuit has been broken, this does not work below about 100 μ A, and so the feature was unavailable to group A.

The device used rechargeable batteries and participants were supplied with a recharger and a spare pair of batteries to avoid missed treatments. Despite the provision of new batteries, several participants reported having to recharge them several times over the whole course of treatment. All participants said they used the alcohol wipes per protocol, but unused materials returned after treatment suggested that may not always have been the case.

7.4 DISCUSSION

The primary aim of this trial was to investigate whether varying the current intensity of MCT affects outcomes in chronic tennis elbow. Although mean improvements in outcomes consistently favoured Group A, the differences were rarely statistically significant. It is clear from the analysis that the study was underpowered for many of the tests. Effect sizes for differences between groups are generally small, as are the corresponding power values, and so there was significant risk of type II error – failure to identify a real difference (of 2.0 units) between the groups when one existed. The test for differences was close to significance for PRTEE function and total score changes by the second assessment, and it passed the significance threshold for improvements in the greyscale score by the final assessment. For other measures, it is not possible to state with confidence whether or not outcomes differed between the two groups. Treatment success rates were significantly in favour of group A at third and fourth assessments. By final assessment, the odds ratio suggests that treatment success was sixteen times more likely in group A than group B. Such a discrepancy is strongly suggestive of a real difference between groups in outcomes that are important to the patient.

The various prognostic indicators that were identified did not differ significantly between groups, and so could not account for the observed differences in outcome. Placebo might have influenced treatment effectiveness, but the same device was used by both groups. Group B received the higher current intensity and reported more sensory stimulation during treatment so the placebo effect might have been expected to favour that group. Yet group A saw greater levels of treatment success. Therefore, it is reasonable to suppose that the consistent pattern of better outcomes observed in that group on most variables represents a real difference. Although effects sizes tend to be small, the differences suggest that MCT does impact upon signs and symptoms of tennis elbow, but the sonographic data is less persuasive regarding structural change.

Although there were statistically significant improvements in most measures over the course of the trial, this cannot be taken as proof that MCT was the cause of those improvements, because the trial did not include a control group. Tennis elbow tends to resolve over time, and so some improvement would be expected even if no treatment were applied. However, if the treatment had no effect, no difference in outcomes would be expected between the groups because they did not differ on significant prognostic indicators. Since they differed significantly by final assessment, both on greyscale score improvements and treatment success rates, it appears that MCT does indeed influence these outcomes. The behaviour of each variable is now considered in more detail.

7.4.1 Tissue healing

The two outcome variables providing the most direct evidence regarding tissue healing are the sonographic greyscale and hyperaemia scores. Structural abnormalities - as quantified by the greyscale score - were mild in a majority of the participants, with no baseline scores greater than 5/12. This limited the scope of the scale to demonstrate improvement. Nevertheless, scores improved over time, and the largest effect size observed was between groups by the final assessment. Although the effect size was large, the absolute difference (1.1) was rather small. In fact, it is less than the minimum detectable change for the scale (2.0) calculated in the reliability study. The confidence interval for the mean difference includes the MDC value, and the variance observed in raw greyscale scores in this study was less than in the reliability study so that the observed mean difference may indeed represent a real change. However, the clinical significance of such a difference is unknown without histological comparison. Calculations using the change data at the second assessment suggest that a total sample size of 110 (55 per group) would provide a power of 0.8 to detect a real difference between groups at that time.

The presence and absence of tears and calcifications in the tendon did not appear to correlate with pain levels and global changes scores; and no significant sonographic changes appeared to accompany the two cases of symptom deterioration. Although the numbers of cases involved are too small to draw general conclusions, these observations suggest that structural changes in the tendon are not necessarily associated with pain levels, at least in cases of chronic tennis elbow. Other factors, such as neural and biochemical changes, may be more significant in determining symptoms.

On initial inspection, variations in hyperaemia scores appear erratic. No significant changes were detected over time or between groups, yet there is a noticeable pattern. Both groups

demonstrated initial rises in hyperaemia after treatment followed by a fall in the three weeks after treatment ceased, and then a further rise by final assessment. At the sensitivities of Power Doppler scanning typically available with equipment used in clinical trials, any detectable blood flow would be regarded as abnormal⁵⁵⁵. However, this does not mean that it is pathological. Rather, it may be a physiological response to tendon damage, since angiogenesis and concomitant increases in blood flow are integral to tissue repair²⁸⁵. Increased blood flow may therefore be a sign of a dormant repair process being re-stimulated. If normal healing resumes, blood flow would be expected gradually to tail off as the proliferative phase gives way to remodelling, the final stage of the process. The data show some consistency with this pattern, although the second rise in hyperaemia does not follow it. This might be explained by re-injury of the tendon in some cases, although none of the seven people in whom such rises were observed reported an obvious recurrence, and no other significant features (such as heavy upper limb use or not wearing a brace) were common among them. A further potentially significant feature arises from the fact that post-treatment assessments were often conducted a few days after treatment was completed. Hence, if the microcurrent was the cause of blood flow increases, the effect was sustained for some time after treatment was completed.

The patterns depicted in Figure 7.3(b) mask a range of individual responses across the whole sample. Intra-tendinous blood flow rose between baseline and first assessment in only 11 of 30 cases, and fell in four. It was unchanged in 14 cases (baseline data was unavailable for one person). Inspection of the data showed that most cases where increases were seen after treatment began with low hyperaemia scores, and all those with decreases had higher baseline blood flow levels. These apparent changes and differences in response could be artefacts, results of random variations or measurement error. On the other hand, individual responses to MCT may have been influenced by some other factor, such as the phase of healing. Blood flow levels change during the healing process: a high level may be a sign of normal neovascularisation that would be expected in the proliferative phase of repair, or it could be indicative of dysfunction at a later stage, when the number of neovessels would normally be expected to reduce. An effective therapy would evoke different responses in each case, depending on the initial status of the tissue. If such effects were occurring in this trial, aggregating data to test for whole group behaviour and inter-group comparisons may be inappropriate. It might account for the non-significance of changes in blood flow analysed at a group level, but the sample size means that sub-group analysis is not viable. This issue is revisited in the report of the second trial and pooled analyses in chapter 8.

If microcurrent was indeed responsible for the changes in blood flow, this raises a number of issues. In particular, how can microcurrent of a single intensity both stimulate and suppress blood flow? It may be that the tissue and cells themselves determine the response. As tissue structures and composition change during injury and healing, their electrical characteristics also change: the presence of more tissue fluid may decrease circuit impedance relative to the surrounding tissue and therefore change the path of applied current and the pattern of current density in the area. Tendinopathy is accompanied by a fall in tendon impedance⁶⁵¹ and so more of the available current would be taken than by a healthy tendon. Macrophage migration in a wound subjected to an electric field has been found to depend on the stage of healing⁷⁹. It is conceivable, then, that microcurrent might bring about different effects depending on the current status of the tissue and disposition of the cells. This is consistent with the findings of the literature review in Chapter 3, that microcurrent of constant intensity can promote quite different aspects of the tissue repair process, such as proliferation, die-back of granulation tissue and prevention of adhesions. Of course, even if microcurrent can both stimulate and suppress blood flow, it is not self-evident that the changes observed in this study are desirable; but they are at least consistent with a model of MCT enhancing the healing process as a whole, not merely one part of the cascade.

Several studies monitoring blood flow levels during treatment for tennis elbow have interpreted reductions in blood flow as an improvement in tissue status^{374, 389, 397, 516}. The argument presented here suggests that this may not be appropriate in all cases. Indeed, a therapy used with the intention of reducing hyperaemia - or more specifically neovascularity - may be contraindicated if an inadequate healing response rather than undesirable blood vessel formation is the problem. This underscores the potential importance of preliminary sonographic assessment to identify the nature of the problem.

The type of tendinopathy present in a particular case might also influence outcome. The composite greyscale score aggregates several forms of structural abnormality, such as calcification or fibrillar disruption, which could itself be secondary to micro-tears or degeneration. In this study, frank tears or signs of joint effusion were occasionally observed, but these were not included in the greyscale score. It may be that some forms of tendinopathy are more responsive to MCT than others, and analysis of outcomes based on different classifications of tendinopathy might provide insights in this matter.

7.4.2 Pain-free grip strength

The analysis of data for this outcome variable was marred by the problems experienced with the dynamometer. Use of the last-observation-carried-forward approach results in a flattening of the response curve for affected individuals and real changes that may have occurred are missed. This is likely to have decreased the calculated mean change values for both groups, since data from participants in each were affected, but the impact on the t-test results is difficult to assess. Imputation was only necessary for four of the final assessment readings, so the calculated changes over the full course of the study are likely to have been depressed only to a minor extent. The mean difference between baseline and final assessments in the better performing group A was 0.31, meaning that PFGS increased by 31% as a ratio of maximum grip strength on the unaffected side. The clinical significance of such a change is unclear – studies investigating the practical implications for the patient of particular levels of improvement have not been reported.

The mean difference between groups in improvements in PFGS by final assessment was 0.1, or a 10% difference between the ratios, which only just exceeds the minimum detectable change value identified in the reliability study. Therefore, although robust conclusions cannot be drawn on this outcome variable because of the low power of the test, the effect sizes for differences between group improvements are so small it seems unlikely there was any meaningful difference between them. In other words, varying the microcurrent intensity probably did not affect improvements in pain-free grip strength. The absence from the trial of an exercise programme focusing on increasing grip strength may have meant that any potential gains due to falling pain levels were not exploited. Had such exercise been incorporated into the treatment programme, any pain relief may have been accompanied by more substantial gains in PFGS.

Clearly, monthly checks on dynamometer calibration were insufficient in this context because the problem affected a significant percentage of the data analysed. However, the low power of the t-tests for grip strength is also a function of the large variance observed in the change scores and the small sample size, reduced still further by exclusion of those with bilateral symptoms and upper limb co-morbidities. Although the preliminary reliability study indicated that this measurement had excellent reliability with a narrow confidence interval, the experience of its use in this trial was less satisfactory. The standard deviation of the mean PFGS ratio in the reliability study with symptomatic participants was 0.24, compared to 0.33 in the baseline values in this study. The lower mean baseline score suggests that more severe presentations were included in the trial, which would contribute to the increased variance.

The limited information available from this outcome measure is unfortunate because it was one of the most objective measures used in the trial. However, this does not necessarily mean that PFGS should not be used in another study – larger effect sizes might well be observed between two other forms of MCT, or between MCT and another type of treatment.

7.4.3 Patient-rated tennis elbow evaluation

Improvements on the pain, function and total scores were observed in both groups over the course of the study. The baseline mean scores on each of these scales were equivalent to 36/100 for group A and 40/100 for group B - indicative of fairly mild presentations of the disorder (although severe presentations were also found in the sample). By final assessment, the pain, function and total scores had fallen respectively by 39%, 51% and 45% of their baseline values in group B and in excess of 70% in group A. Though substantial, the clinical significance of such changes in PRTEE scores has not been established. Studies conducted with single item numerical pain scales have suggested that changes of 30% are clinically significant, correlating with a global rating of “much better”^{652, 653}. Multiple-item pain scales may have lower clinical significance thresholds⁶⁵⁴. By the more conservative standard, changes on the PRTEE-pain scale were clinically significant for group A at both post-treatment and final assessment, and for group B by final assessment only.

If the patterns observed in Figure 7.3 were to represent real differences between group improvements, they would suggest that group A performed better than B initially, and that the scores converged in the longer term. Thus, a worthwhile acceleration in symptom alleviation might be occurring. It is difficult to judge the clinical significance of the different rates of improvement, but the greater change in pain score by first assessment in group A suggests a worthwhile advantage. Calculations with G*power using the computed effects sizes suggest a total sample size of at least 94 would be necessary to achieve a power of 0.8 in identifying differences between groups in pain score changes at either assessment. Fewer (58) would be required for adequate power at second assessment for total scores changes, but many more (276) for functional score changes.

Comparison with the treatment success criterion (based on reported GCS values), offers some useful insights into the significance of the change scores. Like the PRTEE, the judgement of treatment success was based on subjective scoring by the patient. Even though the absolute falls in PRTEE scores did not differ substantially between groups, the treatment success rates did so at all post-treatment assessments. Several factors may account for this apparent discrepancy:

- patients may judge levels of improvement by criteria other than those rated in the PRTEE. However, the instrument was developed specifically as a sensitive measure of change for tennis elbow and has been validated for this purpose. The fact that few participants were able to identify problematic activities other than those identified by the PRTEE suggests that it does have reasonable coverage of functional deficits.
- the lack of an item addressing average pain intensity over the last week may have reduced the PRTEE's sensitivity to change. Estimates of average pain levels in the preceding period is a common outcome variable in tennis elbow trials^{332, 401, 406, 429-437}. Items addressing worst and least pain over the preceding week do not provide the same information. Thus, the PRTEE may be unable to distinguish between two people with the same maximum and minimum levels but very different average pain levels.
- there may be threshold scores on the PRTEE that are significant in themselves for a patient. Thus, as long as the score falls below that threshold, the patient may judge that a significant improvement has occurred, irrespective of the baseline score.

A study that used an anchor-based approach, correlating PRTEE scores with performance on another outcome measure whose clinical significance is already established, could help resolve the issue, but none has yet been reported. Using the global change score as the comparator offers the benefit of a measure whose clinical significance is reasonably straightforward to interpret; but it has the disadvantage of being a purely patient-rated measure – triangulation with an independent measure (such as a clinician rating of success) would increase the credibility of findings.

The charts suggest that pain and function scores followed similar trajectories over time, which is not surprising given that pain was the factor reported by participants as having the greatest impact on activities of daily living. It is likely that, at least in chronic cases, strength losses would follow any reduction in use of the affected limb to avoid painful movements, and so functional deficits may follow. Rates of change were not identical on these subscales however, and this confirms that they were not measuring the same thing.

7.4.4 Patient-specific functional scale

The problems associated with the use of the PSFS were surprising, since it was assumed that all participants would be able to identify at least one additional activity that caused them difficulty. This was not the case. Several of those who were able to identify an activity appeared to find it difficult to rate it consistently, and in many cases the values given were quite at odds with their subjective descriptions of symptoms and their global change ratings. In the study from which the PSFS originated⁵⁴⁰, participants were informed of the numerical rating they had assigned to each item at baseline assessment. The authors speculated that its reliability might be reduced if respondents were unaware of their previous ratings, as was the case in this trial. Guidance on this point is not commonly given by the originators of subjectively-rated scales – none was provided in the PRTEE manual⁵³⁹. If blinding to previous scores reduces the reliability of a scale, this measure may have been similarly affected. Most PRTEE reliability studies have used test-retest periods of two days or less^{355, 457, 655, 656}, so memory bias may have led to inflated estimates of reliability. In this study PRTEE scores appeared broadly consistent with subjective accounts and global ratings, but their reliability – and consequently their responsiveness – may have been reduced by blinding to previous scores. This seems to have occurred with the PSFS.

7.4.5 Global Change rating

As noted previously, tennis elbow is a multidimensional syndrome: very different combinations of tissue damage, sensorimotor deficits and pain behaviour may present in a sample of people with the same diagnosis³⁸¹. Individual outcome variables such as PFGS and function scales cannot encompass the totality of the disorder, which is why several measures were selected for this trial. The global change score is arguably one of the most significant outcome variables precisely because of its non-specificity. Its dependence entirely on patient-rating may be seen as a disadvantage, and it cannot fully compensate for the relatively poor performance of some of the other outcome measures. Its value might have been enhanced if it had been supplemented with a clinician-rated global change score. However, these caveats do not detract from the value of a patient-centred measure that expresses opinion on the totality of the experience of the disorder.

The levels of treatment success noted in group A immediately after treatment, and the significant differences in success rates at subsequent assessments, along with odds ratios substantially in favour of group A, provide strong evidence that the two forms of MCT differ in their impact. Deciding on the clinical significance of differences in success rates is rather

arbitrary, but a criterion of a 25% difference has been suggested^{332, 333}. Using this benchmark, the differences between groups A and B were clinically significant at third and fourth assessments (6 and 15 weeks after baseline). This is consistent with some members of group B having suffered a relapse by third assessment, which also depressed the group's subsequent success rate. The effect sizes at these times, represented by the odds ratio in this study, are substantial and suggest that the treatment provided to group A was considerably more effective than that given to group B.

Reconciling the substantial differences between group success rates with the much smaller differences apparent between them on PFGS improvements is not straightforward. A combination of problems with the dynamometer, small sample size and large variance may have led to an unreliable impression of the differences between groups. It could also be that – where grip strength reductions due to pain are fairly mild – improvements in the PFGS ratio play only a small part in the patient's perception of their condition. However, this begs the question: what other factor or factors determine the judgement of significant improvement in the condition? Perhaps the gripping movement used with the dynamometer does not adequately model those that are used in normal functional activities. Maybe resting pain, rather than pain on gripping, was the dominant feature for some participants. The issue remains unresolved.

7.4.6 Patient experience

The treatment was generally positively regarded by participants. Judging by the diary sheets, compliance was very good. This form of MCT offers the potential attraction of control over various elements of the treatment (e.g. time and location), combined with an essentially passive experience that required relatively little effort on the user's part. Given these features, a longer treatment period might well be feasible. However, if the treatment had also involved an exercise programme, compliance with both may have decreased. This could be a challenge, were MCT to be trialled as part of a broader management strategy.

Reported adverse events were mostly transient but occasionally unpleasant sensory stimulation. The two cases of mild shocks delivered by the device were concerning, given that it had the CE mark of health and safety approval, and the supplier was informed of these events. Both cases were from group A, who were receiving only 50 μ A treatment, so it is probable that the shocks were due to contact with the USB socket rather than the treatment output sockets. It seems unlikely that the case of bilateral leg tingling (in Group B) could reasonably be attributed to microcurrent stimulation received some hours previously.

Sensations reported with the 500 μ A current appeared similar in nature to those experienced with Transcutaneous Electrical Nerve Stimulation (TENS). Some users (though none in this study) may find these sensations unpleasant and MCT at this intensity might be unsuitable for them. Although TENS is used for analgesia, the greater reductions in PRTEE pain scores seen in group A (where sensory stimulation was rarely experienced), suggest that a different mechanism is responsible for pain relief by MCT – see section 9.3 for further discussion of this issue.

7.4.7 Is MCT more effective than wait-and-see?

The significant test results obtained for variables suggests that outcomes differed between the treatment groups. This implies that MCT was responsible for at least some of the observed change. Both groups improved on most of the measures, but the trial itself could not test whether MCT produces significantly better outcomes than if no treatment had been received. This question can be addressed by comparisons with data from other trials that involved a minimal intervention group. No such data is available for the primary outcome measures of tissue change, but comparative data has been published for several of the other variables used in this study. The same definition of treatment success was used in two other trials that involved “wait-and-see” groups^{332, 333}. They received advice, and were allowed ad lib analgesia and brace use, as in this study. The success rates for these groups were 27% and 32% at six weeks after baseline and 55% and 60% at 12 weeks after baseline, respectively. Group A rates (albeit at 6 and 15 weeks) compare favourably with these, comfortably exceeding the 25% clinically significant difference criterion. In the comparator trials, success rates for both minimal intervention and active physiotherapy groups reached 80-85% by 26 weeks, compared with 93% by 15 weeks in group A of this trial. Thus the speed of recovery was superior with MCT. Group B performed poorly on all these comparison, however.

Caution is required in interpreting these comparison. The baseline PFGS ratios and measures of functional disability in the minimal intervention groups suggested that they began with more severe presentations. On the other hand, the comparator studies excluded those with bilateral symptoms, peripheral nerve involvement and a range of upper limb co-morbidities. Such characteristics were common in this trial, and may have depressed success rates compared to the other studies. Hence, there is strong evidence that varying current intensity affects global outcome, and limited evidence that one form of MCT produces a clinically significantly better global outcome than a minimal intervention approach over the specified periods.

Data for minimal intervention groups in several studies are also available for other outcome measures used in this trial. The two studies cited above^{332, 333} measured improvements in mean PFGS ratio values of 50% and 110% of baseline values by 12 weeks. Two other trials measuring raw PFGS scores (rather than PFGS/MGS ratios) in no-treatment groups saw percentage improvements of more than 35% over 12 weeks in one study⁴⁴³ and less than 10% over 7 weeks in another⁴¹⁵. These compare with changes in group A mean PFGS ratios of approximately 15% of baseline by 6 weeks and 50% by 15 weeks. The wide variety of outcomes in the comparator studies presumably reflect different sample characteristics. It seems unlikely that MCT would produce substantially worse improvements in PFGS than no treatment at all, and the problems experienced in dynamometry may account for the apparently poor performance in this trial compared to the best of the others. The variance observed in mean PFGS ratios in this trial (SD = 0.34 at baseline) was high compared to that reported in one of the other studies (SD = 0.22)³³³.

One trial also used the PRTEE as an outcome measure⁴¹⁵ with a minimal intervention group, and recorded changes of 6%, -10% and 4% of baseline pain, function and total scores at 7 weeks. These compared to improvement of over 50% of baseline values on all three scales by 6 weeks in group A of this trial. Relevant information, including symptom duration and a description of the minimal intervention, was absent from the report of the comparator trial and so the groups may have differed in important respects.

Taken together, these comparisons provide limited evidence that using low frequency monophasic MCT of 50 μ A peak current intensity can produce outcomes superior to those obtained from a minimal intervention study.

7.4.8 Study limitations

A number of limitations have already been identified in the conduct of this trial. Perhaps the most significant is that it was underpowered for many of the tests. A combination of rather small effect sizes in some cases and large variances in others, meant that there was limited statistically significant evidence of differences between the groups. The possibility of type II error is evident from the small effect sizes observed. However, significant differences were apparent for the greyscale sonographic score, a primary outcome variable, and the global change score, whose clinical significance is straightforward to interpret.

Inherent in the design of the study was its inability to prove whether MCT was more effective than any other form of management, including minimal intervention. The comparison studies provided the opportunity for some cautious inferences to be made on this question, but the sample size calculated based on the differences in success rates refer only to clinical outcomes and may underestimate the sample required to detect differences in sonographic scales. Those sonographic scales have not been validated, and may not have been responsive enough to register significant changes in tissue status. The aggregation of scores for separate elements increased the number of levels available on the scale but, since all included cases had baseline scores in the lower half of the scale, its scope for detecting changes greater than the MDC was limited. Had the sample contained more severe presentations, the scale may have been more fit for purpose. The lack of more severe cases may have been a result of the method of recruitment – via local advertising rather than through clinics or GP referrals. It may be that potential participants with worse symptoms were already receiving treatment elsewhere. The revision of the greyscale abnormality grading system was intended to increase its reliability, but this was not tested. The inter-rater reliability of the revised scale should be evaluated before use in any other studies.

Several measures could have improved the methodological quality and value of the trial. The randomised list for group allocation could have been generated and held by a person independent of the study to ensure the investigator was blind to allocation. Protocol choices that were based on pragmatic considerations – such as the inclusion of participants with upper quadrant co-morbidities and the lack of control of brace use - may have increased the generalisability of its findings; but they also diminished its capacity to establish a clear cause-effect relationship between independent and dependent variables and may have reduced treatment effect sizes. A longer assessment period may have increased the chances of significant greyscale changes becoming evident, and would have enabled longer term outcomes to be monitored. Although the treatment period was justified on pragmatic

grounds, it was shorter than those found most effective in the bone and skin trials reviewed earlier, and potential benefits of longer treatment times may have been missed. Likewise, the absence of an exercise-based co-intervention – whilst justified on pragmatic grounds – meant that the value of MCT as an adjunct treatment was not considered. Several of these issues are addressed in Chapter 9 when a proposal for a full-scale trial protocol is presented.

The generalisability of findings may be threatened by differences between this study sample and the wider population of people with tennis elbow. The mean age, gender balance, and proportions of participants with bilateral symptoms, dominant arm affected, and attribution of symptoms to sporting involvement appears similar to that observed in epidemiological studies and reviews^{285, 530, 619}. On the other hand, the proportions reporting attribution of symptoms to work activities is somewhat lower than reported in some reviews (30-45%^{339, 530} compared to 13% in this study). There is no direct evidence that this affects outcomes, although those who continue in heavy manual work tend to have worse outcomes^{336, 338} or recover more slowly⁶³¹.

7.5 CONCLUSION

The statistically significant differences and associations detected in this trial suggest that at least one form of treatment appears capable of resolving symptoms more rapidly than a minimal intervention approach; used as an adjunct treatment, MCT may provide more substantial benefits. The evidence for its contribution to tissue healing was mixed. Some greyscale changes were seen over a period of weeks in individual cases, but group trends only became apparent in the longer term, over several months. The changes over time may not have had any clinical significance, and the differences between groups were minor. On the other hand, if the patterns of change in hyperaemia were real, they would suggest a potentially significant physiological effects of MCT. This is worth pursuing, because the data could enhance understanding of the role of bioelectricity and microcurrent in tissue repair. Differences in response observed between individuals suggest that secondary sub-group analysis may be informative. Certainly, further investigation of the apparent patterns of change is warranted because they may have important consequences for the choice of treatment in particular cases. They may also contribute to apparently non-significant group differences in trials where other forms of treatment for tennis elbow are being evaluated. These issues are considered again in the pooled analysis reported in section 8.6.

Because of the lack of available comparable sonographic data, it is uncertain whether the changes observed might have happened without MCT. However, it seems unlikely that the patterns of change observed in hyperaemia would have occurred without any treatment. The potential role of these changes in the healing process have been discussed, but their implications for both tissue repair and clinical outcomes have yet to be explored. Obtaining human tissue samples to assess the impact of MCT on tissue structures would present methodological challenges and ethical concerns; animal studies are probably more feasible. Microdialysis could provide indirect evidence by monitoring the presence of chemical factors involved in matrix and vascular structural changes⁶⁵⁷. The most practical implication of these findings may be to inform further debate about the bioelectric components tendon healing, although the sonographic data provides at least limited evidence that MCT can impact upon the healing process in chronic tennis elbow. However, the differences observed between groups are insufficient to infer that one current intensity has more impact on healing than the other.

The significant changes over time and differences between groups observed in treatment success rates, suggest that MCT can promote resolution of symptoms, and that MCT with the stated parameters is more effective in doing so at 50 μA than at 500 μA amplitude. The most convincing evidence for this conclusion comes from the treatment success rates. The other measures - indicating consistent but non-significant difference in favour of Group - are mostly dependent on patient opinion. The case would be strengthened if significant differences were seen in more objective measures, and a full trial protocol should certainly include at least one.

This trial compared the effects of two current intensities and established that the lower intensity produced the better outcome. As the literature review indicated, many other parameters may also be varied, but little is known about whether they too can be optimised for maximum benefit. Trials comparing the effects of varying these other parameters might enable more precise definition of the therapeutic window. It could be, for example, that the effects of lower intensity microcurrent are enhanced by selection of a particular waveform. The possible combinations are limitless but, given the findings of this study, it would be useful to compare the effects of treatments that deliver similar low intensity current, but differ on at least one other parameter. Conducting another trial with a similar protocol would enable pooling of data from both studies, to make multiple comparisons and explore new avenues of analysis. It would also provide further experience to inform development of a fully powered controlled trial. This work is the subject of the next chapter.

Chapter 8

Further clinical evaluation of microcurrent treatment

8.1 INTRODUCTION

During recruitment for the trial reported in chapter 7, it became apparent that more participants would be available that were required by the protocol. Therefore it was decided to conduct a further trial, comparing the effectiveness of two other forms of MCT. The WeWoThom and the Synapse Tendonworks, which were judged suitable for use in a clinical trial by the laboratory evaluation reported earlier (see section 5.4.1), were selected for the purpose. They deliver similar currents - of the order 25 μ A - for at least part of the treatment time, but their parameters differ in several other respects, including waveform and treatment duration. Hence, this trial compared two different sets of MCT parameters. The Tendonworks is specifically marketed to promote tendon healing and its parameters are based on (but not identical to) those found effective in a trial of MCT for Achilles tendinopathy²⁵¹. The parameters of the WeWo are based on studies (not published in English - see Table 5.1 for source) suggesting that they can reduce musculoskeletal pain and promote microcirculation and tissue healing.

As well as comparing the effects of these two devices, the trial considered adverse events, patient acceptability and ease of use in clinical practice. It was expected that a comparison of outcomes with those of the first trial would provide additional insights into the relative effectiveness of different forms of MCT. Although the two trials were distinct in their recruitment periods, their protocols were similar and their participants were drawn from the same sources, so it was envisaged that pooled analysis of data would be possible. This chapter reports the second trial and the pooled analysis that followed it.

8.2 TRIAL PROTOCOL

The aims of the trial were the same as in the previous study, except that the comparison was between two forms of MCT that varied in several parameters. The WeWo Thom supplied a

nominal 25 μA high frequency balanced biphasic current for six hours; the Tendonworks delivered a three phase programme, with a low frequency monophasic waveform of average intensity 20 μA for 20 of the total 30 minutes. The microcurrent parameters of both devices are described in more detail in section 5.4.1. Treatment with the WeWo Thom was given once daily for three weeks. The Tendonworks required a more complicated schedule, with five days of treatment followed by two days off, repeated for three weeks. In the first week, three treatments per day were given, in the second week there were two treatments per day, and in the third week one treatment per day. Participants were asked to spread these treatments through the day, with a minimum of two hours between each. In addition, the supplier of this device recommended that, before cleaning the skin, it should be gently abraded using a strip of fine sandpaper to remove part of the stratum corneum and so aid electrical conduction. Participants in both groups were asked to do this. Both devices were considerably smaller than the Elexoma Medic, and were held in place during treatment either with surgical tape or a loosely fitting tubular bandage. In all other respects, the experimental protocol was the same as used in the previous trial. Approval for the study, a copy of which appears in Appendix 6, was provided by the investigator's institutional ethics committee, and the trial was registered on www.clinicaltrials.gov (identifier: NCT00905736).

8.3 TRIAL RESULTS

Between May 2009 and August 2009, thirty one eligible participants were allocated into the two treatment groups: group C used the WeWoThom and group D used the Tendonworks. Because the supply of some of the latter devices was delayed, random allocation was not fully realised, and the majority of early enrolled participants were assigned to group C. Once the other device became available, random allocation was re-instituted. Inspection of treatment diaries suggested that all participants completed the allotted number of treatments, apart from one person in each group who missed one treatment each, and two from group D who added two treatments each by mistake. Apart from the two people who received two extra treatments, all participants completed the course of treatment in the allotted 3 weeks. One person in group D was unable to attend one of the follow-up sessions, and the missing data for this case was imputed by carrying forward the last set of data. Figure 8.1 demonstrates the flow of participants through the trial.

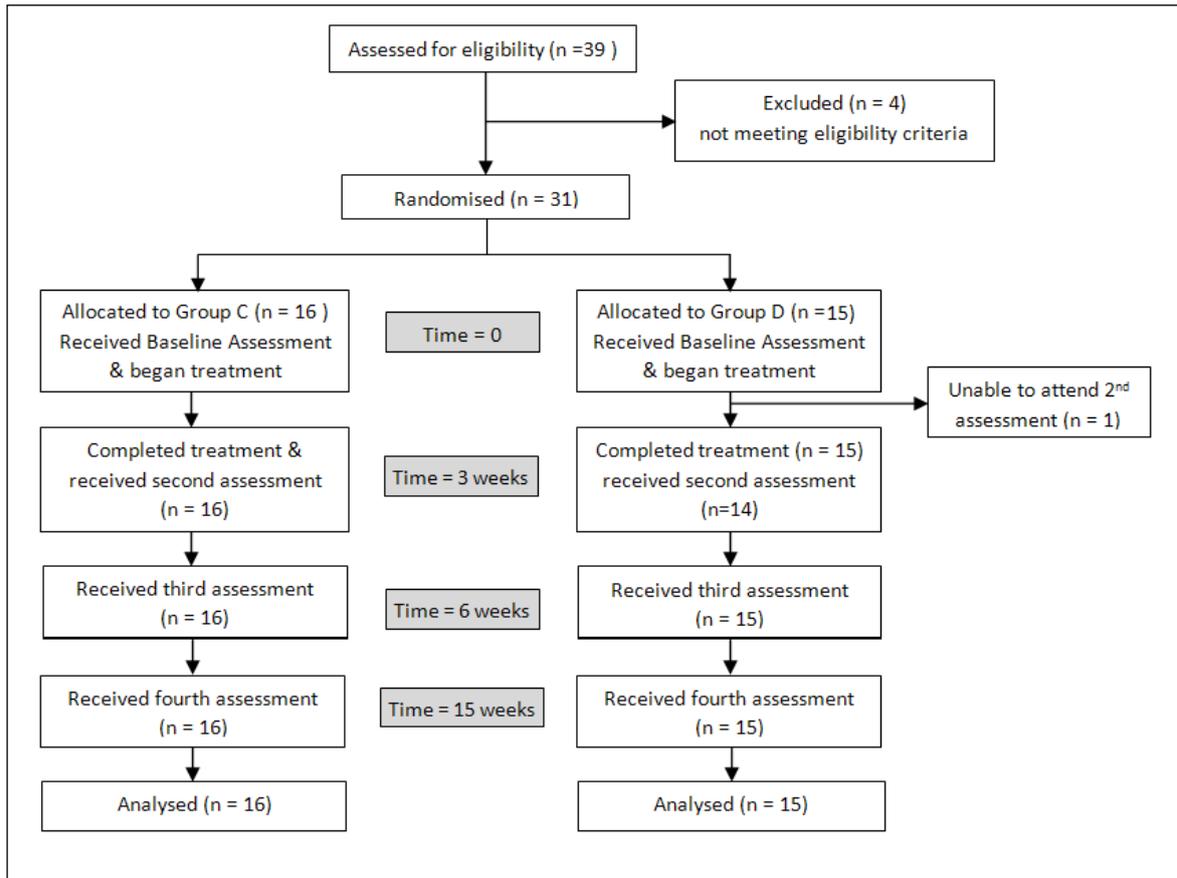


Figure 8.1: Flow chart of participants through second trial

Baseline characteristics for those included in the analysis are given in Table 8.1. Twelve people thought racquets or other sports or were the main cause of the disorder; eight thought it was due to an unaccustomed load; three said it was work-related, one thought it followed trauma, and seven reported no obvious cause. One person in group C had taken sick leave as a result of the current episode. Eighteen people reported ongoing heavy upper limb use during the trial, either because of work activities or competitive sports. Only two of these from group C and one from group D reported using a tennis elbow brace of some kind during the trial. On initial assessment, a half of the whole sample showed signs of radial nerve sensitisation by reporting abnormal sensation in the upper limb on ULTT2B. In eleven cases the test produced pain at the lateral elbow. Three people had bilateral symptoms and five had co-morbidities potentially affecting grip strength measurements so their data for this variable was excluded from the analysis.

As in the previous trial, the use PSFS was unsatisfactory. Fifteen of the 31 participants were unable to identify an activity that caused them difficulty and which was not already listed in the PRTEE. Of those who did, only five were able to provide scores for the selected activities

at every assessment, and no statistical analysis was attempted. Because this trial overlapped with the first, the dynamometer leak also affected data in groups C and D and 23% of the grip strength data in this trial had to be imputed as a result. As before, the last observation carried forward approach was used for imputation of missing data.

Table 8.1: Baseline characteristics of participants included in analysis (PRTEE pain score converted to a score/100)

Group	C	D
n	16	15
Females (n)	9	9
Age mean ± SD (range)	50±4.5 (42-61) years	54±7.7 (43-69) years
Arm dominance (n)	13 Right; 3 Left	11 Right; 4 Left
Dominant arm affected (n)	12	10
Median duration current episode (range)	8 (3-48) months	6 (3-60) months
History of previous episodes (n)	3	8
Ongoing heavy upper limb use (n)	7	7
Positive to cervical tests (n)	10	2
ULTT2B caused lateral elbow pain (n)	7	3
Greyscale total score mean ± SD (range)/12	2.9±1.6 (1-6)	3.4±1.6 (1-6)
Hyperaemia score mean ± (range)/4	1.9±1.1 (0-4)	1.9±0.8 (0-3)
PRTEE pain score mean ± SD (range)/100	46±16 (20-96)	42±15 (16-64)
PRTEE function score mean ± SD (range)/100	34±19 (0-66)	34±18 (10-70)
PRTEE total score mean ± SD (range)/100	40±16 (15-78)	38±17 (14-67)
PFGS/MGS mean ± SD (range)	58±28 (5-96) %	59±33 (11-118) %

Data were inspected with descriptive statistics and baseline variables were compared between groups. Symptom duration was not normally distributed, and neither was the sonographic greyscale score (skewness in group C=0.691, in group D=0.148). Levene's test suggested equality of variance between groups on age ($p=0.115$), sonographic greyscale score ($p=0.909$) PFGS ratio ($p=0.621$), PRTEE pain, function and total scores ($p=0.541$, $p=0.833$, $p=0.577$ respectively) and duration of current episode ($p=0.420$). Tests of baseline equivalence between groups, using parametric and non-parametric procedures as appropriate (see tables 8.3 – 8.5), showed no significant differences for any variable, apart from a positive response to cervical clearing tests, which occurred significantly more frequently in group C than group D. Five cases of outliers were identified in baseline values of outcome variables. Each group had two cases with greyscale scores of 6/12 and one case

in group C had PRTEE pain and total scores above the upper quartile for the group. Re-analysis excluding these cases did not materially alter any of the test results reported below.

Table 8.2: Shapiro Wilk test for normality of selected variables

Variable	Group	Test result	df	sig
Age	C	0.908	16	0.108
	D	0.944	15	0.437
Duration current episode	C	0.767	16	0.001
	D	0.602	15	0.000
Sonographic greyscale score	C	0.878	16	0.036
	D	0.874	15	0.039
PRTEE (Pain)	C	0.856	16	0.017
	D	0.954	15	0.585
PRTEE (Function)	C	0.962	16	0.706
	D	0.946	15	0.465
PRTEE (total)	C	0.963	16	0.715
	D	0.959	15	0.677
PFGS ratio*	C	0.944	12	0.555
	D	0.970	11	0.889

* homogeneity of variance not assumed

8.3.1 Baseline comparisons

Table 8.3: Independent samples t-test for baseline differences between groups on continuous data

Variable	t	df	sig
Age	-1.629	29	0.404
Duration current episode*	-0.358	24.5	0.723
Sonographic greyscale score	-0.906	29	0.372
PRTEE (pain)	0.848	29	0.404
PRTEE (function)	-0.060	29	0.953
PRTEE (total)	0.393	29	0.698
PFGS ratio	0.053	21	0.958

* homogeneity of variance not assumed

Table 8.4: Mann Whitney test for baseline differences between groups on non-parametric data

Variable	U	sig
Duration current episode	111.5	0.754
Sonographic greyscale score	96.0	0.330
Sonographic hyperaemia score	111.0	0.957

Table 8.5: Pearson's Chi-square test for baseline differences between groups on dichotomous data

Variable	χ^2	sig
Females	0.045	1.000
Dominant arm affected	0.860	0.433
History of previous episodes	1.551	0.285
Ongoing heavy limb use	0.285	0.724
Use of brace in study	0.008	1.000
Positive to cervical tests	7.888	0.009
ULTT2B causes lateral elbow pain	1.998	0.252

8.3.2 Analysis of outcome variables

Summary outcomes data for each group are provided in Table 8.6, and charts illustrating the variation of outcome measures over time in the two groups are presented in Figures 8.2 and 8.3. Analyses were conducted to establish whether there were significant changes in the outcome variables over time, and significant differences between group outcomes at follow-up assessments. Table 8.7 summarises the results of repeated measures ANCOVAs conducted with interval and ordinal scales for all follow-up scores, with time as the main effect, treatment group as an interaction effect, and baseline score as covariate. With the exception of the hyperaemia score, Mauchly's test indicated homogeneity of variance for every variable, and Levene's test of error variance showed no significant differences across assessments for any variable.

Table 8.6: Summary outcome data for Groups C and D at all time points

Variable	Mean score \pm s.d.	
	Group C	Group D
Greyscale Score / 12		
Baseline	2.9 \pm 1.6	3.4 \pm 1.6
3 weeks	2.8 \pm 1.4	3.2 \pm 1.5
6 weeks	2.5 \pm 1.4	3.3 \pm 1.7
15 weeks	2.2 \pm 1.4	3.1 \pm 1.6
Hyperaemia Score / 4		
Baseline	0.8 \pm 1.3	1.0 \pm 0.9
3 weeks	2.6 \pm 1.0	2.2 \pm 1.1
6 weeks	2.4 \pm 1.0	2.0 \pm 0.9
15 weeks	2.3 \pm 1.3	2.0 \pm 1.1
Pain-free Grip Strength ratio / %		
Baseline	0.57 \pm 0.26	0.68 \pm 0.32
3 weeks	0.56 \pm 0.27	0.71 \pm 0.31
6 weeks	0.76 \pm 0.26	0.82 \pm 0.46
15 weeks	0.93 \pm 0.28	1.13 \pm 1.04
PRTEE (pain) / 50		
Baseline	23 \pm 8	21 \pm 8
3 weeks	15 \pm 7	17 \pm 8
6 weeks	11 \pm 8	15 \pm 10
15 weeks	10 \pm 9	11 \pm 10
PRTEE (function) / 50		
Baseline	17 \pm 10	17 \pm 9
3 weeks	10 \pm 7	14 \pm 11
6 weeks	9 \pm 9	12 \pm 10
15 weeks	7 \pm 8	8 \pm 9
PRTEE (total) / 100		
Baseline	40 \pm 16	38 \pm 17
3 weeks	25 \pm 14	31 \pm 19
6 weeks	20 \pm 16	26 \pm 19
15 weeks	16 \pm 16	19 \pm 18
Treatment success / %		
3 weeks	25	33
6 weeks	38	53
15 weeks	75	73

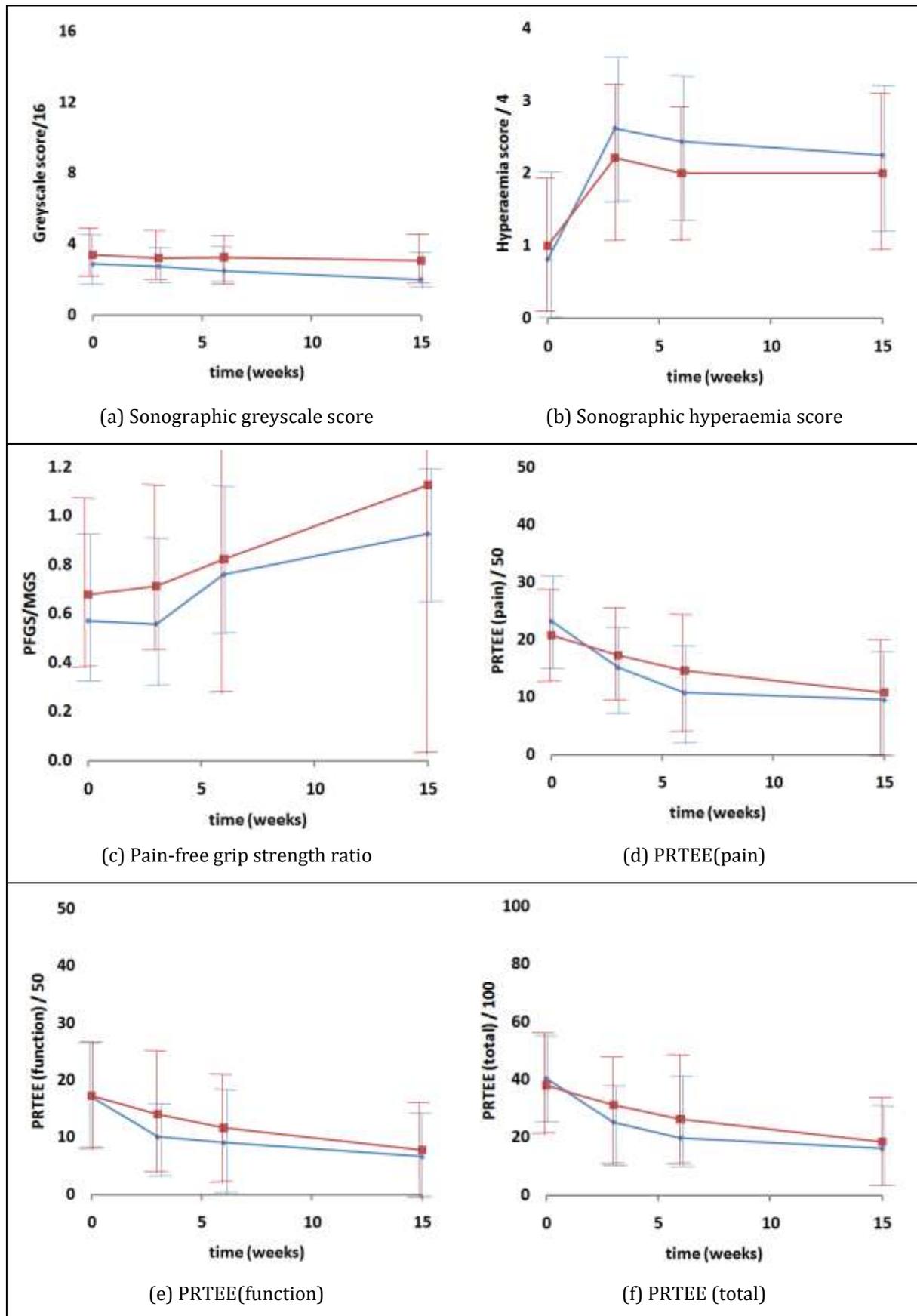


Figure 8.2: Variation of outcome measures in —●— Group C —●— Group D

Table 8.7: Repeated measures ANCOVA for time*group interactions for groups C and D, with baseline score as covariate

Within-subjects time*group interactions			
	df	F	p
Greyscale	2, 54	2.39	0.101
Hyperaemia	2, 52	0.25	0.781
PFGS	2, 40	1.08	0.351
PRTEE-Pain	2, 56	11.03	0.540
PRTEE-function	2, 56	0.603	0.551
PRTEE-Total	2, 56	47.55	0.492

There were no significant interactions between group and time for any variable. The results of independent samples t-tests, conducted on changes in variables at second and final assessments, are presented in tables 8.8 and 8.9 respectively. They found no significant differences between groups in changes of score on any variable, although calculated power values were low, suggesting that the risk of type II error was high. The mean differences between groups were small for all variables, although the confidence intervals were broad and included MDC values for greyscale and PFGS scores.

Table 8.8: Independent samples t-test for differences between groups C and D on change scores at second assessment

	t	df	p	Mean diff (99%CI)	effect size	power
Greyscale*	-1.464	15.0	0.164	-0.13 (-0.38, 0.13)	0.54	0.30
Hyperaemia	.789	27	0.437	0.30 (-0.76, 1.37)	0.31	0.13
PFGS	-1.039	21	0.310	0.05 (-0.17, 0.07)	0.43	0.17
PRTEE-Pain	-1.651	29	0.110	-4.60(-12.27, 3.08)	0.60	0.36
PRTEE-function	-0.242	29	0.811	-0.94(-11.63, 9.76)	0.09	0.06
PRTEE-Total	-1.600	29	0.120	-8.26(-22.50, 5.97)	0.58	0.34

* equality of variance not assumed

Table 8.9: Independent samples t-test for differences between groups C and D on change scores at final assessment

	t	df	p	Mean diff (99%CI)	effect size	power
Greyscale*	-1.480	24.2	0.152	-0.54 (-1.56, 0.48)	0.54	0.29
Hyperaemia	0.781	28	0.441	0.31 (-0.79, 1.42)	0.28	0.12
PFGS	0.556	21	0.584	0.06 (-0.25, 0.37)	0.23	0.09
PRTEE-Pain	-1.034	29	0.310	-3.69 (-13.5, 6.14)	0.37	0.17
PRTEE-function	-1.249	29	0.222	3.70 (-11.87, 4.47)	0.50	0.22
PRTEE-Total	-0.656	29	0.517	-4.60 (-22.89, 5.70)	0.24	0.10

* equality of variance not assumed

The tests showed no significant differences between groups in improvements on any variable at either time point. Table 8.10 compares greyscale changes between groups at final assessment; no correlation between group and score change was found (tau-b = 0.24, exact sig = 0.19).

Table 8.10: Greyscale score change between baseline and final assessment in groups C and D

Group	Greyscale Score change				
	-4	-3	-2	-1	0
C	1	1	2	3	9
D	0	0	2	1	12

Two cases in group C had evidence of frank tears, both which healed by final assessment; two cases of tears were apparent in group D - only one of these healed during the study, but the other reported full recovery by final assessment. There were nine cases of calcification of grade 2 or above at baseline - one in group C and eight in group D. Only one of these (in group D) showed any signs of resolution during the trial. Six reported being much better by final assessment, two somewhat better, and one unchanged.

Related samples t-tests were conducted to calculate the effect size of the treatment between baseline and final assessment for each group. Results, along with effect sizes for each variable are presented in tables 8.1 and 8.12.

Table 8.11: Related samples t-test for differences in scores between baseline and final assessment for group C

	t	df	p	Mean diff (95%CI)	effect size
Greyscale	-2.78	15	0.014	-0.88 (-1.55, -0.20)	0.70
Hyperaemia	1.1	15	0.289	0.31 (-0.29, 0.92)	0.27
PFGS	4.28	11	0.001	0.28 (0.14, 0.42)	1.24
PRTEE-Pain	-4.71	15	<0.001	-13.69 (-19.87, -7.50)	1.18
PRTEE-function	-3.41	15	0.004	-10.44 (-16.96, -3.92)	0.85
PRTEE-Total	-4.36	15	0.001	-24.06 (-35.84, -12.29)	1.09

Table 8.12: Related samples t-test for differences in scores between baseline and final assessment for group D

	t	df	p	Mean diff (95%CI)	effect size
Greyscale	-1.78	14	0.096	-0.33 (-0.73, 0.07)	0.46
Hyperaemia	<0.001	13	1.0	0 (-0.56, 0.56)	0
PFGS	2.52	10	0.030	0.22 (0.03, 0.41)	0.76
PRTEE-Pain	-5.02	14	<0.001	-10.0 (-14.3, -5.7)	1.30
PRTEE-function	-4.09	14	0.001	-9.5 (-14.5, -4.5)	1.04
PRTEE-Total	-4.65	14	<0.001	-19.5 (-28.4, -10.5)	1.20

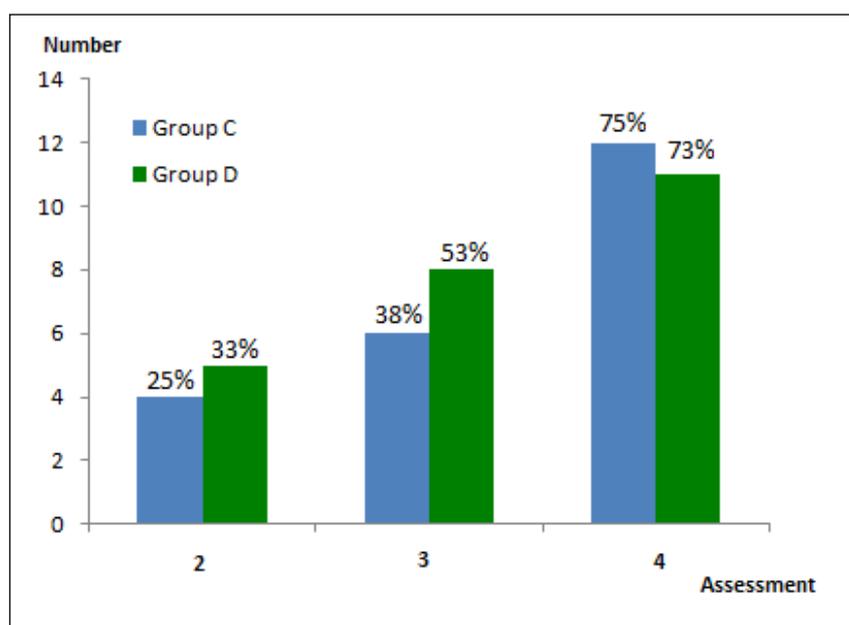
Improvements were seen in both groups on all measures except hyperaemia which, as argued previously, is not necessarily an indicator of pathological severity. In all cases, the improvements were greater in group C than group D, although the differences between groups were not statistically significant and diminished by final assessment. Changes in PFGS and PRTEE scores were significant for both groups; for greyscale scores only group C saw significant change, although in group D the change was close to the significance threshold. Hyperaemia changes were not significant in either group. The calculated power of the test for the greyscale score in group D was 0.5. For hyperaemia, it was 0.17 in group A and zero in group B. Wilcoxon's signed ranks, conducted with the ordinal scales as an additional check for significant change between baseline and final assessment (see Table 8.13), were consistent with the findings of the related samples t-tests.

Table 8.13: Wilcoxon's signed ranks for changes between baseline and final assessment in ordinal variables with groups C and D

Variable	Group C		Group D	
	Z	Exact Sig	Z	Exact Sig
Greyscale	-2.4	0.016	-1.6	0.250
Hyperaemia	-1.1	0.371	-0.3	1.0
PRTEE-Pain	-3.3	<0.001	-3.1	0.001
PRTEE-function	-2.6	0.008	-3.0	0.001
PRTEE-Total	-3.2	0.001	-3.2	<0.001

Following the finding of different blood flow responses apparent in the first trial, patterns were response in this trial were inspected. In group D, hyperaemia changed by one grade at most, compared to up to 3 grades in group C. In group D, blood flow was seen to increase in seven cases (including two with initial scores of 3), and decrease in two. In group C, responses were similar to those observed in the previous trial, with increases only observed in those with low initial scores, and decreases only seen in those with higher initial scores.

The numbers of successful treatments and associated success rates at follow-up assessments are shown in Figure 8.3. There were increasing numbers of successes in both groups at each assessment, with group D initially outperforming group C, but rates were nearly equal by final assessment. No deteriorations in symptoms were reported in either group.

**Figure 8.3: Number of successful treatments and success rates for groups C and D**

Chi square values and odds ratios calculated for each post-treatment assessment (see Table 8.14) show non-significant associations between group and success rates at all three time points. Fischer's Exact test at times 2 and 4, when expected cell counts were not reached, confirmed these findings.

Table 8.14: Differences in success rates and odd ratios for success in groups A and B

Assessment	χ^2	Exact Sig	Odds ratio (95%CI)
2	2.6	0.454	1.5 (0.32, 7.1)
3	0.8	0.479	1.9 (0.45, 8.0)
4	0.01	1.0	0.9 (0.18, 4.6)

8.3.3 Adverse events and side effects

Group C

One person reported tingling in the forearm during the first few treatments. Three people experienced mild erythema under both electrodes, which quickly resolved after each treatment; in the others it was attributable to overzealous use of the sandpaper in skin preparation.

Group D

Nine people reported tingling, two saying it felt strong at times. One person experienced numbness in little and ring fingers during one treatment, one felt post-treatment arm heaviness, and another reported fasciculation of the deltoid muscle for 30 minutes after one treatment. There were three reports of erythema that seemed likely due to vigorous skin abrasion with the sandpaper.

8.3.4 Acceptability and ease of use

Unused materials returned after treatment suggested that skin preparation may not have been per protocol in every case. Because all participants received oral and written instructions on location of the electrodes, their correct placement was not initially checked. However, it later became apparent that some participants were placing the proximal edge of the electrode, not directly over the epicondyle, but 1 or 2 cm distal to it. The current density and configuration at the tendon may have changed because of this misplacement.

Neither device required programming or battery changing, and all participants said they found them easy to use, although several members of group D said that the complicated treatment schedule was not always convenient to follow. Both devices had LED indicators to

show when they were operating, but the LED on the Tendonworks was reported by several participants as difficult to see. Neither had an audible alarm to indicate if the circuit had broken for any reason. Tubular bandaging appeared to be the most efficient way of holding the devices and wires in place, which was particularly important for the Tendonworks as its leads were rather long.

8.4 DISCUSSION

As in the previous trial, significant improvements were seen in both groups on most measures over the duration of the trial. Differences between groups were less marked, however. None of the differences were statistically significant and the values of the mean differences between groups and the effect sizes were generally small, particularly by the final assessment. For greyscale and PFGS scores, the differences did not reach the MDC values calculated in the reliability studies, although the confidence interval for the PFGS score did include it at both second and final assessments. In contrast with the previous trial, treatment success rates show no significant differences between groups as measured by odds ratios. In consequence, there is little evidence that one form of MCT produced superior outcomes to the other.

Both groups improved over time on all variables apart from hyperaemia which, as suggested in the last chapter, is not a simple measure of pathological severity. Excluding this measure, mean improvements between baseline and final assessment were always superior for group C. The changes in greyscale scores did not exceed the MDC value, although PFGS scores did so. Improvements in PRTEE-pain scores were 59% of baseline for group C and 45% for group D, so both passed the criterion for clinically significant change suggested in the previous chapter. Comparisons with outcomes for minimal intervention groups can again be used to investigate whether these forms of MCT are beneficial compared to wait-and-see. Two trials with such groups reported improvements in PFGS ratios of 50% and 110% of baseline values by 12 weeks^{332, 333}, and another reported an improvement of 35% of baseline PFGS raw score over the same period⁴⁴³. These compare to improvements of 48% in group C and 37% in group D at 15 weeks. Compared to the first two studies, these improvements are worse than could be expected by wait-and-see although the confidence intervals for the mean differences are wide and their upper limits would suggest improvements of approximately 70% in each group.

Improvements in PRTEE-scores six weeks after baseline were 53% and 30% of baseline for groups C and D respectively. These compare to a change of 6% observed in a wait-and-see group 7 weeks after baseline, reported in another study⁴¹⁵. Treatment success rates in the minimal intervention groups of two studies^{332, 333} were 27% and 32% at six weeks after baseline and 55% and 60% at 12 weeks after baseline, respectively. Groups C and D performed better than these groups at 6 weeks and 15 weeks by margins of 10-20%. As before, caution is indicated in interpreting these figures because baseline severity was greater in the comparator groups. Nevertheless they provide some indication that MCT with the parameters under test and produce outcomes superior to a minimal intervention strategy over the timescale considered. The impact of the misplacement of the electrodes by some participants is impossible to gauge. It is reasonable to assume that the current reaching the tendon may have been lowered, and its direction will have been more biased longitudinally than if the electrode were placed directly over the tendon. In fact, this may have been advantageous given study findings reported in section 3.3.4, suggesting that charge flow along the tendon stimulates cell proliferation optimally. In any case, since checks on placement began mid-way through the trial it is not known whether the misplacements affected one group more than another. This is a reflection of 'real world' patient-administered interventions, in which per-protocol treatments cannot be guaranteed, and may be a significant determinant of treatment outcome.

In summary, the trial suggests that these two forms of MCT produce outcomes somewhat superior to a wait-and-see approach, and that Group C parameters were somewhat more effective than those delivered to group D. The latter group differed from the others in having fewer cases of positive responses to cervical clearance tests, but this might have been expected to be prognostic of a better outcome for group D since it is unlikely that the treatment affected neck symptoms. So it would not appear that this difference prejudiced the findings. As with the previous trial, low test power was an issue with all of the group comparisons, but differences between groups were small and there is little persuasive evidence that they are clinically significant.

8.4.1 Tissue healing

Greyscale changes were unremarkable and considerably smaller than the MDC value, so there is little evidence of structural normalisation in the tissue. The exceptions to this were the three cases of tears that showed signs of healing, one completely. All of these cases reported substantial improvements in their symptoms by final assessment, but so did a single case in which a tear showed no change. Most examples of grade 2 calcifications showed no signs of change, and the affected individuals had a mix of outcomes from much better to no change. These observations suggest that calcifications and tears need not be painful, and confirm that normalisation of tissue structures is not necessarily associated with clinical improvement.

Group patterns of change in hyperaemia were very similar to those observed in the previous trial, although there was no sign of further rises after treatment. Higher blood flow levels appear to be maintained three months after treatment, but the mean changes observed are smaller than the MDC derived from the reliability data. Group C showed a very similar relationship to groups A and B between baseline hyperaemia score and change by first assessment, but group D tendons behaved quite differently. There were smaller variations in blood flow, and the two cases with the highest initial scores (3) both saw increases in blood flow following treatment. As in the previous study, the changes and the numbers involved are small, so patterns may be coincidental, but it is tempting to speculate that the much shorter treatment time provided in group D (compared to the other three groups) may have contributed to these differences. Application of current for longer periods may be required to necessary to cause larger changes in blood flow.

8.4.2 Parameter dependence

The small differences between group improvements on most variables suggest that the different combinations of parameters did not materially affect outcomes. Drawing firm conclusions about the influence of individual parameters is problematic because several differed between groups. The nominal average current of the WeWo Thom is 25 μA , but it was not current regulated, so may have varied during treatment. The regulated average current intensity of the Tendonworks is 20 μA for 20 minutes, but it is higher (the amplitude varying between 50 and 500 μA) for the other 10 minutes of the programme. Overall then, the average current delivered by the Tendonworks over the course of each treatment is likely to be somewhat greater than delivered by the WeWoThom. On the other hand, the total

charge delivered to the tissue was less because of the much shorter treatment time – this issue is considered in more detail in section 8.6.2.

The similarity in outcomes for both groups suggests that the complex parameter modulation during the Tendonworks programme (and the treatment schedule it required) conferred no advantage over the simpler programme provided by the other device. When asked about the rationale for the programme, the suppliers of the Tendonworks claimed it was based on their own laboratory work, which suggested that a period of biphasic amplitude- and frequency-modulated stimulation “prepared” the tissue cells to respond to the main phase of treatment with monophasic current (Chapman-Jones, private communication), but no data was provided to support this contention. Although the earlier literature review found that the majority of evidence in favour of MCT is from trials using monophasic currents, this trial suggests that a biphasic current can produce similar or better outcomes in some cases. This is consistent with the proposition that the intensity of the current is the critical parameter. On the other hand, had the treatment times been the same, the outcomes may have been quite different. The review suggested that long total treatment durations are most effective, but the monophasic proportion of the current supplied by the Tendonworks was only available for 10 hours in total, which may have been insufficient to outperform the WeWo Thom’s biphasic current that was provided for more than 10 times as long. Further consideration is given to parameter dependence in the pooled analysis presented later.

8.4.3 Patient experience

Reported adverse events were few and mild, which is not surprising given the low current intensity that was delivered by both devices. The reports of excessive skin abrasion suggest that greater attention should be paid to instructions in this technique – if it is used at all. The practice may be unnecessary: abrasion is not recommended with other forms of electrotherapy and its value is questionable if the skin is cleaned and a current-regulated device is used. The size and simplicity of the devices make them a particularly attractive option for patient-controlled treatment, although neither have rechargeable batteries, and they are intended for a single course of treatment only. The small dimensions of the Tendonworks demonstrate that current-regulation does not require a large device.

8.4.4 Study limitations

As with the previous study, underpowering meant that definitive conclusions about differences between groups could not be drawn. However, the small mean differences between the group improvements suggests that, even if a statistically significant difference had been detected, it would probably be clinically irrelevant. The trial was not fully randomised because of the late delivery of devices, and this could have led to an imbalance on some significant baseline characteristic, although the only one detected was in response to cervical clearance test. In principle, this might have been given group D some advantage, but this group performed less well and so the difference between group outcomes may have been greater had this imbalance not been present.

Once again, the problems with the dynamometer and the PSFS measure reduced the data available for analysis. The experience confirmed that the PSFS would be unsuitable for inclusion in a full trial unless used differently. Its value has been proven in other contexts and so it might still be justified to include it, informing the patient of their previous ratings.

Although the trial provided evidence regarding two particular combinations of MCT parameters, its implications for the influence of individual parameters are harder to discern. It may have been that the effects of changing one parameter were counteracted by changes in another. This illustrates a limitation of using off-the-shelf microcurrent devices - very little parameter control was available with either instrument. The only parameter that can be varied with these devices is treatment time, by switching them off before the programmed has ended, or by using them more often. The limited battery capacity of the Tendonworks allows a maximum of 50 treatments (25 hours), so its total treatment time could not have been increased by more than a factor of two. An alternative experimental approach would have been to use the WeWo Thom with both groups and have one group switch off the device after 30 minutes, which would allow substantially different treatment time to be compared.

8.5 CONCLUSIONS

There were no significant differences between outcomes using the WeWo Thom and the Tendonworks when used as described, the differences are unlikely to be clinically significant. Both devices produced patient-ratings of pain, function and treatment success superior to those observed in the wait-and-see groups of other trials, although the participant profiles were not identical with these groups. The apparently worse grip strength outcomes suggest

that caution be exercised in making these comparisons, and placebo may account for at least part of the observed differences.

The differences in group mean values over time for blood flow were not statistically significant, although this may have reflected type II error. An adequately powered trial could test the intriguing possibility that the devices might be able to regulate blood flow in the same manner suggested in the discussion of the previous trial. The fact that a pattern suggestive of such a possibility was seen with the Wewo provides additional grounds for investigating this phenomenon, since it has potential implications for tissue healing.

8.6 POOLED ANALYSES

Since enrolment to the two trials occurred over different periods, and allocation was not randomised across all four groups, primary analysis was conducted separately for each trial. However, participants were recruited from the same sources and the trial protocols were identical in most respects. Therefore the possibility of pooling their data was investigated, since this would allow direct comparisons between outcomes for all four sets of MCT parameters. Only one significant time*treatment group interaction was found in ANCOVAs that were conducted (for groups A and B on greyscale score), and t-tests were underpowered to detect a significant difference between group improvements on most outcomes. Therefore only a limited comparative analysis of pooled data was attempted: global change scores showed both statistically and clinically significant differences between groups A and B, and so these were compared across all groups.

Further analysis was deemed viable using combined data from all the groups, since this should increase the power of the tests. Although the hyperaemia changes observed in each trial were not statistically significant, they were of particular interest because of their potential association with tissue healing and changes in pain levels, so tests of association between hyperaemia scores and other variables were conducted. Combined data was also used to test for prognostic significance of a range of potentially influential factors such as baseline pain and symptom duration.

Baseline equivalence was assessed using a one-way ANOVA for variables that had been subjected to t-tests in the individual trials. If there was inhomogeneity of variance, the Brown Forsythe test was applied⁶⁴⁴ (p347). A Kruskal Wallis test was used for non-parametric data,

and differences between categorical variables were evaluated using Pearson's Chi-square for pair-wise comparisons between all groups.

To investigate differences between groups, contingency tables were constructed between group and global change scores at final assessment. Kendall's tau-b was used to test for associations between group and score, and Pearson's Chi-square tested for associations between group and treatment success. Calculations were conducted pair-wise for all groups, with significance set to $p \leq 0.01$ to compensate for multiple testing. Since hyperaemia has been linked both to levels of pain⁵⁰⁵ and to treatment success in tennis elbow, the relationship between the baseline hyperaemia and pain scores, and between baseline hyperaemia score and outcomes at final assessment, were also investigated using Kendall's tau-b as a measure of association between ordinal variables. Since electrical charge and current density have been suggested as potentially significant treatment parameters in tissue formation⁸⁴, their values were estimated for all groups to investigate whether they might be related to treatment success.

The influence of potential prognostic factors on treatment success was also investigated. Although testing multiple variables for predictive properties runs the risk of identifying apparently significant relationships by chance, the practice is regarded as legitimate for exploratory studies where the factors are selected a priori and with justification. As indicated in the last chapter, higher baseline pain and ongoing stress to the arm have been identified as two factors predictive of poor outcome after a range of conservative treatments for tennis elbow. Several other variables were also considered in this analysis: duration of symptoms, gender, involvement of the dominant arm, use of a brace, psychosocial risk factors (non-zero scores on the depression or anxiety screening questions, taking time off work or involvement in compensation or litigation as a result of the disorder), and whether lateral elbow pain was produced by the ULTT2B. Tests for a univariate relationship between each of these variables and treatment success at final assessment were made using Spearman's rank correlation for ordinal variables and Pearson's Chi-square for categorical variables.

8.6.1 RESULTS

The Levene statistic confirmed homogeneity of variance for all variables tested apart from duration of symptoms. The one-way ANOVA demonstrated no significant differences between groups on any of the continuous baseline variables examined. The Kruskal Wallis test showed that there were no significant differences between groups on baseline on sonographic greyscale and hyperaemia scores and on symptom duration. Pearson's Chi-

square found no significant differences between groups in gender, whether the dominant arm was affected, incidence of previous episodes, radial nerve stressing causing lateral elbow pain, ongoing heavy limb use in the trial and use of a brace in the trial. However, there were differences on positive response to cervical clearing tests. Inspection of the raw data showed that groups A, B and C had 8, 10 and 10 members respectively with a positive response, compared to two members of group D. Table 8.15 shows the mean differences in outcomes at final assessment for all groups.

Table 8.15: Mean differences (95% CI) between baseline and final assessments, and treatment success rates, for all groups

Variable	A	B	C	D
Greyscale	-0.88 (-1.5, 0.20)	0.20 (-0.23, 0.63)	-0.88 (-1.55, -0.20)	-0.33 (-0.73, 0.07)
Hyperaemia	0.13 (-0.52, 0.79)	0.21 (-0.35, 0.78)	0.31 (-0.29, 0.92)	0 (-0.56, 0.56)
PFGS	0.31 (0.05, 0.57)	0.23 (0.08, 0.37)	0.28 (0.14, 0.42)	0.22 (0.03, 0.41)
PRTEE-Pain	-13.5 (-19.3, -7.8)	-7.9 (-12.9, -2.9)	-13.69 (-19.87, -7.50)	-10.0 (-14.3, -5.7)
PRTEE-function	-13.2 (-19.2, -7.3)	-9.7 (-15.6, -3.7)	-10.44 (-16.96, -3.92)	-9.5 (-14.5, -4.5)
PRTEE-Total	-26.9 (-38.1, -15.6)	-17.4 (-17.9, -6.9)	-24.06 (-35.84, -12.29)	-19.5 (-28.4, -10.5)
Treatment success	14/15 (93%)	7/15 (47%)	12/16 (75%)	11/15 (73%)

The mean differences are generally greatest in group A, although the difference between it and groups C and D are small on most measures. Group B performs worst on most measures. The contingency tables for global change scores at final assessment is provided in Table 8.16. There is a consistent pattern of group A performing best and Groups C and D performing better than group B. However, pair-wise group comparisons of success rates using Pearson's Chi-square showed that the only significant difference was between groups A and B, as previously identified. The better performance of group A becomes more apparent in comparing the global change scores: six members of that group recovered completely - a much higher proportion than in any of the other groups. However, pair-wise comparisons between group GCS scores using Kendall's tau-b indicated that these patterns of response were not significantly different. The table also shows that the treatment was not successful for 17 people - more than a quarter of the total sample, although the "failure rate" is reduced to 11% if the data for group B (the least successful group) are excluded.

Table 8.16: Global change scores and numbers of treatment successes at final assessment for all groups

Group	Global Change Score					Treatment outcome	
	-1	0	1	2	3	success	no success
A	0	1	0	8	6	14	1
B	0	5	3	6	1	7	8
C	0	2	2	11	1	12	4
D	1	0	3	10	1	11	4

The associations between baseline hyperaemia and pain scores, and between baseline hyperaemia and outcomes at final assessment, were tested using Kendall's tau-b, pooling all the data from both trials.

Table 8.17: Kendall's tau-b as a measure of association between baseline hyperaemia score and other variables for pooled dataset

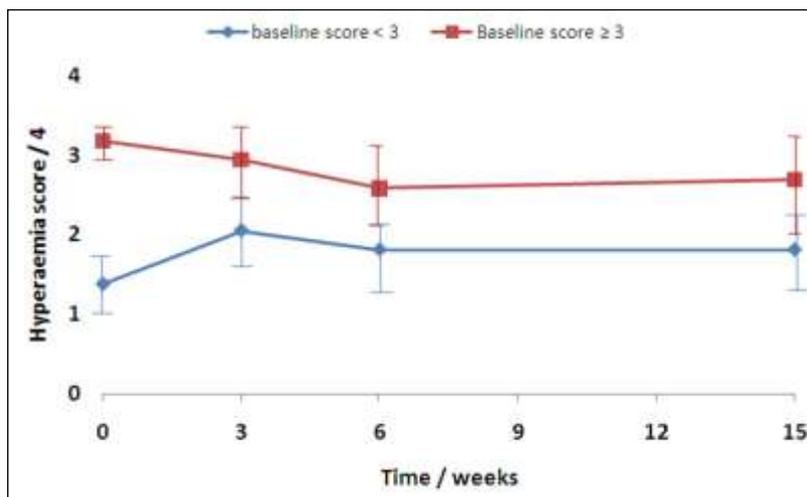
Variable	Tau-b	Sig
Baseline PRTEE-pain	0.02	0.83
Change in:		
- Greyscale score	-0.04	0.73
- Hyperaemia score	-0.38	<0.001
- PFGS	0.08	0.45
- PRTEE-Pain	-0.25	0.005
- PRTEE-function	-0.05	0.61
- PRTEE-Total	-0.27	0.002
Treatment success	0.32	0.005

As Table 8.17 shows, there was no association between baseline hyperaemia and pain scores, or changes in greyscale score, PFGS or PRTEE-function at final assessment. However, there were significant associations with changes in hyperaemia, PRTEE-pain and total scores, and treatment success. These suggest that higher baseline hyperaemia scores are associated with falls in hyperaemia and pain levels, and a better overall clinical outcome, by final assessment. Table 8.18 illustrates this pattern for one variable, treatment success. One baseline Doppler image was lost and so its data is missing.

Table 8.18: Relationship between baseline hyperaemia score and treatment outcome for all groups

Hyperaemia score	Treatment outcome	
	Failure	success
0	3	3
1	7	7
2	4	18
3	2	13
4	0	3
Total	16	43

Figure 8.4 displays the behaviour of hyperaemia score over time using pooled data split into two categories: low (<3) and high (≥ 3) baseline hyperaemia scores. Excluding the data from D, which appeared to behave differently from the other groups in this variable, did not materially change the observed pattern.

**Figure 8.4: Changes in hyperaemia scores over time for all groups, split by high and low baseline scores**

The subgroup means appear to follow a pattern in which low baseline hyperaemia scores lead to an initial rise in blood flow, which fall after treatment and then stabilised at a higher value by final assessment. In contrast, the group with higher baseline values experience a drop on average, which is sustained until the third assessment, when it begins to rise again. Related samples t-tests indicate that the rise in score for the <3 group is significant at 3 weeks ($t = 4.7, p < 0.01$) and for the ≥ 3 group at 6 weeks ($t = -2.8, p = 0.01$). The changes are small, however, falling below the minimum detectable change value calculated previously for this scale. Across both trials, only two cases with blood flow evident at baseline had

hyperaemia scores of zero by final assessment (from initial scores of 2/4 and 3/4). So hyperaemia remained evident in the large majority of tendons three months after treatment was completed – a third had final scores of 3 or 4 - even though symptoms had reduced significantly in many of them.

The results of univariate tests of association between potential prognostic indicators and treatment success at final assessment are presented in Table 8.19. Only gender and elbow pain on ULTT2B showed a close-to significant correlations with treatment success. The odds ratio for success was 2.9 in favour of men, and 4.7 in favour of those with a positive response to the neural tension test.

Table 8.19: Tests of relationships between potential prognostic factors and treatment success at final assessment for participants in all groups

variable	Spearman's r	Pearson's χ^2	Exact Sig
Age	0.151		0.247
Duration current episode	-0.182		0.161
Baseline PRTEE-pain	0.047		0.723
Ongoing arm stress		0.60	0.570
Gender		3.11	0.094
Dominant arm affected		2.75	0.160
Use of brace		0.19	0.760
Psychosocial factors		2.30	0.563
Elbow pain by ULTTB		4.13	0.064

A final pooled analysis was conducted to investigate how current density and total charge flowing varied between the groups, and whether they might be more critical to outcome than current intensity. The current density at the electrode-skin interface is the ratio of the current to the surface area of the electrode, which was approximately 5x5 cm for all groups. Values calculated using the average current for each group are given in Table 8.20, along with the total electric charge (Q) delivered to the tissue, estimated using the formula $Q = I \cdot t$ where I is the average current and t is the treatment time.

Table 8.20: Current density and charge delivered to tissue in each group

Group	Current density $\mu\text{A}/\text{cm}^2$	Charge delivered / 10^{-1} Coulomb	
		Per treatment	Per course
A	1.6	2.4	50
B	16	24.0	500
C	1	5.4	110
D	0.8 – 10	1.2	30

These figures refer to the skin surface – calculation of the charge and the current density in the pathological tissue is problematic⁶⁵⁸. However, they provide some indication of relative magnitudes for comparison purposes. The current delivered to groups A and B was monophasic; to group C it was balanced biphasic so the net charge flowing through the tissue was zero. The current delivered to group D had a complex waveform comprising both monophasic and biphasic stages and the calculations represents an estimate based on data provided by the supplier. The results of these calculations suggest that the total charge delivered in group B was considerably larger than that received in the other groups. Also, although the average current supplied in group C was smaller than in group D, the total charge delivered was larger because of the much longer exposure time.

8.6.2 DISCUSSION

The pooled analysis provides several additional insights into the significance of MCT parameters and of hyperaemia in influencing outcomes. Since all the groups were similar on significant variables at baseline, comparisons between them are legitimate. The pair-wise tests indicated that only groups A and B differed significantly in treatment success rates. However, inspection of the contingency table suggests that the performance of groups A was superior to that of groups C and D, which in turn had better outcomes than group B. Overall, then, the data from the trials are consistent with all the forms of MCT tested giving some clinical benefit and produce changes in blood flow that may play a part in an enhanced healing process; also that the amount of benefit varies between a maximum for group A, a minimum for group B, and a response between these extremes for groups C and D. Improvements in group A were greater than in other groups at each time point, which means that the benefits accrued more quickly for that group – an important consideration, even when longer term outcomes are similar. However, the non-significance of many tests results means that few firm inferences may be made and that an adequately-powered trial is required to confirm whether putative differences are significant.

Two of the comparator studies using the same definition of treatment success as in these trials defined a minimum clinically important difference of 25% in success rates^{332, 333}. Using this criterion, and assuming that the least successful group would achieve 50% success at 3 months, as in this study, a sample size of approximately 60 people per group would be required to detect such a difference.

Parameter dependence

Taken collectively, the comparisons between groups in these trials imply that, even where other parameters differ, lower current intensity treatment is more effective than higher. The small differences between group A and C outcomes suggest that a high frequency biphasic current can achieve success rates similar to a lower frequency monophasic current. In fact, the mean improvements in groups A and C were remarkably similar on all outcome measures. This was somewhat contrary to expectations since the weight of evidence considered in the literature review favoured monophasic currents. Apart from the differences in waveform, groups A and C also had substantially different treatment durations, and it may be that a longer treatment time compensated for a less effective waveform. This might also account for the differences between groups A and D, since the treatment time for group A was more than three times longer than that of group D. A study comparing the effects of substantially different treatment durations for two groups receiving the same monophasic 50 μA low frequency waveform would therefore be worthwhile.

Because similar size electrodes were used in all cases, the current densities are in the same proportions as the currents. Hence their calculation does not offer additional information about differences between the groups, but it does provide an easier comparison with other studies. In chapter 3, effective current densities for a range of tissue types were calculated (see Table 3.1). Comparing the calculated figures, the more effective current densities observed in this trial - a few $\mu\text{A}/\text{cm}^2$ - are at the lower end of the ranges found effective with a variety of bone and skin lesions. This is interesting because the figures for those tissues refer to the site of the lesion itself (since the electrodes were in direct or very close contact with the pathological tissue in those trials), whereas the current densities calculated in this investigation refer to the skin surface; the current density at the tendon would be still lower, perhaps substantially so. It may be that lower current densities could also be effective with other tissues - as Table 3.1 shows, skin grafts and muscle damage have been treated successfully with current densities below 0.1 $\mu\text{A}/\text{cm}^2$. On the other hand, whereas MCT clearly promoted tissue healing in the cases of non-uniting bones and skin ulcers, its apparent effectiveness in the present study may have been for other reasons, such as pain relief. Lower current intensities were associated with greater treatment success rates, but also with fewer reports of sensory stimulation. Therefore, if success is due to an analgesic effect, it is unlikely to be by stimulation of afferent fibres and consequent inhibition of nociceptive signals, the proposed mechanism of action of TENS⁶⁵⁹.

Comparison of the charge delivered during treatment suggests that this is not the critical factor in effectiveness, since there is no clear relationship between charge and effectiveness.

Very little work has been reported addressing this issue. Brighton and colleagues found that bone formation the medulla of an intact rabbit tibia was proportional to the total charge delivered by an inserted electrode, but only at an optimum current level⁸⁴. If the current was too high necrosis occurred, and if too low, there was no bone formation, no matter how much charge was delivered. Total energy delivered may be a factor in treatment success but its calculation requires knowledge of the impedance of the tissue circuit, which was not available in this study.

Adverse events were rare in all groups. As argued earlier, the case of bilateral leg tingling is unlikely to have been caused by the treatment. The two cases of mild electric shocks received from the Elexoma Medic suggest that the device design may need attention in this regard. Subsequent to these trials, the supplier indicated that a redesign was being implemented, which would result in a smaller device with no risk of shocks. These changes should make this device safer and more convenient to use.

The significance of hyperaemia

The results of tests of association between baseline hyperaemia scores and other variables are intriguing. The neovascularity that has been observed in tendinopathy is accompanied by neural ingrowth and increases in concentrations of both pain receptors and their associated neurotransmitters^{510, 596}. This has been suggested as an explanation for the association that has been observed between hyperaemia and pain in various tendinopathies, including tennis elbow^{505, 660}. The data from this investigation suggest that hyperaemia and pain are not simply related, and several other studies have reached the same conclusion^{397, 661}. A certain confusion in terminology may be at issue here. Neovascularity is not the same as hyperaemia – increases in blood flow have been observed in tendons immediately after exercise^{662, 663}, and these are clearly not due to angiogenesis. Conversely, falls in hyperaemia seen in pathological tendons after treatment are not necessarily signs of reduced capillary density in the tissue, although they continue to be interpreted as such in some trials^{397, 664, 665}. The complex relationship between hyperaemia and pain that has been observed in some trials may be because reduced Doppler signals betoken a combination of vascular constriction – which may not reduce pain – and capillary “die-back” – which may.

Nevertheless, the significant associations found here between baseline hyperaemia and several outcomes suggests that it may have prognostic value, at least for microcurrent treatment. In these trials, higher hyperaemia levels at baseline were associated with greater reductions in pain and greater levels of treatment success. Interestingly, the association did not extend to PFGS and function scores, perhaps because motor weakness – which is unlikely

to be affected by MCT – contributes as much to PFGS as pain does. In any case, it appears that hyperaemia and pain are related, but in a complex fashion. Microcurrent was more effective in reducing pain in cases that started with greater intra-tendinous blood flow, although these were not necessarily the most painful cases. A recent study found no association between baseline hyperaemia (which was interpreted as neovascularity) and total PRTEE score after treatment of tennis elbow with a 6 month eccentric exercise programme⁶⁶⁴. PRTEE subscale scores were not reported, so it is not possible to tell whether pain and function scores changed differently, as in this study, although such exercise programmes have been found to reduce both pain and functional disability⁶²⁴. The discrepancy may indicate that the prognostic value of the hyperaemia score depends on the nature of the therapy. Certainly, this study suggests that MCT is most likely to be of value in cases where hyperaemia scores are high. Since the treatment was more successful in these cases, it seems reasonable to speculate that their high levels of hyperaemia were pathological and that reducing them contributed to resolution of the disorder. There are various approaches to reducing the neovascularity associated with tendinopathy, such as sclerosant injections and peritendinous vascular stripping⁶⁶⁶, but if a non-invasive approach such as MCT can achieve similar results this is surely an option worth further investigation. However, the fact that hyperaemia scores in this investigation's trials fell to zero in only two cases, but that symptoms reduced or were abolished in many more, confirms that changes in intra-tendinous blood flow levels do not correlate simply with clinical outcomes.

Figure 8.4 demonstrates the difference in behaviour of the cases with high and low baseline hyperaemia scores, and lends weight to the proposition that MCT may regulate rather than merely stimulate blood flow. It appears that the treatment also differs in the persistence of its effects, since the initial rise in blood flow for the low scoring group was reversed shortly after the treatment ended, whereas the initial fall in blood flow for the high scoring group was sustained for some time after treatment ended. Although all these changes are less than the MDC value calculated earlier for this measure, the consistent patterns observed (at least among groups A, B and C) are consistent with a real underlying pattern of behaviour. Some time after the treatment was stopped, the changes in blood flow may have stopped or been partially reversed. If the changes were beneficial, longer application of MCT may enhance the therapeutic effect. The regulatory role that MCT appears to play is consistent with the theory that it is mimicking endogenous biocurrents that modulate the healing process. Endogenous currents of injury are observed until healing is complete (or at least until tissue integrity is restored) and so, if MCT works by a similar mechanism, application of current for longer periods may be necessary. However, the suggestion that the observed changes in blood flow

are part of that process is as yet speculative. The data also illustrate the risks of drawing conclusions from group averages, because the behaviour of individuals often departed substantially from those averages. Studies with larger samples would facilitate a more sophisticated analysis to investigate whether members of more sharply defined subgroups behave more consistently.

Prognostic factors

Only two of the tested factors were found to correlate significantly with treatment success: gender and lateral elbow pain produced by the ULTT2B test. The better outcome for males is in accordance with other studies^{383, 629}, and could be explained by a variety of factors, including gender-based differences in judging changes in symptoms, differences in work- or leisure-related stresses on the arm, or hormonal influences on treatment effectiveness. The second of these factors may be eliminated because of the lack of correlation between ongoing stress to the arm and treatment success. The significant correlation with a positive response to the radial nerve tensioning test begs the question: why should MCT be more effective where there is evidence of radial nerve involvement? It may be that entrapment or neural sensitisation is the dominant or sole cause of symptoms in these cases, even though tendinopathy is also present. MCT appears effective in the treatment of this form of neuropathy, perhaps more effective than in treating the effects of tendinopathy alone. Possible mechanisms include desensitisation of the nervi nervorum in the radial epineurium, reductions in the concentrations of noxious chemicals in the vicinity, or reductions in compression of the nerve secondary to tendon healing. The lack of significant correlations with other variables, particularly baseline pain and symptoms duration, is encouraging because it suggests that MCT may be of benefit in a wide range of presentations of tennis elbow.

Patient Experience

The flexibility in timing treatment, lack of interference with daily activities and passive nature of the treatment were undoubtedly significant factors in the high rates of compliance with the treatment protocol. Where effectiveness is dependent on substantial treatment durations, as appears to be the case with MCT, compliance is an important consideration. So the fact that participants found the microcurrent devices easy and convenient to use is not trivial. Home-based patient-controlled therapy, if effective, may offer cost savings over conventional therapy, or might encourage the user to comply with other, more demanding forms of therapy⁶⁶⁷.

8.7 CONCLUSION

The pooled analysis, and the two trials that informed it, suggest that a full clinical trial of MCT for tennis elbow is justified, and provide information useful in the development of a trial protocol. They have also produced some intriguing findings relating to the action of microcurrent within the tissue. The low power of the studies diminishes the strength of the evidence for a number of the outcome measures, but the significant differences between groups A and B in greyscale score changes and treatment success rates suggest that peak current intensities of 50 μA or less can produce superior outcomes to currents an order of magnitude higher. They also imply that a simple monophasic current produces outcomes equal or superior to a current with a biphasic or complex multi-phase waveform program. The evidence that MCT can produce better outcomes than a wait-and-see approach depends on comparisons with other studies. These led to inconsistent findings, possibly due to a combination of differences in baseline characteristics, the questionable reliability of PFGS data in this study, and the absence of an exercise program that might have improved functional outcomes. Nevertheless, they provide limited evidence that MCT is superior to a minimal intervention approach.

The analysis suggests that a monophasic current of peak intensity 50 μA or less should be used in the clinical trial. If the current does indeed simulate the biocurrent that would normally drive healing but has failed for some reason, it may be necessary to lengthen the duration of the treatment to ensure that the healing process continues to completion. This would be consistent with the evidence presented in the literature review. The smaller changes in PFGS and function scores suggest that an exercise programme should be used in conjunction with MCT, taking advantage of pain reductions to improve strength and functional capacity, and possibly to assist in remodelling. If the greyscale score were to be used as the primary outcome measure, a sample size of 55 per group in a two-arm trial would be required to detect a difference greater than the MDC; since the pathological significance of such a change (2 units on the scale) is unknown, this is the only meaningful threshold that can be applied. The sample size calculation for success rates cited earlier produced an estimate of 60 people per group to achieve the necessary power at 3 months, therefore such numbers should provide sufficient power for both this and the sonographic outcome measure.

The findings of the analyses of hyperaemia data open up several possible lines of enquiry: what is the physiological significance of the different levels of baseline hyperaemia observed? Can these be used as prognostic indicators of treatment success? Does prognosis differ

according to the treatment? Is there a relationship between hyperaemia and greyscale changes (including features not included in the scoring system used in these trials)? The novelty of some of these findings vindicates the decision to spend considerable time and effort developing a sonographic protocol for use in the trials. However, the variance in group scores and the small number of levels available on the hyperaemia scale suggest that an improved measurement system is required. Hyperaemia scoring using computerised pixel counting offers a more sensitive and objective measurement process and this should be considered in developing a protocol for both the clinical trial and other studies of hyperaemia in tennis elbow.

The second trial and pooled data analysis completed the experimental work undertaken in this investigation. They have added to the evidence provided by the studies reported in previous chapters, and together these enable a reasoned response to the thesis that prompted them. This is delivered in the final chapter.

Chapter 9

Implications and conclusions

9.1 INTRODUCTION

The thesis of this investigation was that microcurrent therapy is capable of promoting healing and alleviating symptoms following damage to soft connective tissue. To test the thesis, two investigative approaches were used: a review of existing evidence concerning the use of microcurrent to treat tissue damage generally, and an empirical examination of its effects when applied to a specific soft connective tissue disorder. The investigation comprised a series of separate studies, with the findings of each informing the development of the next. This has led to a rather unconventional reporting structure, with the aims / methods / data / discussion format being repeated in several chapters. While each study has produced its own outputs, together they provide a body of evidence that may be used to construct a response to the thesis. This aims of this chapter are to discuss the findings of all elements of the investigation in relation to the thesis, and to identify their implications.

Three themes were set out in the introduction to this report, which guided and linked its various components: microcurrent therapy as a distinct therapeutic entity; tissue healing and symptom alleviation; and clinical relevance. The last of these reflected an intention that, whilst the investigation should be founded on theory and basic science, it should be particularly concerned with implications for clinical practice. Hence, the literature reviews gave particular emphasis to clinical trials; the survey sought the views of clinicians to inform the choice of a disorder to treat with microcurrent; the trial protocols included clinically-relevant and patient-rated outcome measures; and the discussions in various chapters addressed the links between tissue healing and clinical change. The other two themes related specifically to the thesis, and this chapter begins with a discussion of the implications of the studies conducted in this investigation couched in terms of those themes. This discussion concludes with a formal response to the thesis. In the next section, the insights and original contributions of this investigation are identified, and some of its limitations discussed. Suggestions for further research are then offered, and the chapter concludes with some summary remarks and reflections on the whole process.

9.2 MCT AS A DISTINCT THERAPEUTIC ENTITY

Microcurrent therapy differs from other modalities that involve application of electric current to the body in two particular regards: its current intensity and its effects within the tissue. Whereas therapies such as transcutaneous electrical nerve stimulation, neuromuscular stimulation and interferential currents typically deliver currents in excess of 1 milliamp, therapeutic microcurrent intensities are 10, 100 or even 1000 times smaller¹¹². This distinction is not merely a matter of degree; the smaller currents can produce quite different effects within body tissue. Many of the other therapies are used to stimulate peripheral nerves to achieve an analgesic effect or cause muscular contraction. MCT rarely does this, because its current characteristics are normally insufficient to cause nerve depolarisation. Thus, if microcurrent has a therapeutic effect, it is likely to depend on a different mechanism. The proposition considered in chapters 2 and 3 is that MCT influences the behaviour of cells that are responsible for the manufacture, maintenance and repair of body tissue.

The literature concerning microcurrent falls into two categories: bioelectric phenomena and therapeutic application. The former comprises theoretical and empirical work on endogenous electricity, its involvement in normal physiology and in the body's response to tissue damage; the latter is concerned with the application of exogenous currents and fields thought to activate or influence tissue healing by simulating endogenous bioelectric cues. Both of these bodies of work were reviewed to establish whether there is a rationale for microcurrent treatment, and to evaluate the evidence regarding its effectiveness. The reviews provided limited support for the clinical application of MCT, but raised questions about whether its mechanism of action is similar to that of endogenous current.

That living tissue demonstrates both passive electrical characteristics and active electrical behaviour is incontrovertible. The energy expended by all cells in the maintenance of electrical potential differences across their own membranes and across a range of tissue boundaries is testimony to the centrality of bioelectricity in the processes of life. Its role has been explored by chemical and electrical manipulation of the cells that generate it^{47, 59, 75}. The former approach – using ion channel activators or blockers – inevitably changes the biochemical milieu of the cells. In fact, because many of the chemical reactions that drive or modulate physiological processes depend on ionic interactions, it is difficult to distinguish between biochemical and bioelectric effects. The latter approach – applying electric fields and currents to tissue – can undoubtedly influence cellular behaviour, and do so in ways that enhance tissue healing. Yet this does not prove that endogenous electricity guides such

behaviour in living tissue. Hence, whilst there are clear associations between bioelectric changes and components of healing, attribution of causality is more problematic. This may explain why, despite the growing corpus of data on bioelectric phenomena, authorities in the field continue to express the uncertainties about their role: 'the signalling function of [the] skin battery remains largely unexplored'⁴⁷; '[electric fields] certainly coexist with the more familiar players that control multiple cell behaviours, and it is now timely that their physiological roles are explored more thoroughly'⁷⁵. These statements are hard to reconcile with others (sometimes made by the same authors) suggesting that causality has been established: 'This electric field... initiates the wound healing process'⁴⁷; 'Proliferation of epithelial cells is regulated by a physiological electric field'⁷⁵; '[endogenous] electrical signals control wound healing'⁶⁶⁸. Arguably, it is only legitimate to say that numerous mechanisms have been identified by which bioelectricity could influence tissue healing.

Even if a causal relationship were to be established, this would not prove that microcurrent therapy brought about its effects by mimicking endogenous currents, as some trial reports and reviews of MCT claim^{183, 184, 253, 255}. If this were so, it might be expected that MCT parameters would resemble those of the biocurrents measured during tissue healing. As the literature reviews showed, this is rarely the case. In some studies, the applied currents have intensities less than 100 μ A and use DC or monophasic waveforms (in which the current is always unidirectional). These are seen most commonly in trials of MCT for bone healing. Some studies involving skin wounds and other forms of tissue damage have used current of similar intensity, but many have not, and their waveforms often bear no resemblance to those occurring naturally in skin wounds.

On the other hand, if certain parameters are key to the effects of biocurrent, it may only be necessary for MCT to reproduce these in order to have similar effects within the body. The clinical trials reported in Chapters 7 and 8 were consistent with current intensity being the main determinant of MCT effectiveness; waveform appeared to be considerably less important – and may indeed be irrelevant – as a mediator of healing. If biocurrent intensity is the most important factor in its influence on healing, then defining MCT primarily in terms of current intensity, and claiming that it mimics the current of injury as a cue for healing, would be reasonable. Clearly, the electrophysiology of healing requires further elucidation before this line of reasoning could be accepted.

Even so, it can still be argued that the therapy has a distinct mechanism of action. As was shown in chapter 2, there is a range of pathways by which microcurrent can influence the healing process – pathways that do not appear to be activated by currents of higher intensity.

Sonographic findings in the clinical trials reported in Chapters 7 and 8 suggested that MCT can both stimulate and inhibit blood flow according to current tissue status. Such an effect has not been reported with other electrotherapeutic modalities. Also, MCT can promote pain relief without obvious sensory stimulation. Hence, the literature review and preliminary trials provided evidence for another mechanism of action by MCT. These different pathways provide the most legitimate justification for considering MCT as a distinct therapeutic entity, and for further investigation of its clinical potential. The narrative and systematic reviews reported in Chapter 3 took this perspective, and in doing so brought together the evidence that is particular to MCT. This reflects a growing awareness that dosage is key to the effectiveness of a variety of electrotherapies, including extracorporeal shockwave therapy³⁶², ultrasound⁶⁶⁹ and laser therapy⁶⁷⁰. Reviews that attempt to synthesise findings from trials without regard to the intensity of the applied energy may reduce the power of the analysis to detect a real effect if there is one – analogous to increasing the risk of a type II error. This may be particularly important where the mechanism of action is thought to involve directly influencing cellular behaviour rather than causing gross changes in the tissue. Such a distinction has been made in modelling the action of therapeutic ultrasound: whilst higher intensities are thought to confer benefits by producing heating effects in the tissue, lower intensities appear to act by altering ion transport mechanisms in cell membranes⁶⁷¹. In this sense, high and low intensity ultrasound may more properly be thought of as different forms of electrotherapy with different indications. This is also true of applied currents. For example, although MCT and TENS involve the same form of energy, possibly with the same waveform and frequency, applied to the body via surface electrodes in either case, they constitute quite different forms of therapy because of the different effects they bring about. Recognising this only provides greater scientific precision, but may also enable more informed clinical decision-making.

9.3 TISSUE HEALING AND SYMPTOM ALLEVIATION

The impetus for this investigation was the proposition that MCT is capable not only of treating the clinical signs and symptoms associated with tissue damage but also of healing the damage itself. This is a particularly attractive prospect because of an implicit assumption that the tissue damage is both the originator and the maintainer of the observed signs and symptoms. If this is so, promoting tissue healing constitutes a more comprehensive management plan than mere symptom management because it addresses underlying causes as well as effects. The assumption has obvious validity where MCT is used to promote healing

in, say, a non-uniting tibial fracture: healing the bone tissue restores the structural integrity that is essential for pain-free and safe weight-bearing. A skin wound may remain a portal for infection, a source of pain and a disfiguring defect until re-epithelialisation has occurred. These examples illustrate the link between tissue healing and clinical outcomes that is clear when MCT is used to treat bone and skin damage.

The link is much less apparent in the treatment of soft connective tissue disorders, however. As the trials reported in chapters 7 and 8 found, normalisation of tendon structure was not necessarily accompanied by clinical improvement, and substantial abnormalities remained in some cases that were regarded as treatment successes. Similar patterns have been reported in other trials using sonography to monitor change during the treatment of tendinopathy⁶⁶⁴. Hence, structural normalisation and clinical improvement are not necessarily correlated. However, this begs the question of what is meant by tissue healing. Along with other forms of soft connective tissue, damaged tendons heal by the deposition of scar, which contains a greater proportion of ground substance, a different mix of collagen types, and a less organised structure than the tissue it replaces^{267, 672}. Even with optimal remodelling, scar tissue remains structurally distinct from its surroundings, but this does not mean that the tendon has not healed. Although the “mend” is somewhat weaker than the original, the new structure may be regarded as satisfactory so long as it can withstand the stresses applied during daily activities of living. This might be called “functional healing”. Some degree of structural normalisation is to be expected, as fibrils align and ground substance levels fall during remodelling, so the sonographic greyscale was an appropriate indicator of one element of healing, but it did not address other important elements of the process, including neural and biochemical changes. These may in fact be more closely related to clinical outcomes – particularly pain – than structural changes are.

Neovascularisation is a key element of tissue healing. During the proliferative phase, the ingrowth of new blood vessels facilitates the transport of oxygen, energy and materials that are required for the production of new tissue. In normal healing, once new tissue has been laid down and remodelling begins, some of the new blood vessels recede as locally increased anabolic activities fall back to previous levels. It is therefore to be expected that hyperaemia will be observed in the earlier stages of tendon healing, and seen to decrease as the repair sequence progresses. In chronic tendinopathy, this pattern is disrupted for some reason: the neovessels do not recede and hyperaemia persists. This has clinical implications because neovascularisation is accompanied by neural ingrowth and increased nociceptor density, which may at least partly account for the maintenance of pain in chronic tendinopathy. The hyperaemia data from the trials appear inconsistent on this point: there was a significant

correlation between changes in blood flow and treatment success, but no correlation was apparent between changes in blood flow and pain levels, nor between baseline blood flow and pain. The charts of change in blood flow over time (see section 8.6.1) suggest that the treatment effects were not fully maintained once MCT ceased, and it may be that the changes were too small and too short-lasting to produce a significant and sustained fall-back of neovessels and their attendant nerves.

On the other hand, pain levels did fall significantly over time, and the differences between groups suggested that MCT had an analgesic effect. If this is not due to a reversal of neurovascular ingrowth, other mechanisms may account for it. The greatest falls in pain levels were seen in the groups receiving microcurrent of lower intensity, which was sub-sensory in most cases, so it seems unlikely that the nerve depolarisation necessary for analgesia by pain gate closure was occurring. Another possibility is that MCT modulated the production of noxious biochemicals or the sensitivity of nociceptors in the area. Sampling of the chemical environment using microdialysis could help investigate these possibilities. Of course, the pain experienced in tennis elbow may have multiple sources – at least 19 have been identified⁵⁰¹ – and MCT may influence some but not others. For instance, local application of microcurrent seems unlikely to reduce the referred pain of cervical radiculopathy^{**}. However, if its analgesic action is through modulation of healing mechanisms, it may have a place in the treatment of multiple possible sources of pain, for instance damage to adjacent tissue such as the radiohumeral ligament, the joint capsule and the epicondylar cortex. Bone spurs and cortical irregularities were common findings in this investigation as in others^{348, 372}; given the evidence for microcurrent's capacity to promote bone healing, such features may respond to MCT (although there is as yet little evidence that they contribute to the pain of tennis elbow).

Persuasive evidence that MCT impacts significantly upon tissue healing in tennis elbow could be provided by a longer-term study that monitors recurrence rates. One of the problems associated with healing by scar formation is that the repaired tendon has lower strength than the original. This is due to the presence of less mature forms of collagen that have weaker cross-links than normal tendon^{544, 611}. The weakness is likely to be part of the reason that both chronicity and recurrence are common in tennis elbow, as in other tendinopathies⁶⁷³. These outcomes are more likely still when the healing process is dysfunctional in some way,

^{**} Although there is evidence that another form of MCT, involving application of microcurrent to the brain via ear clip electrodes (cranial electrical stimulation), may modulate central pain mechanisms (e.g. Tan, G., D.H. Rintala, J.I. Thornby, et al., *Using cranial electrotherapy stimulation to treat pain associated with spinal cord injury*. J Rehabil Res Dev, 2006. 43(4): p. 461-74).

for instance due to ageing, which is a significant factor in the development of tennis elbow⁶⁷⁴. Re-injury while repair is in process, or following return to normal activities after the repair is supposed complete, is more likely when healing is dysfunctional. If MCT can promote functional healing, fewer recurrences might be expected.

Like any other form of tissue healing, tendon repair is a multistage process. The inflammatory phase begins immediately after tissue damage occurs (although there is debate about its occurrence and extent in the tendinopathy that results from repetitive microtrauma^{503, 675}). This is followed by the proliferative phase, in which neovessels form, fibroblast numbers increase and new collagen is synthesised, and then the remodelling phase, when the collagen matures, develops cross links and is aligned according to the prevailing forces acting on the tendon⁶¹¹. The phases are not discrete, but have considerable overlap as the healing process transits between them. Where healing becomes dysfunctional, it appears to be in the transition between the latter two phases, because tendinopathic tissue resembles the granulation tissue characteristic of the proliferative phase²⁸⁵. Hence, if MCT corrects dysfunctional healing, it may be particularly through restoring the dynamic balance of anabolic and catabolic mechanisms that is necessary to progress from one phase to the next. As the literature review showed, successful treatments of skin and bone lesions have usually required the application of microcurrent for many weeks or months. This suggests that the therapy does not merely “kick start” the process but must be continued to sustain it. The same may be true of tendinopathy, and the relatively short treatment period of three weeks in these trials may account for the rather limited changes observed within the tendon.

MCT may also be capable of influencing the other phases of healing. The establishment of a current of injury immediately after tissue damage, and the observed effects of both endogenous and applied currents and fields on cells that are involved in the inflammatory process, provide grounds for supposing that MCT may also have value with acute tissue injuries. As yet, little evidence is available on the matter. Many of the animal studies considered in the literature review applied microcurrent to surgically-damaged tissue. However, investigators appear to have focussed their attention on the later stages of healing and little data is available on the possible influence of applied microcurrent on the inflammatory process. A recent study using MCT on surgically-repaired cruciate ligaments in dogs found that, when used in combination with compression bandaging, it produced greater short-term reductions in swelling than bandaging alone⁶⁷⁶. The literature review reported earlier found only one human study applying MCT to acute tendon damage (after surgical repair of ruptured patellar and Achilles tendons)¹⁴³, but it focussed on the proliferative and remodelling phases, presumably regarding them as the more clinically significant. The review

also cited several studies using MCT for delayed-onset muscle soreness, which is associated with inflammation following heavy exercise^{101, 199-203}. These showed little evidence of a treatment effect on pain. Nevertheless, there would surely be value in investigating the potential of microcurrent in the early treatment of tendon strains and tears, which are both common and debilitating.

Little is also known about the possible effects of MCT on remodelling. Repetitive mechanical loading, either through normal activities or via a programme of controlled exercises, is thought to be a prime motivator of remodelling and provides a rationale for the use of exercise in the management of tendinopathy^{361, 621}. The mechanism by which exercise promotes remodelling is mechanotransduction, whereby forces on the extracellular matrix are transferred to fibroblasts embedded within it and encourage them to remodel the matrix⁶²¹. There is evidence that oscillatory electrical stimulation can also promote remodelling, at least in bone^{40, 677}. The same may be true for tendons but again, little evidence is available specific to this phase. If MCT can promote remodelling, perhaps an oscillatory component is required during this phase. This would be consistent with a recent proposal that mechanical oscillations caused by eccentric contractions in Achilles tendons may promote remodelling after injury⁶⁷⁸. It may be that oscillatory stimulation – whether mechanical or electrical – may be particularly important during this phase. Conversely, a uni-directional current to guide galvanotaxis of cells may be more beneficial in the inflammatory and proliferative phases. Hence, the significance of particular parameters may vary according to the phase of healing: perhaps current intensity is key during the proliferative phase and waveform is more significant in remodelling. This is entirely speculative, but suggests possible avenues of research for the future.

The evidence from the clinical trials conducted in this investigation is equivocal regarding MCT's capacity to promote healing in tennis elbow; it is stronger in relation to symptom alleviation. The patient-rated measure of treatment success was particularly persuasive, and the measures of pain and function were also suggestive of a benefit. Although activity-related pain is the primary symptom of tennis elbow, other features that have been identified include local tenderness, reduced joint range of movement, reduced grip strength and impaired motor control^{285, 466, 679}. In fact all of these clinical features can – at least in principle – be attributed to the pain response: palpating the epicondyle, gripping activities and full extension of the elbow all stress the tendon and so can produce pain⁶⁸⁰; grip strength and motor control may both be impaired by deconditioning following avoidance of activities that might provoke pain⁵⁰². Therefore, reduction in activity-related pain is likely to be essential (though not necessarily sufficient) to address the other features of tennis elbow. If, as has

been argued from the trial data, MCT has an analgesic effect in tennis elbow, it provides the precondition for improvement in the functional capabilities. Since it does not appear to have a neurostimulatory effect, there is no apparent mechanism by which it could directly influence grip strength, proprioception or reaction times. Hence, there is a clear rationale for proposing that MCT's clinical effectiveness will be enhanced by combining it with other forms of treatment that specifically address these features of the disorder. Even if MCT acts only as an analgesic, it has potential benefits over various pharmacological treatments such as non-steroidal anti-inflammatory medication and cortisone injections. Both of these have effects on cellular activity that may be deleterious to the healing process^{681, 682}; possibly in consequence, cortisone injections are associated with higher recurrence rates than other conservative treatments of tennis elbow^{332, 333}. There is no evidence that MCT inhibits healing, at least when the current intensity is within the therapeutic window.

Finally, if MCT is indeed effective in the management of tennis elbow, it may also have value in the treatment of other forms of tendinopathy - such as those affecting Achilles, patellar and rotator cuff tendons - as well as related disorders such as plantar fasciitis. The survey of clinicians reported in Chapter 4 suggests that this would be of great clinical value.

9.4 RESPONSE TO THE THESIS

The response of this investigation to the thesis is that:

There are theoretical grounds and fair empirical evidence to conclude that

- *some forms of microcurrent therapy can promote tissue healing and resolution of symptoms in some cases of chronic tennis elbow in the short and medium term;*
- *outcomes are dependent on treatment parameters, particularly current intensity;*
- *treatment effectiveness may depend on baseline levels of blood flow in the affected tendon.*

This response is hedged with conditional terms. The term "fair empirical evidence" is based on the framework for ranking evidence that was used in the systematic review²¹⁸. According to that scheme, studies ranked as fair "will be at varying degrees of risk of error [and do not] provide a strong evidence base for clinical practice. However, these studies represent initial exploration of interventions and so assist in prioritizing the research agenda."²¹⁸. So the

evidence is not sufficiently convincing to recommend the incorporation of MCT into the clinical management of chronic tennis elbow, but the therapy is worthy of further scrutiny because of its potential to address both symptoms and their causes.

9.5 ORIGINAL CONTRIBUTIONS AND LIMITATIONS OF THE INVESTIGATION

This investigation has produced a number of original findings and other contributions that may be of value to the research and clinical communities. This section identifies these, and discusses some of its significant limitations. Table 9.1 summarises the sequence of arguments developed in the early part of the investigation, which provided the foundation for the experimental work that followed.

Table 9.1: Sequence of arguments proposed in this report

- Cells in the living body generate electric fields across their own membranes and within all body tissues. The fields change when tissue is damaged, and generate electric “currents of injury”, with intensities in the microamp range, that diminish as healing progresses.
- Applying fields and currents similar to those measured in damaged tissue can promote cellular activities that are associated with healing. Disrupting these endogenous fields and currents can inhibit healing. This supports the contention that endogenous currents help drive tissue healing. However, there may be a complex and evolving interplay of biochemical, bioelectric and biomechanical factors as healing progresses.
- A range of applied currents with intensities in the microamp range are capable of promoting healing in a variety of damaged tissues. Evidence of clinical effectiveness is strongest for non-uniting bones, spinal fusion surgery, and several types of skin wound.
- Some apparently effective applied currents do not resemble biocurrents of injury, and these may activate mechanisms different from those involving endogenous currents.
- Effective current intensities appear to differ according to tissue type and form of damage. Other parameters, such as current direction and waveform, may also be significant. Different combinations of parameters may be indicated, depending on the types of tissue

and damage, and on the stage of healing. Few clinical trials have investigated this issue.

- Tissue damage is readily identifiable in tendinopathic disorders, and contributes to their clinical symptoms. Dysfunctional healing is a factor in the development of chronicity and may promote recurrence, which is a common finding in tennis elbow studies. If functional healing could be encouraged by therapy, this might reduce both present symptoms and recurrence.
- Systematic review of clinical trials for tennis elbow have found only limited evidence of benefit for any existing treatment of the disorder, and consistently identify the need for improved methodological quality and reporting. More than 40 outcome measures have been used in published tennis studies, often with no regard to their validity and reliability. Diagnostic and eligibility criteria also vary substantially between them, and are rarely justified. These issues therefore merit particular attention.
- Sonography is capable of diagnosing and identifying tissue changes in tendinopathy, and is increasingly being used as an outcome measure in tennis elbow trials, but little reliability data is available to support this. Assessment protocols and measurement scales vary in ways that may affect reliability and responsiveness.
- A clinical trial is warranted, to assess the effectiveness of MCT in the management of tennis elbow, but preliminary experimental work is required to evaluate a protocol that includes measures relating to tissue healing and clinical variables, and to provide guidance regarding which treatment parameters to employ.

The literature reviews were based on the premise that MCT has a particular therapeutic mode of action making it suitable for specific clinical applications. Some reviews have considered a range of electrotherapeutic modalities including MCT, but not treated it as a separate modality^{166, 683}; others have focussed on the application of MCT to a specific tissue^{184, 194}. None has considered the evidence for MCT across the range of tissue disorders, to investigate whether there are common features between them; and none has focussed on the use of MCT specifically with soft connective tissues. The narrative review conducted in chapter 3 (a report of which has been published in a peer-reviewed journal⁶⁸⁴) strengthened the case for considering MCT as having a unique mode of action, with potential application to a range of tissues and disorders. It also enabled some delineation of its therapeutic windows

(although considerable uncertainty about them remains). The systematic review provided the first rigorous examination of trial data specific to soft connective tissue, and it is intended to submit a report of it for publication.

The quality scoring system used in the systematic review represents both a strength and a weakness in this study. It was developed in response to the criticisms that have been levelled at existing quality scales: that their focus on RCTs downgrades or excludes studies that may provide useful and credible data⁶⁸⁵, and that they give insufficient attention to full descriptions of treatments, co-interventions and participant concordance, which are particularly important in multi-modal treatments commonly used in conservative management strategies²²⁵. By drawing on existing, validated scales and expanding them to address these deficiencies, the quality assessment tool was tailored to the particular requirements of the review, and well-suited to the purposes of this investigation. It may have wider applicability. However, it lacks some legitimacy because some of the guidelines that have been advocated for the development of assessment scales^{227, 686} were not employed. For example, the scale was not submitted to a panel of experts to judge its face validity, nor was it evaluated for inter-rater reliability or internal consistency. Such procedures would be required before the scale could be recommended for broader use. The inclusion of non-RCTs in the review was valuable because it ensured that data on adverse effects and patient acceptability was available, and these are important considerations in the evaluation of a novel therapy.

Strictly speaking, the survey of clinicians reported in Chapter 4 was not an essential component of the broader investigation. It would have been possible to select a soft tissue disorder solely by reference to the literature. A tendinopathic disorder would probably still have been chosen, since the majority of evidence from existing clinical trials, and from relevant animal and cellular studies, relates to tendons. However, the survey provided data that helped in selection of a particular disorder to treat, and also highlighted issues in diagnosis that were used in development of the trial protocol. It also indicated the disorders that are causes for concern in current clinical practice, the variations in management of the disorder, departures from evidence-based recommendations, and the differences in outcomes achieved. These findings may be of interest to the broader clinical and research communities, and an account of them has been published²⁹¹.

The attention given to design and protocol development for the clinical trials was justified both by the aims of this investigation and concerns that have been expressed in the literature. In a recent international survey of course tutors and clinical experts concerned with

musculoskeletal research, the validity, reliability and selection of assessment tools and outcome measures were amongst the most important priorities identified for postgraduate research⁶⁸⁷. As chapter 5 demonstrated, tennis elbow studies have used a vast array of outcome variables and instruments to measure them - at least 50 variables and 40 instruments were identified in the survey of tennis elbow literature. Many of these have been employed with little or no apparent regard for their measurement properties. This appears particularly true of trials of surgical interventions, where effectiveness is often judged in terms of clinician ratings and questionnaires for which no validity or reliability data is available⁶⁸⁸. However, trials of conservative interventions have also used unvalidated outcome measures. In particular, the growing use of sonography as an outcome measure in tennis elbow trials has not been matched by attention to its measurement properties. The survey of the relevant literature conducted for this investigation, and a series of recommendations resulting from it, has been published⁵⁵⁵. These recommendations were followed in the trials reported earlier.

Using sonography both for diagnostic purposes and as a measure of tissue healing was not unproblematic. In the trials, a sonographic diagnosis of tendinopathy was based on evidence of abnormality provided by either greyscale or Doppler images. This criterion may have been too liberal, since greyscale changes due to age-related tissue degeneration would be expected in older participants, even in non-symptomatic tendons. A combination of both greyscale and Doppler abnormalities may have been the more appropriate criterion, since it has been found to be highly correlated with clinically-diagnosed tennis elbow. The trials used a combination of both clinical and sonographic evidence for diagnosis, but it is possible that some participants were misdiagnosed on the basis of similar symptoms from a different cause coupled with greyscale changes due to ageing.

The validity of sonography in identifying structural features of tendinopathy has been established by comparison with histological findings, but its use to gauge pathological severity has yet to be validated, and few reliability studies are available. The significance of changes in the sonographic appearance of the pathological tendon remains moot, and so interpretation of the scale created for this study was not straightforward. In spite of these reservations, sonography was judged the most feasible option in the context of this investigation, and one that could provide useful data on changes occurring within the tissue. The work done to enhance and evaluate the quality and consistency of sonographic assessments provided reliability data that was essential for interpretation of data from the trials. It also provided Minimum Detectable Change (MDC) values that would be needed if the scales were to be employed in other studies.

The reliability studies conducted with dynamometry and pressure algometry were significant in two respects: first, they led to the exclusion of pressure-pain threshold from the trial protocol because of its unreliability, thus avoiding unnecessary patient discomfort and the collection of unusable data; second, they provided confirmation that PFGS measurements could be made reliably, and indicated an MDC value that has not previously been reported. It also underscored the importance of conducting reliability studies with symptomatic populations, amongst whom MDC values may be higher than the normal population because of symptom lability. In retrospect, given the problems experienced later with the Patient Specific Functional Scale, it would have been preferable to subject this measure – as well as the PRTEE – to reliability-testing. This might have led to efforts to improve reliability of the PFGS measurement, as well as providing MDC values for both variables.

Since the trials were conducted, an experienced research group with numerous tennis elbow publications in high quality peer-reviewed journals has published a protocol for a tennis elbow trial⁶⁸⁹. With the exception of sonography, they have selected the same outcome measures chosen for this study, including patient-rated global change, treatment success, the PRTEE questionnaire, pain-free grip strength and adverse events. They also include a measure of anxiety and depression, and pressure pain threshold. The former variables were addressed during baseline assessment in this investigation, and the latter was considered, but dropped after reliability-testing. Their protocol includes additional measures of resting/worse pain (which is questionable since are already measured by the PRTEE), health-related quality of life, kinesiophobia and economic costs. The overlap in outcome measures provides some reassurance that the selection of clinical measures employed in this investigation was appropriate.

This does not represent an inevitable convergence of protocols in tennis elbow trials, however. Other recently published studies continue to use outcome measures of dubious or unproven reliability, such as maximum grip strength or the Nirschl score^{494, 690, 691}. The survey of trial protocols conducted as part of the experimental design process reported in Chapter 5 revealed the heterogeneity in diagnostic and eligibility criteria and assessment procedures used in studies. This can make comparison of findings and meta-analyses of data impossible, which is particularly unfortunate given that pooling of data could compensate for the low study sample sizes commonly reported. The arguments proposed for the outcome measures adopted in this investigation could help inform the development of a common protocol for tennis elbow trials, which would add value to research output^{308, 692}.

The trials themselves produced a data pool and findings that can inform the development of a protocol for a full trial of MCT with tennis elbow - this is discussed later. They provide strong evidence that MCT can treat chronic tennis elbow safely, and successfully from the patient point of view; objective measures were less convincing, however. Pain-free grip strength data may have been compromised by the problems with the dynamometer, and the sonographic changes observed were small. Further work on the sonographic scales, by including other pathological features, increasing the number of level4s or using computer-aided measurement, might increase their responsiveness to change.

The trials were planned as exploratory studies, and were not expected to be sufficiently-powered to detect statistically significant differences between groups on all measures. Nevertheless, the decision not to include a control group receiving either no treatment or a different treatment was a risky strategy: if there had been no observed differences between groups there would have been no evidence that MCT had any effect, because the groups would be expected to improve over time even without treatment. In the event, there were significant differences between groups on some measures but, given the larger than expected recruitment figures, a single trial comparing three groups, two receiving different forms of MCT and one control, might have provided more convincing evidence. In fact, during the investigation consideration was given to an alternative analytical approach: statistical comparison of outcomes with those of another trial involving a minimal intervention group, using data for participants matched on significant baseline variables. Lead authors for two suitable published trials, which used the same outcome measure of treatment success as this investigation, were approached with a view to obtaining a raw dataset, but in the event it was not possible to obtain the data. In any case, matching may not have been possible, and no comparable sonographic data were collected in these studies. Comparisons of group values for treatment success were used, but these were undermined by potentially significant baseline differences between groups.

The trials represented the culmination of several investigative strands in this investigation, each of which has generated its own insights and findings. These are summarised in Table 9.2.

Table 9.2: Original findings and contributions of this investigation

1. There is a dearth of clinical evidence regarding the therapeutic application of microcurrent to other forms of tissue, particularly the soft connective tissues. A systematic review of clinical trials concluded that the evidence is generally of low quality and poorly reported, but sufficient to suggest that certain types of MCT may be of benefit in the management of some soft tissue disorders.
2. A survey indicated that physiotherapists find the tendinopathies amongst the most debilitating and difficult to treat disorders that they see commonly in practice. Frozen shoulder, plantar fasciitis and tennis elbow were rated the most problematic disorders in these regards.
3. A standardised sonographic assessment protocol was developed, using subjective rating scales applied to greyscale and Power Doppler images, to provide measures of tendon structural abnormality and hyperaemia in tennis elbow. Reliability varied depending on the sonographic feature assessed, but ranged from moderate to excellent for aggregate greyscale scores and hyperaemia scores, whether measured by two different raters or the same rater on two occasions. The concurrent validity of the scales was not established, although arguments for their face validity were proposed.
4. The test-retest reliability of pain-free grip strength measurements made with a symptomatic population was established, and Minimum Detectable Change values were calculated for PFGS measurements and the two sonographic scales.
5. Pressure Pain Thresholds and the Patient-Specific Functional Scales were found to be unreliable outcome measures when used as described with people with tennis elbow.
6. Two trials comparing different forms of MCT for chronic tennis elbow were conducted. These concluded that:
 - a. All forms of MCT evaluated were associated with significant improvements in patient-rated outcomes by 3 months after treatment
 - b. MCT with peak current intensity of 50 μA produced significantly better patient-rated outcomes than with intensity 500 μA .
 - c. MCT with a biphasic waveform produced similar outcomes to one with a

predominantly monophasic waveform of similar intensity but applied for a much shorter time.

- d. Higher baseline hyperaemia levels were significantly associated with falls in blood flow after treatment and with greater treatment success rates. Hence, the therapeutic action of MCT may be dependent on baseline intra-tendinous blood flow.
- e. High baseline bloodflow decreased with MCT, with statistically significant falls after 3 weeks of MCT; low baseline bloodflow increased with MCT, rising significantly by 6 weeks from baseline. These observations suggest that MCT may be capable of regulating, not merely stimulating, intra-tendinous blood flow.
- f. Although there were consistent patterns of difference between group means, small effect sizes and/or large group variances meant that the studies were underpowered to detect significant differences between groups on most outcome variables. The trial follow-up period may also have been insufficient to observe significant structural change in the tendon. Hence, type II error may have occurred in these trials.
- g. Adverse effects of treatment were rare and mostly attributable to equipment and other correctable protocol issues rather than the microcurrent itself; patient attitudes to the treatment were positive and compliance with the protocol excellent.
- h. Longer treatment times and the use of co-interventions that promote remodelling may enhance treatment effects.

Although this investigation has sought to maintain a clinical focus throughout, many of these implications are more directly and immediately relevant to the research community than to clinicians. The most clinically relevant conclusion is that MCT cannot at present be recommended for routine use in cases of chronic tennis elbow (or indeed for any of the other soft connective tissues addressed in the systematic review, since the quality of evidence was generally poor). The survey of physiotherapists reported in chapter 4 suggested that MCT is rarely used in the UK at present; however, it appears to be better known and used in other

countries, particularly in North America (Kloth, personal communication). This investigation suggests that its application for tendinopathic disorders does not yet have a firm evidence base, and may only be supported by the experience of individual practitioners. However, further trials are certainly justified, and these may furnish data that will enable clinicians to make more evidence-informed decisions about using this modality.

9.6 RECOMMENDATIONS FOR FURTHER INVESTIGATION

The studies described in preceding chapters suggest a number of avenues for further investigation that may be of value to the research community and to clinicians:

1. The instrument developed for assessment of methodological quality of clinical trials may represent an improvement on some existing tools because it enables consideration of a variety of trial designs, not only RCTs. Evaluation of its inter-rater reliability, discriminatory capacity and internal consistency would enhance its credibility. Alternatively, it could be used as source material for the development of a new scale.
2. The review of trials of treatments for tennis elbow revealed the heterogeneity of protocols used. Although the details of trial methodologies will vary with their aims, there is scope for the development of a common protocol with standard case definitions and diagnostic criteria, as well as validated and reliable outcome measures⁶⁹². A systematic review of the most common outcome measures, identifying the validity and reliability data that exists for each, could help in the development of this protocol.
3. A raw data set gathered from trials using such a common protocol might be valuable to research groups for comparative purposes, and possibly for calculation of effect sizes in pilot studies.
4. Although validation of the sonographic assessment scales against histological data in a longitudinal study is problematic for the reasons identified earlier, a cross-sectional correlation study might be of value. This would involve sonographic assessment and rating of tissue that is about to be excised during surgical treatment of tennis elbow. Intra-operative visual inspection and subsequent histological analysis could provide comparative quantitative data that could be used to assess both greyscale and

hyperaemia ratings. A scale that has been developed to assess changes and vascularity in excised tissue samples from patellar tendons⁶⁹³ could be used for this purpose.

5. The potential effects of MCT on local biochemistry could be investigated using microdialysis. The problem with using this as an outcome measure is that it involves injury to the tendon⁵¹⁰, and so may interfere with the healing process. In fact it may enhance it, since surgical and other invasive procedures may be effective primarily by re-initiating a stalled healing process. New techniques for investigating tendon anatomy and physiology are being developed, but most of these involve some degree of tissue damage⁶⁵⁷. Microdialysis may therefore be the best available option at present for investigating the presence of biochemicals associated with pain, the cardinal symptom of tennis elbow.
6. Baseline hyperaemia levels were prognostic of treatment success in this study. This may be particular to MCT or may have wider applicability. If hyperaemia is measured in other studies, this possibility could be investigated. It might then be of value in clinical decision-making about management strategies.
7. Further development of reliable and responsive sonographic scales is desirable to enhance their credible use in tennis elbow (and other tendinopathy) studies; the experience and data gathered in this study may be useful source material for that work. The improvements in reliability that were obtained in this investigation compared to previous studies suggests that directed training of inexperienced practitioners for a specific application is feasible. This may encourage greater uptake of this imaging modality for both diagnosis and treatment effectiveness studies.
8. Longitudinal sonographic studies have been conducted with other forms of tendinopathy to investigate their natural history^{694, 695}. This should also be done with tennis elbow so that patterns of change, and the predictive properties of particular features, can be investigated.
9. The evaluation of outcome measures enabled Minimum Detectable Change values to be calculated for several of them. It would be useful to both researchers and clinicians to have values for Minimum Clinically Significant Difference (MCSD) values, which appear to be scarce in tendinopathy research⁶⁹⁶. These may be calculated by comparing changes in the variable of interest with changes on a reference scale, such as a global change scale, but the validity of conducting such an analysis

retrospectively has been questioned⁶⁹⁷. MCSD values for the PRTEE and PFGS scores are not available in the literature, and so a prospective study to establish these would be valuable. It has been argued that these, rather than the MDC values, should be used to calculate trial sample sizes⁶⁹⁸.

10. This investigation has concluded that a clinical trial of MCT for tennis elbow is indicated. The preliminary studies provided useful data and experience to inform the trial protocol. These are discussed in more detail in the next section.
11. The proposed clinical trial evaluates a single form of MCT. Uncertainty remains about the influence of parameters other than current intensity. Trials comparing different waveforms, treatment durations and electrode positions – and their effects during different phases of healing - might help further define the therapeutic window.
12. There is evidence of benefit of MCT with acute tissue injuries, such as osteotomies, spinal fusions, skin grafts, fresh fractures and surgically injured or repaired tendons and ligaments. The potential of MCT to promote healing after tendon strains and frank tears should also be investigated, particularly as these may predispose to further injury.

9.6.1 Protocol for a full trial

The protocol used with the preliminary trials described in previous chapters has many elements that appeared appropriate for use in the full trial. However, a number of modifications are required, and this section identifies them.

Aims

This investigation has concluded that of the types of microcurrent evaluated, low frequency monophasic 50 μ A peak amplitude current is most likely to be effective and that its impact may be enhanced by an exercise programme and longer treatment duration. These conclusions provide the rationale for a trial that evaluates the effects of adding MCT to a conventional form of treatment of this disorder. Given the uncertainty about the relationship between tendon tissue changes and symptoms, clinical considerations should determine the primary outcome of interest. However, if MCT can promote tissue healing in tennis elbow, this is significant because it may reduce the chances of recurrence. Therefore the aims of the trial are to investigate

1. whether addition of MCT with specified parameters to a course of standard physiotherapy (including education, advice and an exercise programme) improves short and long term efficacy and reduces recurrence rates in chronic tennis elbow, compared to standard physiotherapy alone.
2. the nature and extent of changes that occur in tissue structure and blood flow during and after this treatment

Design

A well-conducted parallel arm randomised controlled trial is the design of preference because it can provide the highest level evidence of treatment effectiveness. It was argued in Chapter 5 that, since the symptoms of tennis elbow tend to resolve with time, the use of a control group receiving no treatment would enable comparison of the active treatments with a minimal intervention approach. However, group data on outcomes from such an approach is available from two independent trials and can be used for comparative purposes, as was done in this investigation. This enables all participants to receive treatment and so maximises the numbers available for subgroup analysis, which is proposed in this protocol. Like other electrotherapies, MCT may benefit from a substantial placebo effect⁶⁹⁹. A placebo-controlled trial is therefore appropriate, although it is increasingly accepted that evidence of a placebo effect is not necessarily a reason to reject a therapy⁷⁰⁰. Based on data from this investigation, and to compensate for anticipated attrition rates of 15%, a sample size of 70 per arm will be recruited.

Recruitment and Eligibility

The preliminary studies recruited via local advertising and excluded people who were already receiving treatment from another source. As a result, the sample comprised people whose symptoms were not severe enough to drive the individual for conventional treatment, or those who had received such treatment but regarded it as ineffective. In order to recruit a more representative sample, it is proposed to attempt recruitment via local GPs and NHS outpatient physiotherapy departments. A local primary care research network exists, part of whose remit is the facilitation of recruitment to trial from general practices. Recruiting from NHS facilities also has pragmatic justification: it widens the recruitment pool and may also open up avenues of funding for the study. If MCT proves effective, practitioners involved in recruitment may also be more open to using it with future patients.

The main inclusion criterion for this study is a clinical diagnosis of tennis elbow accompanied by both greyscale and Doppler sonographic signs of tendinopathy. The clinical diagnosis is

based on history and examination, but must include a positive response to at least two of provocation tests used in the trials, one of which must be tenderness to palpation over the affected tendon. Symptoms must also have been present for at least three months, which is a somewhat arbitrary cut-off for defining chronicity. These criteria provide the case definition of tennis elbow for use in this trial. In order to make the study as relevant as possible to clinical practice, exclusion criteria will be kept to a minimum. They will include upper quadrant disorders that might contribute significantly to the signs and symptoms of tennis elbow, such as elbow arthritis or cervical radiculopathy. A positive response to the upper limb tension test that will not exclude participation, since this may be present in up to 50% of people with tennis elbow³³⁹. Rather, those with this sign will be taught a simple radial nerve mobilisation technique that may be added to their home exercise programme⁶⁰¹. Any treatment for tennis elbow within the previous three months, other than analgesia and use of a brace, will exclude participation to ensure that any changes observed are more likely due to trial interventions or natural resolution. The eligibility criteria are summarised in Table 9.3.

Table 9.3: Eligibility criteria for proposed trial

Inclusion criteria

- Lateral elbow pain for at least 3 months, and no significant improvement, as judged by the participant, in the previous month
- Pain severity on normal gripping activities of at least 3/10 or a numerical rating scale
- Lateral elbow pain provoked by palpation over the affected tendon and at least one of the following: the chair lift test, resisted wrist or middle finger extension with the elbow extended
- Sonographic evidence of pathology in the common extensor tendon consisting of both greyscale abnormalities and hyperaemia
- Age over 18
- An acceptable understanding of written and spoken English
- Willingness to comply with treatment and follow-up assessments

Exclusion criteria

- Any treatment for tennis elbow in the preceding 3 months
- Concomitant neck or other arm pain that has prevented participation in usual work or recreational activities or necessitated treatment within the last 6 months
- Evidence of other primary sources of lateral elbow pain, including exacerbation of elbow pain with cervical spine clearing tests
- Elbow surgery, malignancy, inflammatory or arthritic disorder

Interventions

Systematic reviews of treatments for tennis elbow continue to conclude that there is little convincing evidence upon which to base the management of tennis elbow^{305, 335, 701}. Expert opinion suggests that a multimodal approach is required, typically comprising advice and education, prevention of further injury, exercise, manual therapy and various forms of analgesia^{285, 702, 703}. Where the promotion of tissue healing is a particular goal, protection of the tissue and repeated mechanical stimulation are likely to be beneficial, therefore these are regarded as key components for the standard intervention in this protocol. Advice, education and the use of a tennis elbow brace have all been proposed as enhancing protection of the area. None of these are firmly evidence-based, although there is weak evidence in favour of the use of counter-force braces^{704, 705}. As for exercise, there are no gold standard guidelines but increasing evidence that eccentric exercises may be of benefit in a range of tendinopathies, including tennis elbow^{678, 706}. No single regime has yet proven superior to others, and existing programmes vary considerably in relation to frequency, loading, progression, whether they should be painful and whether they are supervised or home-based⁶²⁴. Decisions on these matters must therefore be taken on a pragmatic basis.

All participants will be provided with education and advice about the disorder and ways of protecting and reducing stresses on the tendon. Those whose work or recreational activity involves repeated heavy loading of the affected limb will be provided with a counter-force brace, instructed in its use, and advised to wear it when loading is likely to be an issue. A combination of supervised and home-based exercises may benefit from the advantages of both approaches: motivation, progression and correction of technique can be provided by the therapist, and frequency, cost-effectiveness and patient-convenience may be enhanced by self-treatment. The use of MCT as an adjunct may improve adherence to the exercise programme if patients are aware of the potential synergy between the two: understanding that exercise is necessary to help strengthen and remodel the tissue whose synthesis has been promoted by MCT. This provides an additional rationale for using placebo MCT – both groups will then be using microcurrent devices – although the knowledge that there is a 50% chance of not receiving MCT may decrease compliance in some cases.

The exercise programme draws on several that have already been judged effective in clinical trials. It comprises a stretching and strengthening regime involving both concentric and eccentric movements, whose intensity is set so that the eccentric movement is borderline painful but not increasingly painful. Resistance is provided by a resistive elastic therapy band and exercises are progressed by shortening the band. A therapy band is more portable than a weight and so may be used in the workplace if preferred. Wrist extensors and forearm

supinators are both targeted. The exercise programme is conducted once daily, five days a week for eight weeks, and is primarily home-based; however, the participant is asked to attend clinic four times over the eight week period, during which visits the exercises are conducted, monitored and progressed.

Microcurrent treatment is provided by a modified version of the device that was used in the first trial of this investigation. A new model is currently in production, which is smaller than the original and has been redesigned to avoid the possibility of shocks experienced by two participants in that trial. It will deliver current of the same parameters as found most effective in the trial, except that the programmed treatment time will be increased to two hours. The method of application will be the same as before, except that skin preparation will be by cleaning alone, and not involve abrasion. The devices to be used with the control group will be modified so that they deliver no current, but will be otherwise identical to the active devices. Each unit will have a unique number code. The total duration for MCT will be 160 hours spread over eight weeks, delivered 4 hours/day, 5 days/week. This compares to 34.5 hours over three weeks in the preliminary trial, and brings the total treatment duration closer towards those found effective in the bone and skin studies reviewed in Chapter 2. The five-days-a-week regime provides participants with some flexibility in allocation of treatment, and coincides with the exercise programme. It is intended that using the device will remind and encourage participants to carry out the exercises at the same time.

Compliance with treatment will be assessed primarily by requiring the participant to complete a diary that indicates the days on which the treatments were done, whether both exercises and microcurrent treatments were completed, and any problems or issues arising. The diary will also enable the participant to state whether and how they progressed the exercise component of treatment. The possibility of including an electronic compliance meter in the MCT device will also be investigated, along with an audible alarm monitoring circuit integrity. As an additional check, participants will be monitored performing all elements of the treatment during visits to the clinic. A systematic review of strategies to enhance compliance with treatment protocols involving exercise concluded by recommending a combination of diaries feedback and goal-setting³³, all of which are provided by this protocol. Additional supplies of any necessary materials will be provided during visits to the clinic. Participants will be requested to have no other form of treatment apart from analgesic mediation, and compliance with this request will also be checked at the clinical visits.

Assessment

Initial screening will establish whether symptoms have been present for at least 3 months, whether any other treatments are or have been recently received, and willingness in principle to comply with the requirements of the study. Apparently suitable candidates will be invited to baseline assessment, at which medical history and relevant socio-demographic data will be recorded, and a physical examination conducted, using a proforma similar to that used in this investigation. Data on body mass index will also be collected as that has been identified as a potential factor in the development of tennis elbow⁶¹⁶.

The outcome measures will be similar to those used in the preliminary trials, but with a number of additions and modifications. To reflect the patient-centred, clinically-oriented nature of the trial, the primary outcome measures are:

- the patient-rated global change scale and associated measure of treatment success. In addition, the clinical assessor will assign their own global change score, based on their overall subjective and objective assessment of the participant.
- Recurrence rates, defined by a treatment success rating at first or second follow-up and a no-success at any subsequent follow-up assessment⁶⁸⁹. Where recurrence is noted, participants will be questioned to ascertain the nature of the deterioration, and whether any behaviours or environmental factors may have contributed to this outcome.

Secondary outcome measures are:

- Pain, as measured by the PRTEE. The minor word changes to the questionnaire that were made in this investigation will be retained. Average pain over a previous period is a commonly-employed measure in trials of tennis elbow (see section 5.5), and its use will enable some comparison with the results of other studies. Pain over the previous week is addressed by several items in the PRTEE, but not average pain. It will therefore be added to the pain sub-section of the questionnaire but analysed separately.
- Pain-free grip strength, using a Jamar-type isometric grip dynamometer. More specific guidance on technique will be given: for MGS, participant will be asked to build up the grip over a few seconds up to a maximum and then release. PFGS will then be measured the same way, except that the participant will be asked to stop

squeezing as soon as their normal pain is felt at the elbow. No verbal encouragement will be given, and recorded values will be hidden from participants.

- Function, as measured by the PRTEE and the PSFS. On the assumption that the unreliability of the patient-specific functional scale was due to the masking of previous scores, this scale will be used again but with previous scores shown to the respondent. The PRTEE manual gives no guidance on this matter⁵³⁹ and so, for consistency, previous responses to this questionnaire will also be shown to the participant.
- Tissue abnormality. The sonographic assessment scale developed for the preliminary trials would benefit from further development to increase the reliability of scoring for individual features, and to decide which features should be incorporated into an aggregate greyscale score. Further collaboration with radiologists experienced in this area will be necessary. The possibility of more objective scoring – screen calliper-measurement of tendon thickness and tear dimensions, and computer-assisted pixel counts for hyperaemia scoring – will also be investigated. A scale, or several scales using these data, will then be developed for use.

Adverse events, patient impression of the treatment and compliance levels will also be assessed as before. Since recurrence is a primary outcome measure in this study, data collection over the long term is required. Also, patterns of change in tendon structure and hyperaemia are of particular interest, and so regular assessment over the course of the study will be necessary. Six formal assessments over the course of a year are therefore proposed: at baseline and 4, 8, 12, 26 and 52 weeks later. The 4 and 8-week assessments will be mid-way and at the end of the treatment. For participants with radial nerve involvement at baseline, the upper limb tension test will be repeated at subsequent assessments.” A flow chart of the trial process is given in Figure 9.1.

Assessments will probably require more than one person so training in the use of all measures (and common interpretation of sonographic scales) will be provided, and each participant will be seen by the same assessor for all assessments if possible. All clinical assessments will be conducted by a qualified physiotherapist with a minimum two years experience of treating musculoskeletal disorders. Sonographic assessments will be conducted either by a qualified sonographer or radiologist with musculoskeletal imaging expertise, or by a physiotherapist trained specifically for this purpose. Relevant reliability data will be collected before the study commences.

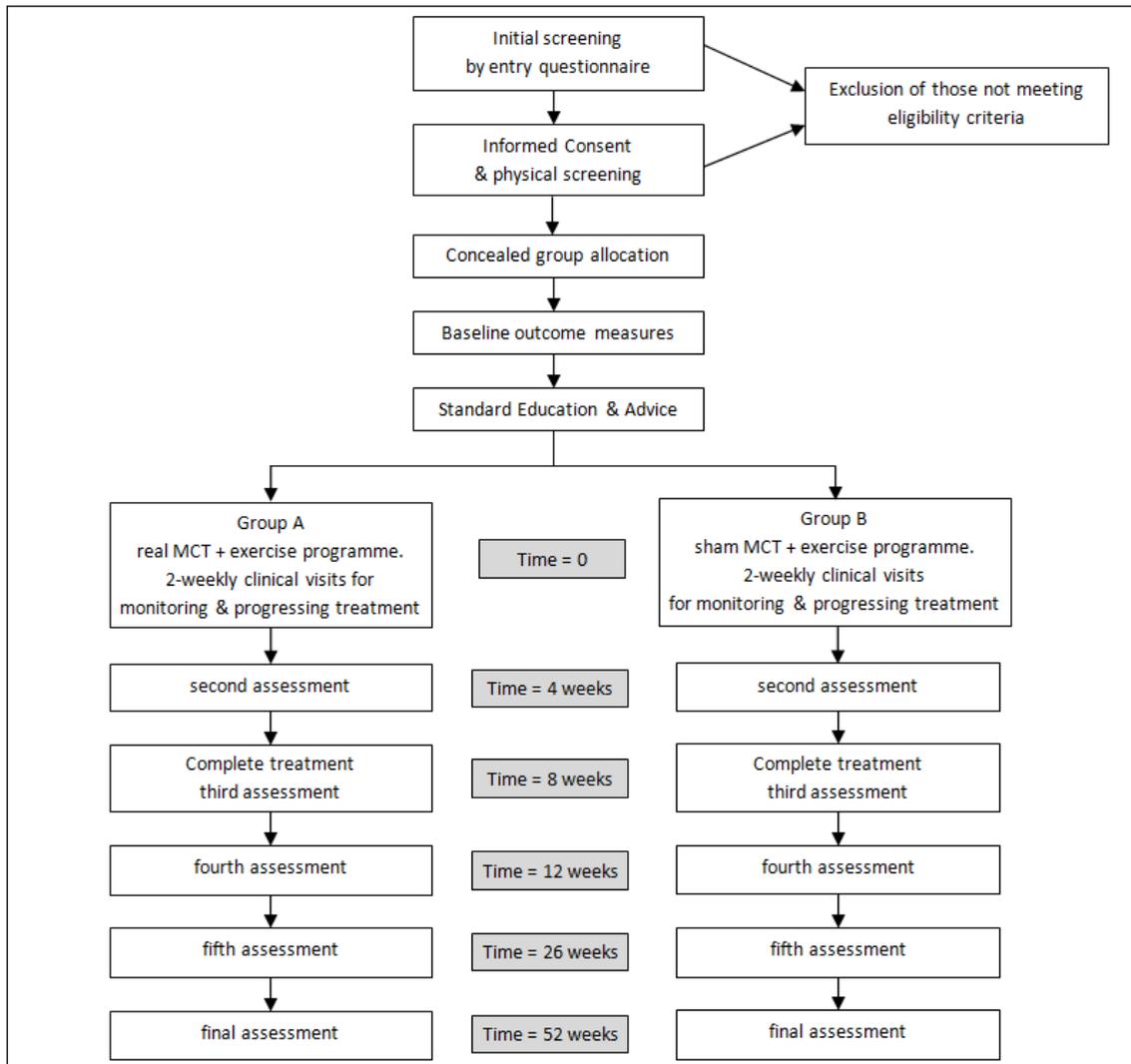


Figure 9.1: Flow chart of proposed clinical trial of MCT

Randomisation, allocation and masking

Participants will be randomly allocated to one of the treatment groups using a computer-generated block allocation sequence as in the preliminary trials. The sequence will be generated and held by an independent researcher not involved in assessment or data collection, and will be communicated as necessary to the clinicians initiating treatment. This researcher will also hold the key to the numerical codes of the MCT devices (indicating whether they deliver microcurrent or not) and will instruct the clinician as to which number device is to be used in each case.

MCT of the chosen parameters was sub-sensory in most cases in the preliminary trial – 2/15 reported a tingling sensation at some point during use. Hence, masking to group allocation cannot be guaranteed. Both participants and assessors will be asked at the end of the treatment to guess their group allocation, so that the success of masking can be gauged. Therapists responsible for assessment will not be blinded to symptoms, but those conducting sonography will be.

Data analysis

All analyses will be conducted on an intention-to-treat basis by an investigator masked to group allocation. Descriptive statistics will be obtained, and data assessed for adherence to parametric assumptions. Tests will be conducted for baseline differences between groups on potentially significant prognostic variables – age, sex, pain, symptom duration, body-mass index and ongoing stress to the tendon. For parametric data, analysis of covariance will be conducted using baseline scores as covariate and changes between baseline and follow-up assessment scores as the dependent variable. Time will be the main effect and group the interaction effect. Dichotomous measures will be analysed by relative risk, and numbers needed to treat calculated. Sub-group analyses will also be attempted, with sub-groups defined by baseline pain severity, greyscale abnormality and hyperaemia score. Correlations between raw and change scores for sonographic and clinical variables will also be investigated.

9.7 CONCLUDING REMARKS

This report has attempted to impose a sense of logical progression on an investigation that evolved in ways that occasionally seemed chaotic and arbitrary. Decisions taken on apparently reasonable and rational grounds sometimes led to unforeseen consequences, or created methodological challenges without obvious solutions. A desire to be rigorous often resulted in the endless consultation of the literature, which often appeared contradictory, and promoted uncertainty rather than clarity. Few of the positivist certainties held at the beginning of this work were intact by the time it was concluded. In hindsight, the investigation is characterised by a methodological complexity that may have reduced its chances of producing a clear and sound conclusion. A simpler approach may have produced a less conditional, more satisfying and clinically relevant response to the thesis.

For all that, the investigation has led to a number of original findings which may enhance understanding of the potential of microcurrent therapy, provide the research community with useful data, and add to an evidence base that may ultimately be of benefit to patients. At the same time it has provided an opportunity to develop a range of research skills, both quantitative and qualitative, an appreciation of the relationship (and sometimes the lack of one) between basic science and clinical practice, and a more critical and structured approach to the planning, conduct and evaluation of research. A number of presentations have been made and papers published on the basis of the work undertaken during this investigation. Several more are in preparation. It is hoped that these will make a worthwhile contribution to the understanding and practice of electrotherapy, as well as being tokens of the research apprenticeship that generated them.

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Appendices

1 Search strategies used to identify studies for potential inclusion in a systematic review of microcurrent treatment of soft connective tissue disorders.

PubMed (1960 - 2009)

- 1 microcurrent*
- 2 "low intensity direct current"
- 3 microamp*
- 4 micro-amp*
- 5 OR/1-4
- 6 Clinical trial randomized controlled trial
- 7 controlled clinical trial
- 8 control trial
- 9 random allocation
- 10 single-blind
- 11 double-blind
- 12 triple-blind
- 13 mask*
- 14 blind*
- 15 random*
- 16 latin square
- 17 placebo*
- 18 comparative study
- 19 evaluation study
- 20 follow-up study
- 21 prospective study
- 22 cross-over study
- 23 non-randomized
- 24 case study
- 25 case series
- 26 prospective
- 27 retrospective
- 28 volunteer*
- 29 OR/6-28
- 30 human [lim]

EMBASE (1980-2009)

- 1 microcurrent*.tiab
- 2 "low intensity direct current" .tiab
- 3 microamp* .tiab
- 4 micro-amp* .tiab
- 5 OR/1-4
- 6 Clinical trial randomized controlled trial
- 7 .tw
- 8 controlled clinical trial .tw
- 9 control trial .tw
- 10 random allocation .tw
- 11 single-blind .tw
- 12 double-blind .tw
- 13 triple-blind .tw
- 14 mask* .tw
- 15 blind* .tw
- 16 random* .tw
- 17 latin square .tw
- 18 placebo* .tw
- 19 comparative study .tw
- 20 evaluation study .tw
- 21 follow-up study .tw
- 22 prospective study .tw
- 23 cross-over study .tw
- 24 non-randomized .tw
- 25 case study .tw
- 26 case series .tw
- 27 prospective .tw
- 28 retrospective .tw
- 29 volunteer* .tw
- 30 OR/6-28
- 31 5 AND 29
- 32 human [lim]

Cinahl (1981-2009)

- 1 microcurrent*
- 2 "low intensity direct current"
- 3 microamp*
- 4 micro-amp*
- 5 OR/1-4

AMED (1980 – 2009)

- 1 microcurrent*.tiab
- 2 "low intensity direct current" .tiab
- 3 microamp* .tiab
- 4 micro-amp* .tiab
- 5 OR/1-4
- 6 Clinical trial randomized controlled trial .tw
- 7 controlled clinical trial .tw
- 8 control trial .tw
- 9 random allocation .tw
- 10 single-blind .tw
- 11 double-blind .tw
- 12 triple-blind .tw
- 13 mask* .tw
- 14 blind* .tw
- 15 random* .tw
- 16 latin square .tw
- 17 placebo* .tw
- 18 comparative study .tw
- 19 evaluation study .tw
- 20 follow-up study .tw
- 21 prospective study .tw
- 22 cross-over study .tw
- 23 non-randomized .tw
- 24 case study .tw
- 25 case series .tw
- 26 prospective .tw
- 27 retrospective .tw
- 28 volunteer* .tw
- 29 OR/6-2
- 30 5 AND 29
- 30 human [lim]
- 31 treatment [lim]

Clinical trials registers (- 2009)**ChiroAccess (1980-2009)****OpenSigle (-2009)**

- 1 microcurrent*.tiab
- 2 "low intensity direct current" .tiab
- 3 microamp* .tiab
- 4 micro-amp* .tiab
- 5 OR/1-4

ISI Web of Science (- 2009)

- 1 microcurrent*.tiab
- 2 "low intensity direct current" .tiab
- 3 microamp* .tiab
- 4 micro-amp* .tiab
- 5 OR/1-4
- 6 surgery, health sciences, pathology, general medical, nursing sports, emergency medicine, human [lim]

Google Scholar

- 1 microcurrent
- 2 microamp
- 3 1 OR 2
- 4 first 100 hits [lim]

Theses.com (- 2009)

- 1 microcurrent*
- 2 "low intensity direct current"
- 3 microamp*
- 4 micro-amp*
- 5 OR/1-4
- 6 tendon*
- 7 ligament*
- 8 fascia
- 9 OR/6-8
- 10 healing
- 11 repair
- 12 electric
- 13 OR/10-12
- 14 5 OR (9 and 13)

2 Study quality assessment tool used in the systematic review of microcurrent treatment of soft connective tissue disorders.

Criteria for all studies		
1	Eligibility criteria specified ¹⁻⁴	2 = comprehensive statement of inclusion and exclusion criteria 1 = partial information about relevant eligibility criteria 0 = no information about eligibility criteria Report describes the source of subjects and a list of criteria used to determine who was eligible to participate in the study. ¹
2	Treatment fully described ^{2,4}	2 = description allowing duplication of treatment provided 1 = partial description 0 = essential elements of description absent Including the microcurrent parameters, treatment method and timings, and description of any co-interventions and comparison group treatment
3	Treatment standardised ^{4,5}	2 = clear statement of how standardisation was achieved 1 = statement suggesting standardisation 0 = not standardised / unclear / no evidence presented For MCT, any co-interventions or comparison group treatment. Includes adherence to protocol by patient
4	Key baseline characteristics stated ^{4,6}	2 = data presented for key characteristics that might affect outcome 1 = data presented for some characteristics that might affect outcome 0 = no relevant data
5	Key outcome measures validated ^{2,5}	2 = evidence given for valid use of key outcome measure for this application 1 = key outcome measure has face validity for this application 0 = no evidence of validity of application Key outcomes are those outcomes which provide the primary measure of the effectiveness (or lack of effectiveness) of the therapy 1
6	Key outcome measures reliable ^{2,5}	2 = evidence given for reliable use of key outcome measures for this application 1 = partial evidence regarding relevant reliability data presented 0 = reliability of application not established or unclear Inter-rater, intra-rater or test-retest reliability as appropriate.
7	Drops outs and Intention to treat analysis ^{1-4,7} bias ⁸	2 = statement that all received intended treatment, or ITT analysis 1 = clear statement of withdrawal numbers and reasons 0 = unclear or no information presented Where subjects did not receive treatment (or the control condition) as allocated, and where measures of outcomes were available, the analysis was performed as if subjects received the treatment (or control condition) they were allocated to. This criterion is satisfied, even if there is no mention of analysis by intention to treat, if the report explicitly states that all subjects received treatment or control conditions as allocated ¹

		<p>Participants who were included in the study but did not complete the observation period or who were not included in the analysis must be described⁷.</p> <p>This item combines criteria that appear individually in other scales - the inclusion of ITT analysis and a description of drops outs. The former gives the stronger evidence of bias control; the latter allows the reader to judge the potential level of bias. The scores reflect this.</p>
8	Appropriate statistical analysis ^{1, 2, 4}	<p>2 = apparently appropriate analysis used 1 = incomplete analysis presented 0 = inappropriate or no relevant analysis</p> <p>A between-group comparison: may be comparison of outcomes measured after the treatment was administered, or a comparison of the change in one group with the change in another. The comparison may be in the form hypothesis testing (which provides a “p” value, describing the probability that the groups differed only by chance) or in the form of an estimate (for example, the mean or median difference, or a difference in proportions, or number needed to treat, or a relative risk or hazard ratio) and its confidence interval¹. Statistical power analysis should be used if trends are not statistical significant.</p>
9	Point & variability estimates for at least one key outcome ^{1, 3, 4}	<p>2 = appropriate graphical or numerical data provided 1 = partial presentation of data 0 = inappropriate or no data</p> <p>A point measure is a measure of the size of the treatment effect. The treatment effect may be described as a difference in group outcomes, or as the outcome in (each of) all groups. Measures of variability include standard deviations, standard errors, confidence intervals, interquartile ranges (or other quantile ranges), and ranges. Point measures and/or measures of variability may be provided graphically (for example, SDs may be given as error bars in a figure) as long as it is clear what is being graphed (for example, as long as it is clear whether error bars represent SDs or SEs). Where outcomes are categorical, this criterion is considered to have been met if the number of subjects in each category is given for each group.¹</p>
10	Key outcomes measured for >85% of subjects in each group ¹	<p>2 = numbers allocated and measured stated, and criterion satisfied 0 = cannot tell, or <85% in each group measured</p> <p>This criterion is only satisfied if the report explicitly states both the number of subjects initially allocated to groups and the number of subjects from whom key outcome measures were obtained. In trials in which outcomes are measured at several points in time, a key outcome must have been measured in more than 85% of subjects at one of those points in time¹</p>
11	No competing interests ⁹	<p>2 = clear statement of no competing interests 0 = potential conflict / no statement / unclear</p> <p>Competing interests were not significantly associated with authors' conclusions¹⁰</p>
Additional criteria for experimental studies involving comparison between groups		
12	Method of group assignment	2 = full description allowing duplication

	described ^{4, 6, 9, 11}	<p>1 = partial description 0 = inadequate or no description</p> <p>Were the patients in different intervention groups, or were the cases and controls recruited from the same population? Were study subjects in different intervention groups, or were the cases and controls recruited over the same period of time?¹¹</p>
13	Satisfactory method of randomisation ^{1, 3, 7}	<p>2 = clear evidence of satisfactory randomisation 1 = partial evidence of randomisation 0 = no evidence</p> <p>The report states that allocation was random. The precise method of randomisation need not be specified. Procedures such as coin tossing and dice-rolling should be considered random. Quasi-randomisation allocation procedures such as allocation by hospital record number or birth date, or alternation, do not satisfy this criterion.¹</p> <p>Method allowed each study participant to have the same chance of receiving each intervention and the investigators could not predict which treatment was next. Methods of allocation using date of birth, date of admission, hospital numbers, or alternation should be not regarded as appropriate⁷</p>
14	Groups balanced on key baseline characteristics ^{1-4, 6, 11}	<p>2 = no significant difference on all key baseline characteristics of completers, or adjustment in analysis 1 = no significant difference on most key baseline characteristics of completers, 0 = not stated or differences not dealt with</p> <p>At least one measure of the severity of the condition being treated and at least one (different) key outcome measure at baseline. The rater must be satisfied that the groups' outcomes would not be expected to differ, on the basis of baseline differences in prognostic variables alone, by a clinically significant amount. This criterion is satisfied even if only baseline data of study completers are presented¹.</p> <p>Patient groups matched for significant prognostic variables, or effect of any differences evaluated in valid statistical analysis⁹</p>
15	Allocation concealment ^{1, 3, 4}	<p>2 = clear evidence of satisfactory concealment 1 = partial evidence of concealment 0 = no evidence</p> <p>The person who determined if a subject was eligible for inclusion in the trial was unaware, when this decision was made, of which group the subject would be allocated to. A point is awarded for this criterion, even if it is not stated that allocation was concealed, when the report states that allocation was by sealed opaque envelopes or that allocation involved contacting the holder of the allocation schedule who was "off-site".¹</p>
16	Subjects blinded to treatment ^{1, 3, 4, 7}	<p>2 = clear evidence of satisfactory concealment 1 = partial evidence of concealment 0 = no evidence</p> <p>Subject did not know which group s/he had been allocated to. In addition, subjects are only considered to be "blind" if it could be expected that they would have been unable to distinguish between the treatments applied to different groups¹.</p>

		Study participant could not identify the intervention being assessed, or if in the absence of such a statement the use of active placebos, identical placebos, or dummies is mentioned ⁷
17	Therapists blinded to treatment ^{1,3,4}	2 = clear evidence of satisfactory concealment 1 = partial evidence of concealment 0 = no evidence
18	Assessors blinded to treatment ^{1-4,7}	2 = blinding clearly achieved 1 = partial evidence of blinding 0 = no evidence presented Stated that the person doing the assessments could identify the intervention being assessed, or if in the absence of such a statement the use of active placebos, identical placebos, or dummies is mentioned ⁷ In trials in which key outcomes are self-reported (eg, visual analogue scale, pain diary), the assessor is considered to be blind if the subject was blind ¹

3 documentation relating to survey of clinicians

From: Leon Poltawski
 Sent: 24 January 2007 12:57
 To: queries@corec.org.uk
 Subject: query

Dear COREC

Apologies for this query but I could not get a clear answer from your website FAQs. I am planning a questionnaire that will be sent to physiotherapists in many Trusts in southeast England. The questionnaire is to ascertain clinician perceptions about particular types of condition they treat. It does not involve information about specific patients, nor does it enquire about perceptions of their work-place or their employers - the focus is purely clinical. The questionnaire will be sent to clinicians at their workplace but does not need to be completed there.

Will our own University REC be sufficient to provide ethical review of this study? If not, how can ethical approval be obtained when the questionnaire will be sent to clinicians in many different Trusts?

Thanks for your advice.

Leon Poltawski
 Researcher in Electrotherapy
 School of Health & Emergency Professions -
 Physiotherapy University of
 Hertfordshire College Lane Hatfield
 Herts AL10 9AB

01707 284556

RE: query

Queries [queries@corec.org.uk]

Sent: 24 January 2007 14:40
 To: 'Leon Poltawski' [L.Poltawski@herts.ac.uk]

The following reply has been provided by Jo Downing, Information Officer

Thank you for your query. When asked to advise on the requirement for ethical review by an NHS Research Ethics Committee (REC) we consider the information sent to us and use the criteria in the attached table to reach a conclusion.

Based on the information provided, our advice is that the study may be classified as service evaluation. On this basis it does not require review by a NHS REC. The main remit of NHS RECs, as set out in paragraph 3.1 of the Governance Arrangements for NHS Research Ethics Committees (GAfREC), is to review research involving NHS patients. GAfREC is available on our website at www.corec.org.uk/applicants/help/guidance.htm

Although independent ethical review by an NHS REC is not necessary in this case, all types of study involving human participants should be conducted in accordance with basic ethical principles for example informed consent and respect for the confidentiality of participants. When processing identifiable data there are also legal requirements under the Data Protection Act 2000. When undertaking an audit or service evaluation, the investigator and his/her team are responsible for considering the ethics of their study with advice from within their organisation. You may find it helpful to discuss your study with the relevant R&D Office and your Data Protection Officer.

Where exceptionally an audit or service evaluation is felt to raise significant ethical issues and the host

organisation considers independent ethical review to be essential, an application may be made to an NHS REC under GAfREC paragraph 3.2.

I hope this helps.

Regards

Queries Line

Central Office for Research Ethics Committees
(COREC)

National Patient Safety Agency

Website: www.corec.org.uk

<<http://www.corec.org.uk>>

Ref: 041/01

**

This reply may have been sourced in consultation with other members of the COREC team.

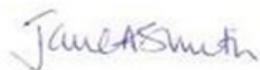
**UNIVERSITY OF HERTFORDSHIRE
FACULTY OF HEALTH AND HUMAN SCIENCES
ETHICS COMMITTEE FOR HEALTH AND EMERGENCY PROFESSIONS**

Protocol Number: HEPEC/06/07/45
Name of Investigator: Leon Poltawski
Name of Supervisor: Tim Watson
Programme: PhD Physiotherapy
Title of Study: Physiotherapist perceptions of selected refractory soft tissue lesions

Thank you for your application. The Committee has approved your study and you may now proceed with your project.

On completion of your study, please would you ask your supervisor to return the attached Quality Monitoring Form to the Clerk to the Committee, Rachel Stirton.

On behalf of the Committee, I would like to wish you all the best with your study.



Jane Smith
Chair of Ethics Committee

cc Tim Watson, Supervisor
2007

Date: 27 June



University of Hertfordshire

HEPEC/03/07/37

Hatfield Herts
AL10 9AB
UK

23rd March 2007

Switchboard 01707 284000
Maincom 01707 284000
Fax 01707 284115
www.herts.ac.uk

I am writing to invite your participation in a survey concerned with the treatment of soft tissue conditions, such as such as tendinopathies and ligament sprains. Taking part involves completion of a questionnaire, which should take about 20 minutes.

The survey aims to establish which are the soft tissue conditions that physiotherapists find most resistant to treatment. Chronic soft tissue conditions are a significant source of pain and disability, and can require substantial inputs of health-care resources, sometimes with unsatisfactory outcomes. The results of this survey, which we aim to publish, may assist in prioritising resources for the development and use of more effective treatments. If you wish, a report of the study findings will be sent to you.

The questionnaire forms part of a doctoral study of electrotherapy, under the supervision of Professor Tim Watson, at the University of Hertfordshire. You have been invited to participate because you are an experienced clinician in musculoskeletal physiotherapy, with links to the Physiotherapy Placement Information Management Service, from which your contact details were obtained.

I am enclosing a copy of the questionnaire, along with a stamped addressed envelope for its return. In order to be eligible, the person who completes the questionnaire must

- Be a physiotherapist registered with the Health Professions Council
- Have a minimum of 2 years (full time equivalent) experience treating musculoskeletal conditions.

If you are unable to complete this questionnaire, we would be grateful if you could pass it on to another clinician in your physiotherapy department who meets these criteria.

The questionnaire is coded to enable analysis of results by geographical area and type of health-care institution. However I would like to stress that neither you nor your place of work or employer will be identified in any publication arising from this research.

Please contact me if you would prefer a form you can complete on computer and return by email. Many thanks for considering being involved.

Yours sincerely

Leon Poltawski BSc, MCSP
School of Health & Emergency Professions - Physiotherapy

Tel: 01707 284556
Email: L.Poltawski@herts.ac.uk



A Charity Exempt from Registration under the second Schedule to the Charities Act 1993

QUESTIONNAIRE: TREATING SOFT TISSUE LESIONS

The aim of this questionnaire is to establish which are the common soft tissue conditions that physiotherapists find most resistant to treatment. Some of the most common are listed here.

Rotator cuff tendinopathy	Trochanteric bursitis	ACL / PCL lesion
Frozen shoulder	Hamstring tendinopathy	Knee bursitis
Bicipital tendinopathy	Adductor tendinopathy	Patellar tendinopathy
Tennis elbow	Quadriceps tendinopathy	Knee cysts
Golfer's elbow	ITB syndrome	Achilles tendinopathy
Wrist tendinopathy	MCL / LCL lesion	Ankle ligament lesion
Carpal tunnel syndrome		Plantar fasciitis

1. In the table below, list 5 or more conditions from this list that you find particularly resistant to treatment, i.e. signs and symptoms change little or slowly with treatment.
2. Grade each condition in your list according to how commonly you see it, its impact on the patient, and its resistance to treatment. 1=least and 5 = most. An example is given.
3. Mark any form of electrotherapy you use treating each condition. Ten = TENS; Int = Interferential; Psw = Pulsed shortwave; Las = Laser; US = ultrasound; O = other electrotherapy.
4. Be more specific about the position or nature of the lesion if you wish. An example is given.
5. If you wish, you may add conditions that do not appear on the list above. However do not include back pain, neural or arthritic conditions.

Conditions that I find most resistant to treatment	Seen commonly in my practice	Severity of impact on patient	Resistant to treatment	Electrotherapy treatment						
				Ten	Int	Psw	Las	Us	O	
<i>e.g. Wrist tendinopathy (de Quervain's)</i>	3	2	4		✓				✓	

Cont/

Please answer the following questions:

Indicate if a particular patient group predominates in your practice	Elderly / athletes / manual workers / other (specify)
How many years experience do you have treating musculoskeletal conditions?	years (full time equivalent)
Have you ever used microcurrent electrotherapy to stimulate healing of soft tissue lesions?	YES / NO / NOT HEARD OF
If so, please describe the treatment and your opinion of its effectiveness	
The findings of this questionnaire may be used to inform more detailed follow-up work. May we approach you again to invite your participation in this follow-up?	YES / NO
Would you like to receive a report of the findings of this study?	YES / NO
If you answered yes to either of the above, please state your name and provide us with a preferred contact number, postal address or email address	

Many thanks for your help in participating in this survey. Your participation is taken to indicate your consent for the data collected to be used for research purposes. No information that may identify you, your workplace or your employer will be disclosed in any publication or presentation of findings.

Please return this form in the envelope provided, or request an electronic version to return by email, to:

Leon Poltawski
 School of Health & Emergency Professions - Physiotherapy
 University of Hertfordshire
 College Lane
 Hatfield, Herts AL10 9AB
 Phone: 01707 284556 Email: L.Poltawski@herts.ac.uk

4 Documentation relating to development of outcome measures

**UNIVERSITY OF HERTFORDSHIRE
FACULTY OF HEALTH AND HUMAN SCIENCES
ETHICS COMMITTEE FOR HEALTH AND EMERGENCY PROFESSIONS**

Protocol Number: HEPEC/04/08/60
 Name of Investigator: Leon Poltawski
 Name of Supervisor: Tim Watson
 Programme: PhD Physiotherapy
 Title of Study: Variation in normal forearm strength, tenderness and tendon structure.

Thank you for submitting the information requested plus the information you have submitted via your email concerning contact details. Approval is granted and you may now proceed with your project.

On completion of your study, please would you ask your supervisor to return the attached Quality Monitoring Form to the Clerk to the Committee, Rachel Stirton.

On behalf of the Committee, I would like to wish you all the best with your study.



Jane Smith
Chair of Ethics Committee

cc. Tim Watson, Supervisor

Date: 17 April 2008

**UNIVERSITY OF HERTFORDSHIRE
SCHOOL OF HEALTH & EMERGENCY PROFESSIONS**

CONSENT FORM FOR STUDIES INVOLVING HUMAN SUBJECTS

Title of research project:

Variation in normal forearm strength, tenderness and tendon structure.

	YES	NO
The purpose of this study has been explained to me	<input type="radio"/>	<input type="radio"/>
I have been informed of the details of my involvement in the study	<input type="radio"/>	<input type="radio"/>
My questions regarding this study have been answered to my satisfaction	<input type="radio"/>	<input type="radio"/>
I understand that I am not obliged to take part in this study and may withdraw at any time without the need to justify my decision.	<input type="radio"/>	<input type="radio"/>
I understand that any personal information obtained as a result of my participation in this study will be treated as confidential and will not be made publicly available	<input type="radio"/>	<input type="radio"/>
I, the undersigned, agree to take part in this study	<input type="radio"/>	<input type="radio"/>

Signature of subject:.....

Name of subject:..... (Please print)

Signature of investigator:.....

Leon Poltawski

Name of investigator: Leon Poltawski

Status of investigator: Research Physiotherapist

Date:.....

ELBOW ASSESSMENT STUDY

Participant Information Sheet

Thank you for considering taking part in this study. It is part of an investigation into tennis elbow, which can be painful and disabling. Later on we will be looking at people who are affected by this condition, but in this part we want to gather information about the elbows of people who are not affected. This will help us to see what differences are caused by tennis elbow. The study is being conducted within the Physiotherapy Division of the School of Health and Emergency Professions as part of a doctoral research programme.

Who can take part?

Ideally we are looking for individuals who do not have any problems with their arms. However if you have any pain in your neck, shoulder, arms or hands, we would still like to do a partial assessment.

What is involved?

At an initial meeting, you can ask any questions and get more information before committing to participating. If you agree to be involved, you sign a consent form and then you will be asked some questions about your general health and your daily activities that might affect your arm. After that, your elbow will be assessed. First, your elbow will be scanned using ultrasound – this is a painless procedure that allows the inside of your arm to be imaged; then your grip strength will be measured by asking you to squeeze a device called a dynamometer; and lastly the tenderness of your elbow will be measured by pressing a device called an algometer onto it. This is pressed until it becomes uncomfortable for you and is then stopped. The strength and tenderness readings will be taken 3 times and both of your elbows will be assessed. The whole process should take about 50 minutes.

If you are agreeable and available, the tests will be repeated again after a fortnight. This enables us to check the reliability of the measurements, and to see if there have been any changes in that time. The second meeting should not take more than about 30 minutes. The assessments will take place in the Physiotherapy Research Laboratory, which is on the top floor of the Wright Building. If you are unable to attend both assessments we would still like to collect one set of information from you.

over/

ELBOW ASSESSMENT

Name	ID	Date
------	----	------

DOB:	M / F	Hand dominance: L / R / Ambi
------	-------	---

PMH									
-----	--	--	--	--	--	--	--	--	--

RA	OA	DIAB	NECK	SHOULDER	UL# / SURG	ULOTHER	TENDINOPATHY	ELBOW
----	----	------	------	----------	------------	---------	--------------	-------

--

STEROIDS: SYSTEMIC / TOPICAL / INJECTION	ANALGESIA
--	-----------

--

Strenuous / repetitive UL activities in work / home / recreation
--

--

Are there any risks or possibilities of harm?

The tenderness test causes some discomfort, but this should subside as soon as the test finishes. There are no known risks associated with any of the procedures that are used. You can withdraw from the study at any time without giving any reason.

Are there any benefits to being involved?

By participating, you will be helping to deepen our knowledge of tennis elbow, and the data you provide may help in the development of a new treatment for it.

What happens to the information collected?

We hope to gather data from at least 30 people. This will be used to compare healthy elbows with those affected by tennis elbow. The information collected may be published in a professional journal, but nothing will be released that identifies any of the participants in the study. Any personal information collected about you will be kept confidential to the research group and will not be divulged to anyone else without your permission.

What if I am unhappy about any aspect of my involvement?

You should raise the issue with the researcher in the first instance. If this does not resolve the matter you can contact the research supervisor, Professor Tim Watson, whose details are given below.

What next?

If you are happy to go on to the next step, please contact me by telephone or email. We can then arrange to meet.

Researcher:

Leon Poltawski
Physiotherapy Research Group
University of Hertfordshire
Hatfield AL10 9AB

01707 284968

L.Poltawski@herts.ac.uk

Research Supervisor:

Professor Tim Watson
School of Health & Emergency Professions
University of Hertfordshire
Hatfield AL10 9AB

01707 284970

T.Watson@herts.ac.uk

ASSESSMENT DATA

1	Date	Time	ID
Analgesia / TOP / P resisted <u>Wr</u> E / P resisted MF E / P <u>Wr</u> E stretch			

<u>Ax</u>	Algometer		Dynamometer	
	L	R	L	R

USI	L	R
Grey scale		
Doppler		

2	Date	Time	ID
Analgesia / UL problems / Change in activity			

Ax	Algometer		Dynamometer	
	L	R	L	R

USI	L	R
Grey scale		
Doppler		

5 Documentation relating to reliability assessment of outcome measures

**UNIVERSITY OF HERTFORDSHIRE
FACULTY OF HEALTH AND HUMAN SCIENCES
ETHICS COMMITTEE FOR HEALTH AND EMERGENCY PROFESSIONS**

Protocol Number: HEPEC/02/08/48
Name of Investigator: Leon Poltawski
Name of Supervisor: Tim Watson
Programme: PhD Physiotherapy
Title of Study: Changes in outcome measures over time in tennis elbow

Thank you for submitting the information requested. Approval is granted and you may now proceed with your project.

On completion of your study, please would you ask your supervisor to return the attached Quality Monitoring Form to the Clerk to the Committee, Rachel Stirton.

On behalf of the Committee, I would like to wish you all the best with your study.



Jane Smith
Chair of Ethics Committee

cc Tim Watson, Supervisor

Date: 7 February 2008

TENNIS ELBOW STUDY

Participant Information Sheet

Thank you for considering taking part in this study. It is part of an investigation into the condition called tennis elbow, which can be painful and disabling. People with tennis elbow normally have pain in the outer part of the elbow, made worse by gripping and lifting things. It may be caused by repetitive and strenuous use of the arm at work or in sports activities.

This study aims to gather information about its effects on people, and to see how these change over time. It is also investigating factors that affect how long the disorder lasts, for instance age and type of work done. The study is being conducted by the Physiotherapy Division of the University of Hertfordshire.

Who can take part?

We are looking for people who have symptoms of tennis elbow at the moment. You may have been diagnosed with the condition by a health professional, but if you have the typical symptoms and are not sure, we would still like to meet you.

What is involved?

You can ask any questions and get more information before committing to participating. If you agree to be involved, you will be asked to sign a consent form and answer some initial questions about your tennis elbow. Some simple tests will be then carried out to confirm whether you have the condition. If you do, a more detailed assessment will be done. This includes questions about your occupation and lifestyle, any treatment you have had for the condition, and any other medical problems you have. Physical tests include measuring the strength of your gripping muscles and looking at movement in your neck and arm joints. An ultrasound scan will also be made of the area. This provides an image of the tendon that is affected by tennis elbow and allows any changes to be seen. It involves moving a probe over the skin – it is painless with no known risks. The whole assessment process takes about an hour.

We want to see whether these things change with time, and so would like to make similar measurements about a fortnight later and – if possible – six months after this first meeting. These assessments should not take as long as the first one. If you are unable to attend for these meetings we would still like to collect one set of information from you. The venue is negotiable: they may happen where you saw this study advertised, at the University of Hertfordshire, or you may be visited at your workplace or at home.

The study does not involve any treatment for tennis elbow, although information about the condition and advice on its management will be available. Later on we will be conducting a study that involves treatment of the condition and, if you still have it then, it may be possible for you to participate in that study.

Are there any risks or possibilities of harm?

The physical tests that will be carried out may cause some discomfort or slight pain – this is necessary in order to diagnose tennis elbow and to measure its effects, and should subside as soon as the test finishes. There are no known risks associated with any of the tests that are used. You can withdraw from the study at any time without giving any reason. If your tennis elbow should flare up during the study, a referral letter can be given to you to take to your GP if you wish.

Are there any benefits to being involved?

You will be given an opinion as to whether you have tennis elbow, and information about the condition and its management, but no treatment is being offered at this stage of the study. It is hoped that information gathered will increase knowledge of the condition and help in the development of its treatment, which may be of benefit in future to people suffering with it.

What happens to the information collected?

We hope to gather data from at least 30 people with tennis elbow. This will enable us to spot patterns in how it develops and what affects its progress. The information will also be used in preparing for the next stage of research, which is looking at a new treatment for the condition.

The information collected may be published in a professional journal, but nothing will be released that identifies any of the participants in the study. Any personal information collected about you will be kept confidential to the research group and will not be given to anyone else without your permission.

What if I am unhappy about any aspect of my involvement?

You should raise the issue with the researcher in the first instance. If this does not resolve the matter you can contact the research supervisor, Professor Tim Watson, whose details are given below.

What next?

If you are happy to go on to the next step, please contact me by telephone or email. We can then arrange to meet.

Researcher:

Leon Poltawski
Physiotherapy Research Group
University of Hertfordshire
Hatfield AL10 9AB

01707 284968

L.Poltawski@herts.ac.uk

Research Supervisor:

Professor Tim Watson
School of Health & Emergency Professions
University of Hertfordshire
Hatfield AL10 9AB

01707 284970

T.Watson@herts.ac.uk

ELBOW ASSESSMENT

Name		Study ID		Assessment date	
------	--	----------	--	-----------------	--

Contact details

DOB:	M / F	Hand dominance: L / R / Ambi.
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PRESENT EPISODE

Rx

Previous episodes

PSFS (TODAY: 0 = unable to perform; 10 = able to perform same level as pre-problem)

Ass 1	Study ID		Assessment date	
-------	----------	--	-----------------	--



	Appearance	Color	MF E	WR E	STRETCH	SUP
L						
R						

	MGS / PFGS	GS 1	GS 2	GS 3
L				
R				

	PPT1	PPT2	PPT3
L			
R			

ROM/STR	Sh Ab.	Sh HBB	Elb FI	Elb Ex +OP	Finger FI	Elb velúvác
L						
R						

	C6 quad; + comp / distract	ULTT2B
L		Sh dep → Elb E → IR → Wrist FI → Sh Ab. → C6 LF
R		Sh dep → Elb E → IR → Wrist FI → Sh Ab. → C6 LF

PMH								
Neck Sp	Other UL	CTS / TA	OA / RA	Diab	Systemic	Steroids	Smoker	Analgesia
PSH								
Work			leisure					
Sick leave	Compensation litigation	Down/depressed/hopeless in last month	Little interest/pleasure doing things in last month	Anxious/worried a lot in last month				

Ass 2	Study ID		Assessment date	
-------	----------	--	-----------------	--

Changes since last time: symptoms / activities / analgesia

GRS	Much worse	Little worse	Same	Little better	Much better	Fully recovered
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R L

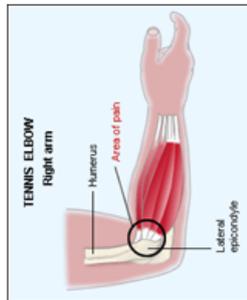
	Appearance	Ed/p	MF E	WR E	SUP	STRETCH
L						
R						
Ed/p FI						

	MGS / PFGS	GS 1	GS 2	GS 3
L				
R				
	PPT1	PPT2	PPT3	
L				
R				

Tennis elbow

Introduction

Tennis elbow is a problem in the area around the bony bump on the outer side of the elbow (called the lateral epicondyle). Similar symptoms can occur on the inner side of the elbow, which is sometimes known as 'golfer's elbow'.



Tendons controlling some muscles in the forearm are attached to the lateral epicondyle. When this area is inflamed or damaged, it can be painful to carry out movements using the forearm and wrist.

The elbow joint is surrounded by muscles that move your elbow,

wrist and fingers. Tendons in the elbow join the bones and muscles together, and tennis elbow happens when one or more of these tendons become damaged. The pain you feel is at the point where the tendons from the forearm muscle attach to the bone.

Symptoms

Tennis elbow is characterised by pain and tenderness in the elbow, sometimes extending into the forearm. This is made worse by using the wrist, particularly for gripping and twisting movements. Symptoms vary, but may include:

- recurring pain on the outside of the forearm just below the bend of the elbow. Sometimes pain may be felt down the arm towards the wrist;
- elbow pain caused by lifting things;
- pain when writing or when gripping even small objects such as a pen;

- pain on twisting the forearm, for example, when turning a door handle.
The pain caused by tennis elbow normally lasts for 6 to 12 weeks. Some people have pain for as little as 3 weeks, while others may experience discomfort in the elbow joint for several years.

Pain ranges from a mild discomfort when the elbow is used, to severe pain that can be felt even when the elbow is still, or when sleeping. You may have stiffness in your arm, which gets progressively worse as tendon damage builds up. As the body tries to compensate for the weakness in the elbow, you may also get pain or stiffness in other parts of the affected arm, the shoulder, or neck.

Causes

Excessive or repeated use of the muscles that straighten the wrist can cause injury to the tendons, leading to tennis elbow. These injuries consist of tiny tears in the tendons where it attaches to the bone. If these injuries are not allowed to heal fully, they can tear again, which leads to the

formation of scar tissue. An inflamed tendon can pinch the radial nerve, one of the major nerves controlling muscles in the arm and hand. This may also cause pain when the arm is used.

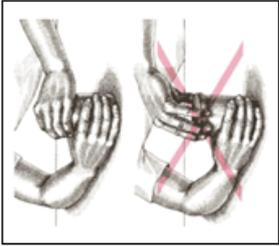
Tennis elbow can be caused by overuse of the forearm muscles in repeated actions such as:

- occupations that involve repetitive turning or lifting the wrist, such as painting, plumbing or typing
- sports that involve lots of wrist action such as racquet games or throwing;
- using scissors or shears;
- gardening and some forms of housework.

Even if you are used to these types of work or sports, you can still overdo it, or do it the wrong way.

Treatment

Some cases of tennis elbow clear up with rest and support, and by avoiding or changing activities that put stress on the tendon. Over the counter painkillers can be taken to treat any mild pain.

<p>Allowing symptoms to get better without further treatment can take several weeks or months; tendons are slow to heal.</p> <p>Your GP may prescribe anti-inflammatory painkillers to ease pain and inflammation. Some are available in creams or gel form, which can be rubbed over the affected joint. Some anti-inflammatory painkillers can be bought over the counter; ask your pharmacist for advice.</p>  <p>Some people find a tennis elbow strap helpful. This is fastened snugly just below the elbow and can help protect the tendon from further damage while it heals. Such straps are available at pharmacists.</p> <p>if tennis elbow is particularly painful and making movement difficult, other treatment may be necessary. Cortisone injections</p>	<p>are sometimes given to reduce inflammation and pain. They are usually delivered with an anaesthetic, but they can be painful for a while afterwards. Sometimes several injections are needed over a few weeks if the first does not work. Some people find that pain returns after steroid injections, which can be a result of putting too much strain on the arm too quickly. As with any injury, you should gently build up to normal activities to prevent the problem coming back. Steroid injections can be very helpful in pain relief, but may make it more likely that the problem will recur in the future.</p> <p>In some cases, referral to a physiotherapist may be advised. Physiotherapy treatment may include exercises to stretch and strengthen the forearm muscles, electrotherapy such as ultrasound, and the use of splints or supports to protect the tendon and allow it to heal.</p> <p>if the problem resulted from playing sport, professional advice on technique may be necessary. Or, in the workplace, attention to</p>
<p>use of equipment, posture or working practices may be needed.</p> <p>A small number of people require surgery to relieve symptoms.</p> <p>Prevention</p> <p>The best way to avoid tennis elbow is to avoid putting too much stress on the tendons in the elbow. The following measures may help:</p> <ul style="list-style-type: none"> • Stop the activity that is causing you pain or find a different way of doing it. If you use your wrist and elbow more than the rest of the arm, try to spread the load so that the larger muscles of the shoulder and upper arm work too. • if you play a sport that uses repetitive movements, such as tennis, try to get some professional advice about your technique so that you do not strain your elbow. 	 <ul style="list-style-type: none"> • Warm up and gently stretch the muscles before playing sport. • Enlarging the grip size on rackets or tools and decreasing their weight can also help to prevent you putting excess strain on the tendons. • Wearing a splint when you are using your arm, and taking it off when you are sleeping or resting can help prevent further damage to the tendons. Ask your GP for advice about the best type of splint for you to use. • Increasing the strength of your forearm muscles can help to prevent tennis elbow occurring.

The information in this leaflet is adapted from an article published on the NHS Direct website: www.nhsdirect.nhs.uk

6 Documentation relating to clinical trials of MCT

UNIVERSITY OF HERTFORDSHIRE
FACULTY OF HEALTH AND HUMAN SCIENCES
ETHICS COMMITTEE FOR HEALTH AND EMERGENCY PROFESSIONS

Protocol Number: HEPEC/10/08/05
Name of Investigator: Leon Poltawski
Name of Supervisor: Tim Watson
Programme: PhD Physiotherapy
Title of Study: Effectiveness of microcurrent in the treatment of chronic tennis elbow – a preliminary study

Thank you for your application and attending the meeting. The Committee has approved your study.

On completion of your study, please would you ask your supervisor to return the attached Quality Monitoring Form to the Clerk to the Committee, Rachel Stirton.

On behalf of the Committee, I would like to wish you all the best with your study.



Jane Smith
Chair of Ethics Committee

cc Tim Watson, Supervisor

Date: 22 October 2008

**UNIVERSITY OF HERTFORDSHIRE
FACULTY OF HEALTH AND HUMAN SCIENCES
ETHICS COMMITTEE FOR HEALTH AND EMERGENCY PROFESSIONS**

Protocol Number: HEPEC/03/09/74
Name of Investigator: Leon Poltawski
Name of Supervisor: Tim Watson
Programme: PhD Physiotherapy
Title of Study: The influence of parameter variations on the effectiveness of microcurrent treatment of chronic tennis elbow

Thank you for your application and attending the meeting. The Committee has approved your study but before you proceed to your data collection would ask you to amend your application in line with the discussions and Committee's comments.

- A13 Tick the section on 'poster and 'advertisement'.
- A22 Explore the inclusion of a letter to GPs, as per discussion with the Committee.
- A33 Ensure more detail in future applications, as discussed.

Please send both paper and electronic copies of your amendments to Rachel Stirton, Clerk of the Committee, 1 F264 Postgraduate Office, Wright Building.

On completion of your study, please would you ask your supervisor to return the attached Quality Monitoring Form to the Clerk to the Committee, Rachel Stirton.

On behalf of the Committee, I would like to wish you all the best with your study.



Jane Smith
Chair of Ethics Committee

cc Tim Watson, Supervisor

Date: 18 March 2009

**UNIVERSITY OF HERTFORDSHIRE
SCHOOL OF HEALTH & EMERGENCY PROFESSIONS**

Microcurrent treatment of chronic tennis elbow – a preliminary study

	YES	NO
The purpose of this study has been explained to me	<input type="checkbox"/>	<input type="checkbox"/>
I have been informed of the details of my involvement in the study	<input type="checkbox"/>	<input type="checkbox"/>
My questions regarding this study have been answered to my satisfaction	<input type="checkbox"/>	<input type="checkbox"/>
I understand that I am not obliged to take part in this study and may withdraw at any time without the need to justify my decision.	<input type="checkbox"/>	<input type="checkbox"/>
I understand that any personal information obtained as a result of my participation in this study will be treated as confidential and will not be made publicly available	<input type="checkbox"/>	<input type="checkbox"/>
I, the undersigned, agree to take part in this study	<input type="checkbox"/>	<input type="checkbox"/>
I understand that all equipment is provided on loan. I will use it as instructed and return it when requested.	<input type="checkbox"/>	<input type="checkbox"/>

Signature of participant:.....

Name of participant: (Please print)

Signature of investigator



Name of investigator: Leon Poltawski

Status of investigator: Research Physiotherapist

Date:..

TENNIS ELBOW STUDY

Participant Information Sheet

Thank you for considering taking part in this study. It is part of an investigation into the condition called tennis elbow, which can be a painful and disabling condition. People with tennis elbow normally have pain in the outer part of the elbow, sometimes extending into the forearm. It is made worse by gripping, twisting or lifting things. It may be caused by repetitive and strenuous use of the forearm at home, work or in sports activities.

This study aims to investigate whether a form of treatment called microcurrent can be helpful in cases of chronic tennis elbow. This treatment has been shown to help healing in other conditions such as bone fractures and skin wounds, but we do not yet know whether it can help with tennis elbow. The treatment involves passing a very small electric current through the elbow – so small that it cannot be felt. It is described in more detail later. The study is being conducted by the Physiotherapy Division of the University of Hertfordshire.

Who can take part?

We are looking for people who have had symptoms of tennis elbow for at least 3 months, and who are finding that things have not improved significantly in the last few weeks. You may have been diagnosed with the condition by a health professional, but if you have the symptoms described above and are not sure, we can assess you to check. Unfortunately you cannot take part if you are currently being treated for tennis elbow by someone else.

What is involved?

If you are interested in taking part, you will be asked to complete a short questionnaire which will help us decide whether you are eligible. If you are, we will invite you to a meeting where you will be assessed to confirm that you have the condition. This involves asking you about the problem and about your general health and lifestyle, and then carrying out a range of physical tests on your arms. These include testing your muscle strength and looking at the movement of different parts of your arms. An ultrasound scan will also be made of each elbow. This provides an image of the tissue under your skin and allows any changes to be seen. It involves moving a probe over the skin and is painless with no known risks. Finally you will be asked to complete a questionnaire that asks you to rate the pain a difficulty caused by your tennis elbow. The whole assessment process takes about an hour.

Once all of that information has been collected, you will be shown the microcurrent device. This is about the size of a portable CD player, and it attaches to your elbow via wires leading to two sticky pads that are placed on either side of the affected area. You will be shown how to use the unit because the treatment needs to be applied for 2 hours every day for 3 weeks, so you will be taking it home with you and treating yourself with it every day. The unit is portable, and can be hung from a belt or held in a large pocket, so using it should not stop you from doing your every day activities.

It is very important that you use the microcurrent unit as directed, every day for 2 hours. If you think this will be very difficult, it is best that you do not take part in the study. We will ask you to tick a sheet each day to confirm that you had the treatment. After 3 weeks, the treatment is complete and you will be asked to come back for another assessment, which involves similar tests to the first time we see you. We will also ask to see you one more time, a further 3 weeks later, to check whether things have changed at all during that time.

During the period of the study we ask that you do not treat your tennis elbow in any other way, apart from using pain-killers and a tennis elbow brace, if you already use one. We will also ask that you do not take any

HEPEC approved: 10/05/05

cont/

pain killers on the days when you are assessed. We will contact you a few days into your treatment period to make sure that all is going to plan, and to answer any questions you may have. You will also be able to contact us during office hours if you have any concerns.

Are there any risks or possibilities of harm?

The physical tests that will be carried out may cause some discomfort or slight pain – this is necessary in order to diagnose tennis elbow and to measure its effects, and should subside when the test finishes. There are no known risks associated with any of the tests that are used, and side effects of the microcurrent treatment are very rare if it is used as instructed. If you do experience any worrisome symptoms because of the treatment you should stop it immediately and contact us. You can withdraw from the study at any time without giving any reason. If your tennis elbow should get worse during the study, or if you wish to get alternative treatment, a referral letter can be given to you to take to your GP if you wish.

Are there any benefits to being involved?

We are investigating this form of treatment because it has proven helpful with other conditions, and we think it is reasonable to expect that it may be helpful with tennis elbow. It may help relieve your symptoms, but it may not. The point of this study is to see whether microcurrent does make a difference. Whatever the outcome, you will have helped improve our knowledge of tennis elbow and of microcurrent treatment. Everyone enrolled in this trial will receive microcurrent treatment.

What happens to the information collected?

We hope to gather data from up to 30 people with tennis elbow. If the treatment appears to be helpful, the next stage in our research will be to compare it to existing forms of treatment so see whether it should be recommended as an addition or alternative to them. Information from the current study will help in the planning of that next stage.

The information collected may be published in a professional journal, but nothing will be released that identifies any of the participants in the study. Any personal information collected will be kept confidential to the research group and will not be divulged to anyone else without your permission.

What if I am unhappy about any aspect of my involvement?

You should raise the issue with the researcher in the first instance. If this does not resolve the matter you can contact the study supervisor, Professor Tim Watson, whose details are given below.

What next?

If you have any questions or concerns before deciding whether to take part, please contact Leon Poltawski – details below. If you are happy to go on to the next step, please complete and return the attached entry questionnaire. If you are eligible to take part, we can then arrange to meet.

Leon Poltawski
Physiotherapy Research Group
University of Hertfordshire
Hatfield AL10 9AB

01707 284968
L.Poltawski@herts.ac.uk

Study Supervisor:
Professor Tim Watson
School of Health & Emergency Professions
University of Hertfordshire
Hatfield AL10 9AB

01707 284970.
T.Watson@herts.ac.uk

TENNIS ELBOW STUDY – ENTRY QUESTIONNAIRE

Name

Do you currently have a painful elbow?	Yes No
Does the pain get worse when you grip, twist or lift things?	Yes No
Roughly how long ago did the problem start? (If you have had it before, say how long ago the <u>current</u> episode began)	
Has the condition changed significantly in the last month? If so, please say how	Yes No
Has a doctor or other health professional said that tennis elbow is the problem?	Yes No
Is anyone currently treating you for your tennis elbow? If so, please state their profession and briefly describe the treatment	Yes No
Do you have any other problems with your affected arm or hand? If so, please briefly describe	Yes No

Please provide us with a contact telephone number or address (email or postal).

When you have completed this you can return the questionnaire either by post using the reply-paid envelope provided, or email it to L.Poltawski@herts.ac.uk.

If you have any questions please don't hesitate to contact us by email or telephone (01707 284968)

PATIENT-RATED TENNIS ELBOW EVALUATION QUESTIONNAIRE

Name		Study ID		Assessment date	
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The questions below will help us understand the amount of difficulty you have had with your arm in the past week. You will be describing your **average** arm symptoms **over the last week** on a scale 0-10. Please provide an answer for all questions. If you did not perform an activity because of pain or because you were unable, then you should circle a "10". If you are unsure, estimate to the best of your ability. Only leave an item blank if you never perform that activity. Please indicate this by drawing a line completely through the question.

1. PAIN IN YOUR AFFECTED ARM

Rate the average amount of pain in your arm **over the last week** by circling the number that best describes your pain on a scale from 0 to 10. A zero (0) means you did not have any pain, and a ten (10) means that you had the worst pain imaginable.

	No pain										Worst pain imaginable
When you are at rest	0	1	2	3	4	5	6	7	8	9	10
When doing a task with repeated arm movement	0	1	2	3	4	5	6	7	8	9	10
When carrying a bag or case by the handle	0	1	2	3	4	5	6	7	8	9	10
When your pain was at its least	0	1	2	3	4	5	6	7	8	9	10
When your pain was at its worst	0	1	2	3	4	5	6	7	8	9	10

2. DISABILITY

Rate the amount of difficulty you experienced performing each of the tasks below **over the last week**, by circling the number that best describes your difficulty on a scale from 0 to 10. A zero (0) means you did not experience any difficulty, and a ten (10) means that it was so difficult you were unable to do it.

	No difficulty										Unable to do
Turn a door knob or key	0	1	2	3	4	5	6	7	8	9	10
Carry a bag or case by the handle	0	1	2	3	4	5	6	7	8	9	10
Lift a full cup or glass to your mouth	0	1	2	3	4	5	6	7	8	9	10
Open a jar	0	1	2	3	4	5	6	7	8	9	10
Pull up trousers	0	1	2	3	4	5	6	7	8	9	10
Wring out a wet cloth	0	1	2	3	4	5	6	7	8	9	10

3. USUAL ACTIVITIES

Rate the amount of difficulty you experienced performing your usual activities in each of the area listed below **over the last week**, by circling the number that best describes your difficulty on a scale from 0 to 10. By "usual activities" we mean activities that you performed before you started having a problem with your arm. A zero (0) means you did not experience any difficulty, and a ten (10) means that it was so difficult you were unable to do any of your usual activities.

	No difficulty										Unable to do
Personal activities (dressing, washing)	0	1	2	3	4	5	6	7	8	9	10
Household work (cleaning, maintenance)	0	1	2	3	4	5	6	7	8	9	10
Work (your job or everyday work)	0	1	2	3	4	5	6	7	8	9	10
Recreational or sporting activities	0	1	2	3	4	5	6	7	8	9	10

Comments:

USING THE ELEXOMA MEDIC

If you have any problems using the device please let us know as soon as possible by telephoning 01707 284968.

Care of the equipment

Keep the Elexoma in its protective case if you are moving around when using it.

When not using the electrodes, stick them on the plastic sheet and seal them in the bag provided. This will help them to last longer.

Check the battery indicator each day. If it shows that the batteries are beginning to run out, recharge them before using the Elexoma.

Treating your elbow

Connect the electrodes to the Elexoma using the cable, which should be plugged into the left hand socket on the top of the device, labelled I.

Clean the elbow using the alcohol swabs. To improve electrical contact, dampen the sticky surfaces of the electrodes with a wet finger and wait 10-20 seconds till tacky. Then stick the electrodes with the black plug over the tendon, and the one with the red plug just behind the elbow, as you have been shown. If they still don't stick well, try using the tape to hold them in place. If they aren't sticking at all, use a new pair. It's important that the electrodes don't peel away from your skin.

Switch on the Elexoma by pressing button A. Make sure the right program is selected by pressing button A repeatedly until Program 5 is displayed.

Press button B so 10 μ A is displayed.

Press button C until the treatment current changes to μ A (press button D to reduce it, if you overshoot)

Hold down button E until the treatment time changes to its maximum value of 99 minutes.

The treatment has started. If the machine beeps continuously it means the current isn't flowing – check that the electrodes are firmly attached to you and the leads are all connected.

The timer counts down to zero and then the Elexoma beeps briefly and stops delivering current. It switches itself off automatically after a few seconds.

Peel off the electrodes, disconnect them from the leads, stick them on the plastic sheet and place the sheet in the sealable bag.

Mark your use of the Elexoma on the diary overleaf, and make a note of any problems.



DIARY OF ELEXOMA USE

NAME STARTING DATE

Please tick the box every time you give yourself a treatment

If you miss a day, put a zero in the box

If there are problems on any day, put an asterisk in the box and make a note of the problem under the table.

You should treat yourself a total of 21 times

	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Week 1							
Week 2							
Week 3							
Week 4							

7 Dissemination of study findings

Presentations given

Bioelectricity & Microcurrent therapy
School of Life Sciences Research Seminar
University of Hertfordshire
October 2009

A trial of Microcurrent therapy: rationale & methodology
School of Health & Emergency Professions Research Seminar
University of Hertfordshire
May 2010

Microcurrent therapy in the management of chronic tennis elbow
School of Health & Emergency Professions Research Forum
University of Hertfordshire
September 2010

Reports

Microcurrent therapy in the management of chronic tennis elbow
Final Report to suppliers of microcurrent devices
September 2010

Microcurrent therapy in the management of chronic tennis elbow
Report to participants in clinical trials
September 2010

Abstracts submitted to World Physical Therapy Congress 2011

Microcurrent therapy in the management of chronic tennis elbow: an exploratory investigation.

Using sonography for the evaluation of tendon pathology in tennis elbow: reliability of assessment scales.

Physiotherapists' perceptions of problematic musculoskeletal soft tissue disorders

Leon Poltawski, Tim Watson, Geraldine Byrne

Aims: Many common musculoskeletal disorders are resistant to existing management strategies, causing long-term pain and disability. While arthritic and spinal problems have been prioritized for research, several soft tissue disorders may be equally burdensome for individuals and difficult to treat successfully. Identifying those that are least responsive to treatment may help focus the limited resources available for research and treatment provision. This study aimed to rank the most problematic disorders, and identify contributory factors, to inform the debate on research and service priorities in the management of musculoskeletal disorders.

Methods: The views of practising physiotherapists on the most problematic soft tissue disorders were sought using a postal questionnaire survey and telephone interviews. The questionnaire was sent to 193 experienced musculoskeletal physiotherapists working in National Health Service and private clinics in south-east England.

Findings: The response rate was 48%. The top three problematic disorders were identified as frozen shoulder, plantar fasciitis and tennis elbow. Subsequent interviews with 20 respondents indicated that inadequate differential diagnosis, triaging and differences in therapeutic practice may account for some of the observed variation in outcomes.

Conclusions: A greater focus on these particular disorders and issues by both clinicians and the research community is warranted.

Key words: ■ Musculoskeletal disorders ■ physiotherapy ■ therapist perceptions ■ research priorities

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Musculoskeletal disorders are sources of considerable pain and disability, and can impose major costs on those affected, on health service providers and on society at large (European Commission, 2003). International reports have identified rheumatoid arthritis, osteoarthritis, osteoporosis and spinal disorders as the most burdensome conditions (European Commission, 2003; World Health Organization, 2003; European Bone and Joint Health Strategies Project, 2004). Their findings and recommendations may inform the agendas of the research community and their funders. However, other musculoskeletal disorders may be severely debilitating for individuals and unresponsive to existing treatment options. Work- and sports-related soft-tissue disorders, such as tendinopathies and carpal tunnel syndrome, have been identified as significant and growing problems (Jones et al, 1996; Kcavet and Hazes, 2003; Staal et al, 2007). A recent

pan-European report (European Bone and Joint Health Strategies Project, 2004) emphasized the need for more detailed research into such disorders. Their prevalence, impact on those affected and the inadequacy of existing treatment strategies have been identified as indicators of the burden they impose on the individual and society (European Commission, 2003; World Health Organization, 2003; European Bone and Joint Health Strategies Project, 2004). Data on these factors can help formulate research priorities and identify areas of clinical practice that may be improved.

Health surveys and clinical trials can provide relevant evidence, but the views of clinicians involved in the management of these disorders also require investigation. Strategies for improving musculoskeletal health recognize that the awareness and perceptions of health professionals is key to improving outcomes (Akesson and Woolf, 2007; Rowe and McDaid, 2007). Practice may vary

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Research

considerably between therapists, even where the evidence base is sufficient to provide robust treatment guidelines (Eve et al, 1996; Swinkels et al, 2005; van der Wees et al, 2007). In some cases this may be owing to a failure to take account of the opinions and daily experience of clinicians (Eve et al, 1996). An appreciation of their perspectives and priorities may help in focusing research and drawing up treatment recommendations that are seen as relevant to clinical practice.

AIMS

The aims of the study were to:

- Rank common disorders by clinicians' opinions of the problems they impose on patients and their recalcitrance to treatment
- Identify some of the issues that may need to be addressed to improve outcomes in the management of these disorders.

The factors identified in the reports cited above—prevalence, impact on those affected and the inadequacy of existing treatment strategies—were used to formulate criteria for evaluating these disorders. Hence, study participants were asked to rank disorders according to how commonly they were seen in practice, the severity of problems they cause to the patient, and their recalcitrance to treatment. The questions posed by the study were:

- Which are the common musculoskeletal disorders that are currently proving most problematic for patients and most difficult to treat successfully?
- What are the clinical issues that may impede their successful management?

Providing answers to these questions may assist in the formulation of research priorities.

METHODS

Design

A postal questionnaire was used to obtain quantitative data on clinicians' opinions. This was followed by telephone interviews with a sub-sample of respondents to gather richer data on perceptions of treating the three most problematic disorders. Approval for the study was obtained from the investigators' institutional Ethics Committee, and written or oral consent was obtained from all participants. National Health Service (NHS) ethical approval was not required as the study was a combination of service review and clinical audit.

Participants

Musculoskeletal physiotherapists were selected as the population of interest because they encounter many of the common soft tissue disorders in their practice. A convenience sample of experienced musculoskel-

etal physiotherapists was identified from a database of NHS physiotherapy services and private practices, which is used to provide clinical placements for physiotherapy students in the south east of England. The database aims to include all NHS services in the region. A total of 193 outpatient musculoskeletal clinics were identified, and the questionnaire was sent to a named contact at each clinic. The covering letter stated the inclusion criteria: that respondents must be physiotherapists registered with the UK Health Professions Council, and have a minimum of 2 years' full-time equivalent experience treating musculoskeletal disorders. Following analysis of responses to rank the disorders, all responders who had chosen the top three problematic disorders were invited to participate in a follow-up telephone interview.

Instruments

A questionnaire was designed specifically for the study. A range of orthopaedic and musculoskeletal textbooks and epidemiological papers was consulted (Cunningham and Kelsey, 1984; Hertling and Kessler, 1996; Dandy and Edwards, 2003; Walker-Bone et al, 2004; Huisstede et al, 2006) to identify the most common soft tissue disorders. Spinal problems, arthritides and specifically neural and bone disorders were excluded. A draft questionnaire was drawn up and modified following peer-review, before being piloted with ten randomly-selected clinicians from the sample. These clinicians were asked to complete it and identify any difficulties with its interpretation and completion. Six responses were received with no problems reported. The questionnaire was judged fit for purpose and sent to the rest of the sample. Illustrative content from the questionnaire is given in *Table 1*.

For the follow-up telephone interviews, a semi-structured format was used. Several opening questions were chosen to address relevant areas:

- Are some presentations of these disorders less responsive to treatment than others?
- What management strategies do you typically adopt?
- What factors do you find limit their successful management?

These were followed by appropriate subsidiary questions to explore respondents' opinions in more detail. After piloting with an experienced musculoskeletal physiotherapist, this interview format was deemed suitable and adopted. Interviews lasted approximately 20 minutes and were digitally recorded for subsequent analysis, in which recordings were audited for common themes and areas of divergence. Interviews were conducted and audited by one author (LP); analytical method and interpretation were agreed with another author (GB), an experienced qualitative researcher.

FINDINGS

Survey

Completed questionnaires were returned by 93 physiotherapists, representing a response rate of 48%. The mean experience of respondents in musculoskeletal physiotherapy was 10.7 (± 7.5) full-time equivalent years. *Figure 1* shows the proportion of the sample that identified each disorder as problematic in terms of the three chosen criteria. The top three disorders—frozen shoulder, plantar fasciitis and tennis elbow—were each chosen by more than 55% of respondents. The various tendinopathies

were the most commonly cited disorders: 97% of respondents chose at least one tendinopathy.

Figure 2 plots the sums of points allocated by all respondents for the top ten disorders (see *Table 1* for point system). Charting by total points gives more weight to disorders that were chosen by more respondents. A plot of mean scores would give undue weight to disorders that few respondents reported as problematic. Ranking disorders by points on each criterion places them in a similar order to that of *Figure 2*, the main exception being rotator cuff tendinopathy, which ranks fourth in terms of frequency of presentation.

Table 1.
Rating system and instructions used in questionnaire

QUESTIONNAIRE: TREATING SOFT TISSUE LESIONS

The aim of this questionnaire is to establish which are the common soft tissue disorders that physiotherapists find most resistant to treatment. Some of the most common are listed here:

Rotator cuff tendinopathy	Trochanteric bursitis	ACL / PCL lesion
Frozen shoulder	Hamstring tendinopathy	Knee bursitis
Bicipital tendinopathy	Adductor tendinopathy	Patellar tendinopathy
Tennis elbow	Quadriceps tendinopathy	Knee cysts
Golfer's elbow	ITB syndrome	Achilles tendinopathy
Wrist tendinopathy	MCL / LCL lesion	Ankle ligament lesion
Carpal tunnel syndrome		Plantar fasciitis

1. In the table below, list 5 or more conditions from this list that you find particularly resistant to treatment, i.e. signs and symptoms change little or slowly with treatment.
2. Grade each condition in your list according to how commonly you see it, its impact on the patient, and its resistance to treatment. 1 = least and 5 = most. An example is given.
3. Be more specific about the position or nature of the lesion if you wish. An example is given.
4. If you wish, you may add conditions that do not appear on the list above. However, do not include back pain, neural or arthritic conditions.

Conditions that I find most resistant to treatment	Seen commonly in my practice	Severity of impact on patient	Resistant to treatment
e.g. Wrist tendinopathy (de Quervain's)	3	2	4

MCL=medial collateral ligament; LCL=lateral collateral ligament; ACL=anterior cruciate ligament; PCL=posterior cruciate ligament; ITB=iliotibial band

Research

Frozen shoulder, plantar fasciitis and tennis elbow are the most problematic disorders in terms of the proportion of respondents voting for them, and of the combined scores of respondents for frequency of presentation, severity of symptoms and recalcitrance to treatment. A number of factors might account for the observed recalcitrance: existing therapies may be insufficiently effective in dealing with these particular disorders; they may be less effective with particular sub-sets of those affected; or best practice may not be implemented in the management strategies adopted by clinicians. These questions were addressed in the interviews that followed.

Interviews

Of the 26 questionnaire respondents whose selected problematic disorders included the top three from the whole sample, 20 agreed to follow-up interviews. Their mean experience in musculoskeletal physiotherapy was 13.3 ± 7.9 years. Responses are summarized in Table 3. Several common themes emerged from the interviews:

- Meeting the patient when the disorder had already become chronic was seen as a problem with all three disorders. Whether owing to a delay in the

patient seeking help, low priority being attached to the referral by a GP, or long waiting lists, chronicity was commonly seen as a major obstacle to managing the disorder effectively.

- Poor or non-response to treatment was seen as sometimes arising from inadequate assessment or mis-diagnosis. This was particularly observed in the first stage of frozen shoulder, when limitation of movement might not follow a capsular pattern and pain could be impossible to localize. Less experienced clinicians were judged by some respondents as prone to treat frozen shoulder as a rotator cuff lesion and so exacerbate the problem. Unrecognized neural involvement was suggested by some as accounting for the apparent recalcitrance of all three disorders.

- A range of management strategies are commonly employed, but the disorders were often found to be slow to resolve. Many respondents felt they followed a natural course that was resistant to therapeutic modification. Some admitted that they had developed a defeatist attitude to the most recalcitrant disorders, and might tell patients early on not to expect much improvement from therapy. A minority expressed a concern about therapists continuing to treat when there is no reasonable expectation of improvement.

- Clinical practices varied, with some clinicians adopting a much more interventionist approach than others. Most respondents concluded that hands-on physiotherapy is not appropriate for frozen shoulder, particularly in its early phases. A significant minority disagreed with this standpoint, claiming that interventions in both phases could lessen symptoms and improve function. A difference in opinion was also apparent in accounts of treating plantar fasciitis; some therapists claimed excellent success rates and expressed surprise that others found the disorder recalcitrant.

- Some interviewees were specialist practitioners with particular skills relevant to these disorders, such as biomechanical analysis; others had many years of general experience, but admitted to lacking specialist knowledge that might change their practice. Referral to other specialist services was mentioned in some cases. With plantar fasciitis, referral to podiatry services for biomechanical assessment was described, but a concern also expressed that immediate referral might deny the patient access to skills particular to physiotherapists.

DISCUSSION

The study identifies the soft tissue disorders that clinicians presently find particularly challenging to manage, and the interviews provide some

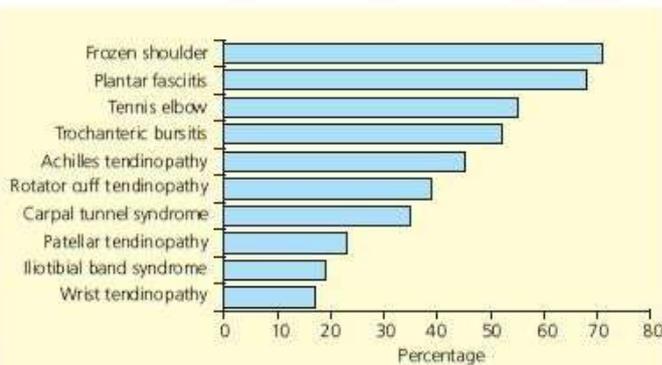


Figure 1. Proportion of respondents identifying top ten problematic disorders

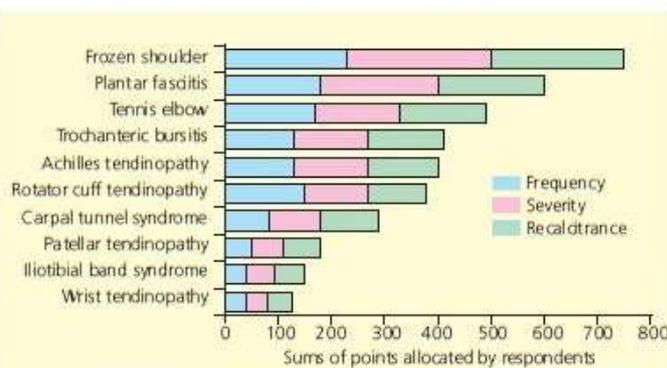


Figure 2. Individual and combined scores for frequency of presentation, severity and recalcitrance to treatment of top ten disorders.

insight into potential contributory factors. Since frozen shoulder, plantar fasciitis and tennis elbow appear to be the disorders that clinicians find particularly problematic, directing research into the more effective management of these particular disorders may be warranted. Comments made in the interviews suggest that several lines of enquiry may be valuable, drawing on both clinical research and service reviews.

Differential diagnosis and identification of concurrent pathologies are recognized in the literature as significant issues for all three disorders (Neviaseer and Neviaseer, 1987; Bamji et al, 1996; Vicenzino and Wright, 1996; Singh et al, 1997; Cornwall and McPoil, 1999; Nirschl and Ashman, 2003). Improving existing skills in this area, by in-service training on their diagnosis for example, could be helpful. Studies evaluating the sensitivity and

Table 3.
Clinician opinions and experiences with the top three problematic disorders

Frozen shoulder	Plantar fasciitis	Tennis elbow
<p><i>Less responsive presentations</i></p> <ul style="list-style-type: none"> ■ Painful phase: only symptomatic relief seen as possible (minority said could prepare for later impact on quality of life) ■ Stiff phase: disorder seen as virtually impervious to treatment by most interviewees 	<ul style="list-style-type: none"> ■ Chronic phase 	<ul style="list-style-type: none"> ■ Chronic phase
<p><i>Management strategies commonly adopted with each disorder</i></p> <ul style="list-style-type: none"> ■ Painful phase: refer for injection, scapular setting, education and advice, reassurance that it will get better; use of electrotherapy (TENS) and acupuncture for pain ■ Stiff phase: for most therapists—see once or twice to show self-management, stretches; for some therapists—soft tissue release, muscle balance, scapular tracking, joint mobilization, sustained joint glides ■ Treat co-factors such as spinal, muscular, neural problems 	<ul style="list-style-type: none"> ■ Exercise (especially stretching) ■ Cryotherapy ■ Trigger points ■ Addressing problems higher up, such as core stability) ■ Electrotherapy (most commonly ultrasound) ■ Lifestyle, work adaptation ■ Education about disorder ■ Treat co-factors, such as muscular and neural problems ■ Refer for corticosteroid injection ■ Refer to podiatry for more expert biomechanical assessment – often big improvement after orthotics organized ■ Focus on symptoms rather than causes 	<ul style="list-style-type: none"> ■ Cryotherapy ■ Taping, strapping ■ Home exercises, stretch and strengthening (especially eccentric) ■ Manual therapy (deep frictions, massage, mobilizations with movement) ■ Electrotherapy (most commonly ultrasound) ■ Lifestyle, work adaptation ■ Education about disorder ■ Treat co-factors such as spinal, neural problems ■ Refer for corticosteroid injection
<p><i>Factors thought to limit successful management of the disorder</i></p> <ul style="list-style-type: none"> ■ Inadequate differential diagnosis leading to inappropriate management ■ Some therapists felt they could have more impact if they saw patients more; others felt resources were not an issue ■ Only seen when already in chronic phase ■ Age-related degeneration may limit response to therapy ■ Therapist tendency not to look deeper for related problems 	<ul style="list-style-type: none"> ■ Difficulty identifying and addressing all contributory factors ■ Centralization of pain in chronic cases ■ Lack of biomechanics skills of clinician ■ If referred to podiatrist, attention may not be given to neurodynamics or muscle balance work ■ Contributory co-morbidities, e.g. diabetes 	<ul style="list-style-type: none"> ■ Inadequate differential diagnosis leading to inappropriate management ■ Difficulty identifying and addressing all contributory factors ■ Only seen when already in chronic phase – seen as a low priority by referring doctors ■ Centralization of pain in chronic cases ■ Tendency to re-injure: difficult to get patients to rest the area or change work patterns / lifestyle ■ Contributory co-morbidities e.g. diabetes ■ Psychosocial contribution

Research

specificity of diagnostic tests for these disorders are required. At the same time, more reliable diagnostic tools might be developed for use in the clinical setting. For instance, in the cases of tennis elbow and plantar fasciitis, the extent of pathological tissue changes observed with diagnostic ultrasound in the laboratory may correlate with common clinical tests (Torp-Pedersen et al, 2002; Sabir et al, 2005; du Toit et al, 2008). Respondents find tennis elbow and plantar fasciitis more recalcitrant once they have become chronic. Therefore outcomes may improve if higher priority is assigned to them in the triaging process. Referral guidelines may need to be revised accordingly.

Differences in opinion about the efficacy of physiotherapy were apparent among the interviewees. This may be a result of differences in practice rather than the inherent recalcitrance of these disorders. Therapy departments that have more success managing these disorders might consider what they can do to inform others of their strategies. More detailed research should identify variations in practice and outcomes in the treatment of these specific disorders. Despite the many management strategies advocated in the literature, there remains uncertainty about which interventions are most appropriate at each phase of the disorders' natural histories, and for different patient sub-groups. Systematic reviews of treatments for these disorders have criticized the quality of published research (Cleland and Durall, 2002; Struijs et al, 2002; Buchbinder et al, 2006; Wood et al, 2006).

The choice of physiotherapists as the target population meant that the views of other clinicians were not sought. Disorders regarded by physiotherapists as recalcitrant might respond more readily to treatment by other health professionals, as evidenced by successful outcomes following referrals to podiatry reported by some respondents. This underscores the value of interdisciplinary research and collaboration in their management, as recently proposed for frozen shoulder (Morrissey, 2007).

Study limitations

A number of potential limitations in this study can be identified. The questionnaire return rate of 48% is at the lower end of rates typical for research published in medical journals (Asch et al, 1997). Ethical approval for the study was granted on condition that reminders were not sent, as the questionnaires may have been passed on to other clinicians. A higher rate might have been achieved if this condition had not been imposed. The questionnaire was created specifically for this survey and its reliability has not been established. However, the survey was intended to be exploratory rather than definitive in nature, drawing attention to disorders and opinions that require further investigation.

CONCLUSIONS

This exploratory study has identified several soft tissue musculoskeletal disorders that are particularly problematic for both patients and clinicians. Its findings may be helpful in several respects. Service managers may be challenged to focus resources more specifically on these particular disorders, which have been identified by frontline clinicians as in need of more effective management. The research community may be encouraged to develop more effective diagnostic techniques and to audit clinical practice for variations in treatments and outcomes. Finally, where clinicians are obtaining relatively good outcomes with these disorders they may publicize their experience and contribute to the development and dissemination of best practice guidelines. These responses may enhance the service and improve the outcomes of treatment offered to those suffering with these debilitating and costly disorders. **UTR**

Conflict of interest: none

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KEY POINTS

- This study explored the views of practising physiotherapists working in National Health Service and private clinics in south-east England on the most problematic soft tissue disorders, using a postal questionnaire survey and telephone interviews.
- Frozen shoulder, plantar fasciitis and tennis elbow are viewed by physiotherapists as particularly problematic disorders to treat.
- Issues of diagnosis, triaging and differences in management approaches may be contributing to the apparent recalcitrance of these disorders.
- More resources dedicated to service reviews and research concerned with effective assessment and multidisciplinary management of these disorders is warranted.

COMMENTARIES

This is an interesting and informative piece of research which, unfortunately like many other reports, stimulates more questions than it provides answers. This is not a criticism of the work but is a general statement regarding research in the field of physiotherapy and physical therapy techniques. The concluding statement of much published material in this area could be 'more research required in this area!' However, the authors should be congratulated for seeking the views of clinicians before embarking on further research. Indeed, if clinical research is to be successful it is fundamental that it links to the needs of the profession.

The findings highlight many of the problems encountered in the clinical arena, such as the development of chronic conditions related to waiting times for treatment, the differing views of clinicians regarding diagnosis, treatment and the relevant success or otherwise of these interventions. Indeed this is reiterated

in other work (Scott and Ashe, 2006) where it is suggested that the reporting of common tendinopathies demonstrates contradiction in the definition and description of the pathology. This work adds to other research published in this area. A report by Picavet and Hazes (2003) highlighted patients self-reported musculoskeletal disorders; the most common being 'tendonitis or capsulitis' in over 15% of male and over 17% of female respondents.

The authors of this study remark that previous literature reviews are critical of the quality of reported studies of common musculoskeletal disorders. There is often little to be taken away from the published literature that the clinician can apply in their day-to-day treatment of patients. The research may be poorly reported, the intervention may not be comparable to that used in clinical practice or the researchers only look at certain parameters of treatment. Perhaps we should be learning

from our colleagues involved in acupuncture research where there is now an expectation that researchers will report studies in a certain manner so that the treatment technique could be easily reproduced in clinical practice or indeed future research (MacPherson et al, 2001). Taking this further many journals will not accept papers unless there is an adherence to these reporting guidelines.

This article highlights the problems associated with the development of chronic conditions as a result of referral systems and waiting times. These problems may well become a thing of the past if open access and self-referral systems are encouraged by health service providers. The authors mention service reviews and dissemination of good practice, which are both useful in improving the care of our patients. Indeed, perhaps as therapists we should be looking to the use of information technology and the easy access to and sharing of information in

interactive websites. These sites allow clinicians to discuss ideas and difficult case scenarios and, similar to this piece of work, give researchers an insight into the questions that clinicians have about patient care. Thus development of future, clinically relevant research topics will be stimulated.

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Scott A, Ashe MC (2006) Common tendinopathies in the upper and lower extremities. *Curr Sports Med Rep* 5: 233–41

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Research

This article on experienced physiotherapists' perceptions of problematic soft tissue disorders brings to light some interesting points not only for clinical practitioners but also for service managers, researchers and higher education institutions.

It is clear from the study findings that much of the difficulty in managing the conditions highlighted in the article appears to be a result of the development of chronicity. The importance of addressing this is reflected in the emphasis given to self-management and health promotion in the recently launched Scottish Adult Rehabilitation Framework: *Co-ordinated, Integrated and Fit for Purpose* (Scottish Executive, 2007). This phase of the rehabilitation journey is sometimes called 'prehabilitation'. As the conditions mentioned in the article potentially had a strong work- or sports-related origin, it would appear that a good starting point for musculoskeletal soft tissue disorder prehabilitation would be in the workplace and in culture and leisure centres. It would have been interesting to know what percentage of the disorders listed had been associated with the patient's

vocational or leisure activities.

It is interesting that the authors used the terminology 'treatment' rather than 'condition management'. Certainly, in Scotland at present, with the launch of the aforementioned Rehabilitation Framework, the focus is less on impairment management and more on maximizing the active participation of the patient in his/her social setting. It would be illuminating to correlate the perceived level of symptom severity of the particular conditions outlined in the article and the patient's level of disability and quality of life. This could, perhaps, form the basis of another study on this topic.

As alluded to in the article, there is no doubt that early intervention for soft tissue disorders is of paramount importance. One would hope that with the increasing number of primary care providers offering direct access to physiotherapy, clients would be able to obtain speedy diagnosis and suitable management (Holdsworth and Webster, 2004). However, it appears that there is a need for the profession to promote better public awareness of the scope of physiotherapy

practice, for appropriate self-referral to take place. Recent research from Scotland has identified that patient knowledge about the physiotherapy profession is poor; indeed, less than 23% of respondents in a national survey of physiotherapy service users claimed to be knowledgeable about physiotherapy (Webster et al, 2008).

Another issue raised in this article was the referral to other disciplines for specialist services. At present, there are several drivers in Scotland for a single access point for all rehabilitation services, which, hopefully, would encourage genuine multi-disciplinary team working and joined-up care (Scottish Executive, 2005; Scottish Government, 2007). However, at this point in time although this ideal 'seamless' care provision is evolving slowly it still tends to be rather sporadic.

Finally, the findings of this study are pertinent to physiotherapy educators in universities. Undergraduate students and novice practitioners would find it extremely reassuring to be informed that when presented with the types of conditions considered problematic

by experienced physiotherapists that they were not alone in finding them difficult to manage. Armed with this knowledge and in conjunction with the ever-expanding evidence base for practice, they should be able to facilitate a more satisfactory outcome for the patient.

Holdsworth LK, Webster VS (2004) Direct access to physiotherapy in primary care: now?—and into the future? *Physiotherapy* 90(2): 64–72

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Bioelectricity and microcurrent therapy for tissue healing – a narrative review

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Background: Microcurrent therapy (MCT) uses electric currents similar to those produced by the body during tissue healing. It may be a particularly beneficial where endogenous healing has failed.

Aim: To review evidence regarding microcurrent in tissue healing and the application of MCT.

Methods: All peer-reviewed studies concerning microcurrent and MCT were sought, and representative literature was synthesised to indicate the scope and weight of current evidence.

Results: Microcurrent appears to play a significant role in the healing process, and MCT can promote healing in a variety of bone and skin lesions. The evidence for other tissues is encouraging but presently scant.

Conclusion: MCT may have unrealised potential in the treatment of dysfunctional tissue healing and deserves greater attention by researchers and clinicians.

Keywords: bioelectricity, electrotherapy, microcurrent, tissue healing

Introduction

Contemporary accounts of tissue healing are typically expressed entirely in terms of biochemistry.¹⁻⁴ The actions of substances such as cytokines and growth factors are said to initiate and mediate the various stages of inflammation and repair that normally follow tissue damage.⁵ Yet evidence which has accumulated over many decades suggests that a full description of the physiology of healing must also include the role of bioelectricity – accumulations and flows of charge that are generated endogenously, within the body. The importance of bioelectricity in functions such as nervous system signalling and muscle contraction has been long appreciated, but it is also involved in many other physiological processes. These include the development, adaptation, repair and regeneration of tissues throughout the body.⁶⁻⁹

Recognition of bioelectricity's role in tissue healing provides a rationale for the therapeutic application of electrical stimulation, particularly in cases where natural repair processes have broken down. Microcurrent therapy (MCT) is an example of this. Uniquely amongst the various electrotherapeutic modalities, MCT involves application of voltages and currents of similar magnitude to those generated endogenously during normal

tissue healing. Although relatively unknown and currently little used by physiotherapists outside North America, MCT has been shown to be of benefit in several types of tissue healing and it may be effective in others. It appears to stimulate healing generally, and not just one element of the process; it has very few side effects; and it may offer an effective treatment for musculoskeletal disorders such as chronic tendinopathies where normal healing has become dysfunctional.

This paper outlines current thinking on the role of bioelectricity in healing, presents empirical evidence regarding MCT for the promotion of tissue healing, and suggests implications for both clinical and research communities. The majority of published research in this area is concerned with bone and skin lesions, but patterns and mechanisms of healing in these tissues share features with those seen in damaged tendons, ligaments and other musculoskeletal structures.¹⁰⁻¹² Therefore the evidence presented here is of relevance to researchers and clinicians concerned with a variety of musculoskeletal disorders.

Bioelectricity and healing

The human body, in common with other living organisms, expends a significant proportion of its

energy generating electricity.¹³ In fact the body is a conglomeration of electric batteries. Every cell maintains a voltage across its external membrane, and across the membranes of its organelles.^{14,15} This is achieved by the active transport of ions, particularly sodium and potassium, against their concentration gradients, establishing charge separations that constitute a potential difference or voltage across the membrane.¹⁶ Aggregates of cells also set up voltages across various tissue layers, including cutaneous and corneal epithelium, vascular and intestinal walls, and the cortex and periosteum of long bones.^{14,15,17–21} These voltages are of the order of millivolts (mV) in magnitude, and where there is a conducting pathway they cause the movement of ions within tissue, constituting a bioelectric current, typically in the microamp (μA) range.¹⁴

At the cellular level, bioelectricity is involved in the transport through the membrane of ions that can influence cell behaviour. Even in non-excitable cells there are voltage-gated channels controlling the passage of such ions.²² At the tissue level, endogenous fields are intrinsic to a number of metabolic processes, including development, adaptation and repair. They can influence cell morphology and the growth of body parts during foetal development;^{13,23,24} they are generated when connective tissues such as bone and tendon are stressed, and can influence adaptive modifications in the extracellular matrix,^{25–28} and when tissue is damaged they set up currents that appear to drive elements of the healing response.^{17,29–32} The currents diminish as healing progresses, with normal values being re-established once healing is complete.^{17,23,32,33}

That bioelectricity is intrinsic to such processes – rather than a mere by-product – has been established by a wealth of experimental evidence. Perhaps the most convincing is that setting up a voltage in opposition to the endogenous one, or blocking the passage of biocurrents, can slow or abolish the healing response in a variety of tissue types.^{15,33–35} In vitro studies have also demonstrated that application of electric fields and currents similar to those generated within the body can cause significant changes in the structure and behaviour of cells. Application of microcurrent to tissue has been found to boost the number of organelles responsible for cellular activities, and to increase concentrations of ATP, the cellular currency of energy.^{36,37} These changes can facilitate cell proliferation and protein synthesis, which have been found to increase when microcurrents are applied to the constituent cells of

skin,^{38,39} tendons,^{40,41} cartilage⁴² and bone.⁴³ Such effects are highly parameter-dependent, however. Larger currents or alternating microcurrents at certain frequencies have been found to reduce cell proliferation or induce cell death in some cases.^{44,45}

Ion channels in cell membranes may migrate under the influence of an applied field, resulting in cytoskeletal modifications, including creation of membrane projections that enable cell movement.^{24,37} Directed movement of cells within an electric field – known as galvanotaxis – has been observed with many cell types. These include leukocytes and macrophages, which are key mediators in different stages of healing,⁴⁶ as well as a variety of cells responsible for tissue formation, such as keratinocytes, vascular endothelial cells, osteoblasts, osteoclasts, chondrocytes and fibroblasts.^{24,37,47,48} Different cell types have been found to move in opposite directions, and reversing the field reverses the direction of migration.^{37,49}

At the tissue level, unidirectional fields and direct currents (DC) can promote vascular permeability⁵⁰ angiogenesis⁵¹ and neural sprouting^{31,52} as well as formation of new skin, bone, cartilage and soft tissue.^{39,53–57} Such findings are significant because they suggest that applying fields and currents with similar parameters to bioelectricity may be used to stimulate tissue healing. Cell migration, proliferation and synthesis of new tissue are all essential components of the healing process.^{1,46} If applied electricity can mimic endogenous electrical signals that guide cellular behaviour, then a therapeutic option may be available where natural healing has failed.

Therapeutic microcurrent

There are various forms of electrotherapy that may deliver average currents in the microamp range, such as high voltage pulsed current, and high frequency alternating currents induced by electric or electromagnetic fields, e.g. pulsed short-wave or non-thermal pulsed radio frequency. However, the waveforms produced by these modalities are quite unlike those of any observed endogenous currents and voltages, which tend to be unidirectional, and of constant or slowly varying amplitude.¹⁴ Since MCT is predicated on the basis that it mimics endogenous bioelectric signals, the main focus here is on those studies that use electrical stimulation with similar parameters. A good deal of evidence regarding the effects of microcurrent on tissue healing has accumulated over recent decades. Where clinical trials have been reported, they are presented, though

reference to *in vitro* and animal studies is also made where clinical trial data is scarce.

Bone

Electrical stimulation was used for promotion of bone healing in the early nineteenth century. English physician John Birch applied DC to the ends of a 13-month-old non-uniting tibial fracture via percutaneous electrodes.⁵⁸ After 6 weeks of treatment the fracture had consolidated. Other historical examples of electricity being used in this way are recorded, but the therapy later fell into disuse. It was revived in the mid-twentieth century, when a scientific rationale for its application was developed on the basis of *in vitro* and animal experiments. In the 1950s several workers found that application of microcurrent to bone could initiate osteogenesis in both normal and damaged bone.^{59,60} Later studies investigated the effects of parameters such as current size, polarity and electrode material and configuration on the process.^{61–63} New bone could be laid down by DCs of about 20 μA , with maximal formation occurring at the cathode (the negative electrode). Currents above 30 μA could cause bone resorption or osteonecrosis.^{55,62,64} Such data provide a persuasive rationale for the use of microcurrent to stimulate bone healing, and subsequent *in vivo* animal studies suggested that it might be beneficial for several clinical applications, including fresh fractures, delayed and non-uniting fractures, osteotomies and spinal fusions, although parameter choices varied considerably and not all applications were successful.^{65–70} Reviews of such studies are available.^{71,72}

Clinical studies

The earliest modern application of MCT for human bone healing was to non-uniting fractures. In 1971, Friedenbergs and colleagues published a case study in which a malleolar fracture, which had failed to unite after more than a year, was healed within 9 weeks by treatment with DC of 10 μA via a cathode inserted into the fracture site.⁷³ Several larger studies followed, in which MCT was applied to delayed or non-uniting fractures. Delayed unions are those that take longer than would be expected for the particular fracture site and patient characteristics; non-union is said to occur when healing stops and union is not achieved after 6–8 months.⁷⁴ In 1977 Brighton and colleagues reported a study involving treatment of 57 lower and upper limb non-unions with 10–20 μA , delivered to the site by 2–4 cathodes for 12 weeks, followed by 12 weeks of continued immobilisation.⁷⁵

Of those treated, 76% went on to develop full union, with most failures accounted for by insufficient current delivery or breakage of electrodes. In a follow-up multi-centre study 84% of 178 non-unions treated using a similar protocol achieved union. Complications were reported as minor.⁷⁶ Another multicentre trial in a different country used the same current but delivered through a single cathode to 84 patients with either delayed or non-union,⁷⁷ mostly of the tibia or femur. Time to achieve union varied between 12 and 36 weeks. A 10-year follow-up assessment of 37 of the patients enrolled in this trial found normal bone remodelling, continued union and no side effects of the electrodes that were left *in situ* (the remaining participants were unavailable for review).⁷⁸

Microcurrent pulsed at 20 Hz has also been evaluated and found beneficial with a mixed caseload of non-uniting fractures, congenital pseudarthroses, osteotomies and leg-lengthening procedures.⁷⁹ DC of pulse amplitude 20–25 μA and duration 30 ms was applied via a cathode wrapped around or threaded through the fracture site and with the anode implanted in the medulla (as opposed to the subcutaneous positioning used in other trials). Treatment times varied according to case until union was observed radiographically, and varied between 2 and 12 months. The overall success rate was 87% although adjunctive treatments and individual characteristics varied considerably. Authors of one of the earlier studies⁷⁵ reported that they found that constant DC always produced superior outcomes to pulsed current, although they presented no relevant parameter or outcome data.

Some of these studies are rather dated and do not meet contemporary reporting standards for clinical trials. The absence of a formal control group is justified by the fact that usually no bone healing had been observed for months, and spontaneous recovery in such cases is rare, so participants were considered to be acting as their own controls.⁷⁶ However placebo and time effects cannot be ruled out when evaluating their evidence. The lack of more recent studies may reflect the greater popularity of less invasive electrotherapies, although MCT appears superior in selected cases. A comparison with capacitative and inductive coupling as adjuncts for bone graft treatment of tibial non-unions reported in 1995 found that microcurrent was more effective with high risk cases such as those with atrophic non-unions or previous graft failure.⁸⁰ Where there were no identified risk factors, none of the electrotherapies was superior to graft alone.

Although non-invasive forms of electrotherapy have superseded MCT for some applications, it has continued to be employed with lumbar spinal fusions, where there is evidence of its superiority over other types of electrical stimulation. Such fusions are used in cases of disabling joint instability or disc degeneration, and normally involve a bone graft and instrumentation. Failure rates can be as high as 40%,⁸¹ but may be reduced substantially by the application of MCT. After its first clinical use was reported in 1974,⁸² DC application, typically of 20 μA applied by a single or multiple cathodes to the fusion site for 5–6 months, was subject to evaluation in several trials.^{83–85} In these studies patients receiving MCT in addition to standard treatment had successful fusion rates of 81–96%, compared to 54–81% for those on standard treatment alone, as assessed by radiographic and clinical criteria. Results for methodologically sound controlled trials consistently indicate statistically significant outcomes in favour of DC MCT compared with control groups.⁸⁶ It is particularly effective when used in high risk cases such as those with previous failed fusions, multiple level surgery, smokers and those with co-morbidities such as diabetes and obesity,^{87–89} and has a stronger favourable evidence base than either capacitative or inductive coupling, particularly for posterior fusions.⁹⁰ An economic evaluation of the therapy as an adjunct in spinal fusion surgery⁹¹ also found that it provided significant cost savings and shorter in-patient stays.

Smaller studies have suggested that DC MCT may be useful in other bone lesions, including high risk ankle and hind-foot fusions^{92,93} and selected congenital pseudarthroses.^{94–97} Their findings have yet to be confirmed by larger trials. Two controlled trials have suggested that MCT may also accelerate healing in fresh fractures,^{98,99} though this application is still largely unexplored.

Systematic reviews of trials have concluded that the best evidence for promotion of bone healing by application of small electric currents is in cases of non-uniting lower limb fractures and spinal fusions.^{71,86,88,90,100–105} Meta-analyses have been weakened by pooling data from trials using heterogeneous groups and treatment parameters, and even different forms of electrotherapy.^{86,101} Nevertheless, consideration of the evidence regarding MCT in particular suggests that its application, usually for several months, may enhance tissue healing in a variety of bone lesions.

Skin

Since it is easily accessible for study, skin is the tissue in which the bioelectrics of healing have perhaps been subject to the greatest scrutiny. Reviews providing accounts of *in vitro* and animal studies are available,^{53,72,106} and only the human and clinical studies are dealt with here. Several authors have identified the seventeenth-century use of charged gold leaf for resolution of smallpox lesions as the first example of electrotherapy for human skin healing.^{53,107,108} In fact there is no mention of electric charge in the cited source.¹⁰⁹ Charged gold leaf, which would deliver a small and diminishing current to adjacent tissue, was used successfully in the 1960s to assist healing in surgical vascular wounds and cutaneous ulcers.^{110,111} However, charging appears to have been considered an aid to adherence of the leaf rather than an agent of healing in itself. Nevertheless, more recent studies have consistently concluded that electrical stimulation, including MCT, can indeed promote healing in various types of human skin wounds, particularly ulcers. The first of these was reported in 1968 by Assimacopoulos who, following successful use of microcurrent to accelerate healing of surgical scars on rabbit ears,¹¹² tried the treatment with recalcitrant leg ulcers in three patients.¹¹³ DC between 50 and 100 μA was delivered continuously for several weeks via a stainless steel mesh cathode soaked in saline and placed on a moist dressing on the wound, and an anode affixed to the thigh or abdominal wall. All the wounds healed within six weeks and no side effects of treatment were reported.

In a larger study, Wolcott and colleagues used MCT with 83 ulcers of varying aetiology in 67 patients.¹¹⁴ A measure of control was introduced by assessing but not treating additional ulcers in eight of the sample patients. 'About three quarters' of the patients had failed to respond to other conservative treatment. DC between 400 and 800 μA was applied via a copper mesh cathode over the wound and anode on skin 15 cm proximal. The current level was determined individually, adjusted so as to avoid bleeding or excess exudate production, and was delivered for 2 hours, thrice daily for several weeks, in some cases months, until healing occurred (a full breakdown of durations was not given). The protocol involved a polarity-swapping element, based on early experience that healing would often plateau after a few days and could be restarted by reversing the polarity of the electrodes. Over a mean treatment time of 7.7 weeks, there was a mean volume reduction in treated wounds of 82%, with a mean

healing rate of 13.4% per week. Thirty-four lesions (40%) healed completely. These figures mask a wide range of individual and group responses, with paraplegic patients (presumably mostly spinal cord injured) consistently responding less well to treatment. Of the eight patients (mostly paraplegic) with microcurrent-treated and control ulcers, mean volume reductions were 93% (range 75–100%) in the MCT ulcers and 33% (range 0–75%) in the control ulcers. The study evidence is weakened by the lack of information on duration of ulcers, the inclusion of patients for whom standard treatments had not been tried, early termination of electrotherapy protocol in more than half of the sample, and the small size of the control group. Even so, it began to build the case that MCT could assist healing in a variety of skin ulcer types.

MCT using similar protocols – and various alternatives – were later used in several larger controlled trials by other groups.^{115–121} These involved several skin ulcer types including those due to venous and arterial insufficiency, secondary to diabetes, and pressure ulcers following spinal cord injury. MCT typically involved currents of several hundred microamps, often continuous DC but sometimes pulsed or low frequency biphasic. Where currents were unidirectional, the anode was normally placed on the wound, within a moist dressing. Treatment times were usually 1 hour or more each day for several weeks or even months. Healing was measured in terms of percentage reductions in wound surface area or volume over a defined time, and in the majority of cases ulcers receiving MCT as an adjunct to conventional treatment healed more quickly and completely than those receiving conventional treatment alone.

More recent studies have suggested that MCT may also be effective with other types of skin wounds. In a trial involving 30 patients, microcurrent was found more effective than conventional treatment in promoting skin graft healing following thermal injury.¹²² A DC current between 50 and 100 μA was applied continuously for several days via an anodal dressing on the wound. Stimulated wounds closed in an average 4–6 days compared to 7.2 days for controls. A series of case studies involving application of monophasic microcurrent to pressure sores, an infected venous ulcer and a recalcitrant pilonidal sinus also found evidence of benefit in terms of accelerated healing and reduction of bacterial load.¹²³ The novelty of these cases was that the current (of unspecified magnitude) was provided by a

proprietary dressing with an integrated circuit, battery and electrodes.

Reviews of electrical stimulation for skin wound healing have consistently concluded that the weight of evidence is in its favour when it is used as an adjunctive treatment with other conservative management strategies.^{53,86,108,124–128} In the USA, government and private medical insurers pay for its use with recalcitrant ulcers due to pressure, arterial or venous insufficiency and diabetes.¹²⁷ However, most reviews have not considered the different modalities separately, because the numbers do not justify subgroup analysis. Where MCT studies are considered alone, the range of protocols employed means that optimum parameters cannot yet be identified. Both continuous and pulsed, monophasic and biphasic, anodal and cathodal stimulation seem capable of promoting healing. The parameters that are supported by a majority of studies are current size (in the hundreds of microamps), treatment time (typically several weeks, for hours rather than minutes each day) and application directly to the wound bed. Monophasic or ‘unbalanced’ currents (those with a net delivery of charge) are more common in the studies indicating MCT effectiveness.

Tendons and other tissues

Data from *in vitro* and animal studies, and a small number of human trials, suggest that there may be unexplored potential for microcurrent treatment of lesions in soft connective tissue, particularly tendons and ligaments. In these structures, the extracellular matrix (ECM) is laid down by phenotypes of the fibroblast, a cell that has been shown to migrate, proliferate and increase synthesis of ECM proteins under the influence of applied electric fields and currents.^{40,41,129–132}

Tissue and animal studies

By using explants, whole tissue samples taken from animals and maintained in laboratory cultures, investigators have been able to conduct well-controlled studies of the effects of applied current on tendons and ligaments. Nessler and Mass reported using these methods in 1987, when they applied continuous 7 μA current for up to 6 weeks to surgically transected and sutured rabbit flexor tendon explants.¹³³ Bioassay and histological analysis showed greater and more rapid fibroblast proliferation, protein synthesis and collagen deposition consistent with normal tendon healing in stimulated explants compared to their controls. These changes

were observed distant from the cathode, which had been placed into the lesion, and the authors speculated that the current density was too great close to the cathode. Soon after, Cleary and colleagues investigated the influence of various microcurrent parameters by applying pulsed monophasic microcurrent to chicken flexor tendon explants for 3 days, varying current amplitude, direction and pulsing frequency.¹³⁰ They found that levels of fibroblast proliferation, protein synthesis and collagen fibroplasia at the cut surfaces of stimulated explants were significantly greater than those of unstimulated controls. Effect sizes were greatest at current densities of about $1 \mu\text{A}/\text{cm}^2$, and at pulse frequency 1 Hz, and dropped off at higher values. Applying the current longitudinally maximised the effects, whilst no significant differences between treated and control explants were found with transverse application. This observation was explained by other studies showing that fibroblasts lay down collagen fibres parallel to the direction of the applied field.^{134,135}

In a study using explants of rabbit flexor tendons and their sheaths, longitudinal stimulation with various DC microcurrent levels was applied for up to 2 weeks.⁴¹ Investigation of the cut surfaces revealed evidence of cell proliferation and collagen deposition in both treated and control samples, with adhesions forming in the epitenon-sheath as a result. Application of microcurrent caused different effects according to current size. Above $1 \mu\text{A}$ there was evidence of tissue degeneration and cell death, but at $0.5 \mu\text{A}$ proliferation continued in the tendon substance but was significantly reduced in the sheath. This observation rather astonishingly suggests that microcurrent can selectively inhibit proliferation that would lead to counterproductive adhesion formation during sheathed-tendon healing.

In the first reported *in vivo* animal study, low level current was applied to surgically wounded flexor tendons of six ponies via a cathode implanted in the wound and an anode 3 cm distal.¹³⁶ No gross or histological differences were seen between treated and contralateral control tendons at 4, 5 or 6 weeks post-injury. The author speculated that the (unmonitored) current, provided by a bimetallic strip, may have been too low to affect healing. Later studies were more encouraging, though a wide range of parameters was adopted, making generalisation from their results problematic. Stanish and colleagues transected the medial portion of the patellar tendons of nine dogs and divided them into three groups, receiving plaster immobilisation, brief compression bandaging or constant $20 \mu\text{A}$ current applied via a

cathode wrapped around the tendon.¹³⁷ After 6 weeks the dogs were killed and the tendons removed with their contralateral counterparts for comparison. Breaking strengths as a percentage of the normal tendon values were 47 and 50% for the first two groups, and 92% for the MCT group. Though the sample sizes were small, the difference is striking.

In a larger study,¹³⁸ the patellar tendons of 45 rabbits were transected bilaterally and cathodes sutured into the lesions, anodes mounted on the tissue surface. One limb was left untreated, the other given $10 \mu\text{A}$ DC continuously, with tendons removed at 3, 5 or 7 weeks for evaluation. Mechanical strength was found to increase more rapidly in the early weeks in stimulated tendons, whilst mature collagen formation was greater in the later weeks, compared to controls. This suggested that MCT could accelerate healing in both proliferative and remodelling phases of healing.

Subsequent studies with rat Achilles tendons, knee ligaments and joint capsules have consistently suggested that MCT with a range of parameters can accelerate repair and result in stronger tissue and reduced contracture formation after injury, compared to unstimulated controls.^{56,139-143} Microcurrent has also been observed to promote rabbit cartilage growth⁵⁷ and repair,¹⁴⁴ as well as rat peripheral nerve regeneration.⁵² DC or unbalanced biphasic current was used in all the tendon studies, but alternative current was also successfully employed with other tissues. Treatment times varied between 1 and 24 hours a day for between 1 and 4 weeks. Where currents were modulated, their amplitudes were of the order of $100 \mu\text{A}$ (with considerably lower average values), and electrodes were implanted, usually delivering current parallel to fibre orientation. The strength of the studies is in their use of contralateral controls, allowing a cause-effect relationship to be established. However their findings cannot be aggregated because of heterogeneity in their treatment parameters. They all used surgical means to create lesions and animal models that are imperfect analogues of human tissue disorders. The lack of histological data also means that conclusions cannot be drawn about repair processes. Despite these limitations, they provide evidence that microcurrent can promote resolution of tissue damage, and have justified progression to clinical trials of MCT.

Human studies

Following their work with surgically wounded canine tendons, Stanish and colleagues reported on a series

of more than 100 patients in which MCT was used after surgical repair of torn Achilles and patellar tendons and anterior cruciate ligaments.¹³⁷ A DC of 20 μ A was applied (for an unreported time, presumably several weeks) via a cathode wrapped around the lesion and a subcutaneous anode and power-pack. The authors reported accelerated return to full weight-bearing and function, and histological analysis of 45 reconstructed ligaments 9 months after surgery showed the tissue to be revascularised with mature and well organised collagen. This was not a formally controlled trial, however, and little numerical data is provided for scrutiny.

MCT has been subject to trial with several examples of chronic tendinopathy. One involved 48 people with Achilles tendinopathy of at least 3 months' symptom duration, randomly assigned to receive either microcurrent or conventional conservative treatment.¹⁴⁵ A monophasic square wave of amplitude 40 μ A and frequency 10 Hz was applied via surface electrodes placed transversely across the lesion. Treatment was for 30 minutes daily over 14 days, followed by a regime of eccentric exercises. Numerical measures of patient-rated pain and stiffness and clinician-rated clinical status were recorded at baseline and at 3, 6 and 12 months after treatment. Statistically significant differences in favour of the MCT group were found in these measures. Sonography, which can be used to image changes associated with tendinopathy,^{146,147} was also employed. The authors reported that sonographic findings were 'in agreement' with these outcomes, though specific data were not given. Improvements were most marked in the first 3 months after treatment. The study is weakened by non-standardisation of the conventional treatment and a complex and unvalidated scoring system used with the outcome measures. However, the data are encouraging.

A more recent pilot controlled trial has used MCT for chronic tennis elbow.¹⁴⁸ Sixteen people with symptoms lasting at least 3 months were randomly assigned to receive either a 6-week standardised exercise programme or exercise plus MCT. Biphasic square wave current, with a variety of parameters including amplitudes 40 or 300 μ A and frequencies of 0.3, 3 and 30 Hz, was used. Treatment was administered via probes contacting the skin at various points on the elbow and forearm for several minutes, 10 times over 3 weeks. Outcome measures were pressure pain threshold at the tendon, grip strength and pain on gripping, recorded at baseline and 1, 2, 3 and 6 weeks later. All participants improved but no

significant differences between groups were seen in any of the outcome measures. The conclusions may have been affected by the small sample size of the study, but in any case it was hampered at the outset by the use of MCT of very short duration and methods of application that were given no scientific justification by the authors.

Trials using microcurrent have been reported for a range of other soft tissue lesions, including plantar fasciitis,¹⁴⁹ delayed-onset muscle soreness (DOMS),¹⁵⁰⁻¹⁵² radiation-induced fibrosis¹⁵³ and osteoarthritis.¹⁵⁴ The outcomes of these trials suggest – though not unequivocally – that MCT may have an analgesic effect that is not due to sensory stimulation, since the treatment is normally sub-sensory. Pain relief may account for the improvement in other outcome measures such as range of movement and function. In one study there was also evidence of mediation of the healing process. Serum creatine kinase (CK) levels, which elevate following muscle damage, were found to be lower in DOMS-induced muscles after MCT than in an untreated control group. The microcurrent was delivered by a skin-mounted charged dielectric pad, providing an average 20 μ A over 48 hours, and the CK level differences were significantly lower in the treated group 4–7 days after injury.¹⁵¹

Drawing firm conclusions from these human studies is hampered by various factors. In particular, the use of proprietary devices delivering microcurrent whose parameters are based on little if any scientific rationale. The outcome measures they adopt often give only indirect information about tissue status, and some studies are poorly constructed or reported. Nevertheless they suggest that MCT may have potential in promoting the resolution of various musculoskeletal soft tissue disorders, and indicate the need for well-conducted clinical trials. The normally sub-sensory nature of microcurrent means that double-blind placebo-controlled trials, which could provide convincing evidence, are practicable. However, at least for the present, the most persuasive evidence in favour of MCT for soft tissue lesions is provided by cellular and animal studies.

Conclusions

The evidence in support of MCT is convincing enough to justify its inclusion in the clinician's repertoire for treatment of several examples of recalcitrant bone and skin lesions. Indeed federal and private health insurance providers in the USA have accepted its use (along with other forms of

electrical stimulation) for spinal fusions and hard to heal skin ulcers for some years.^{53,83} In contrast, the lack of substantial and robust human trial evidence for the use of MCT with musculoskeletal soft tissue lesions is frustrating. Clinicians are justifiably cautious when presented with yet another form of electrotherapy, especially when the case for those that are more familiar and well-used, such as therapeutic ultrasound, has been questioned in several reviews.¹⁵⁵⁻¹⁵⁷

Yet MCT has several significant features in its favour: there is already substantial evidence that it can promote healing in a variety of tissue types and disorders, especially where other approaches have failed; it may help redress an underlying physiological dysfunction as well as reducing its symptoms; its mechanism of action appears to be as a trigger or facilitator of the whole healing process, unlike some new approaches such as exogenous growth factors, which have specific targets in the healing cascade. Reported side-effects of MCT are few and minor, and it can be provided by a small, portable generator, over an extended period where necessary, requiring minimal therapist supervision once initiated. The therapy has been shown to be most beneficial when it is used as part of a broader management strategy. Given these characteristics, the potential for MCT in a range of recalcitrant musculoskeletal disorders is worthy of closer attention by both research and clinical communities.

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Review

Measurement Issues in the Sonographic Assessment of Tennis Elbow

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ABSTRACT: Sonography is increasingly being used for assessment in tennis elbow research and clinical practice, but there are a lack of data regarding its validity, reliability, and responsiveness to change for this application. Studies using the modality were reviewed to establish current levels of evidence for these measurement properties. There is reasonable evidence regarding its validity for identifying tennis elbow tendinopathy, but a lack of data addressing its reliability and responsiveness. Practical issues affecting image quality are discussed, and recommendations for further investigation are suggested, to enhance the credible use of sonography with this debilitating condition. © 2010 Wiley Periodicals, Inc. *J Clin Ultrasound* 38:196–204, 2010; Published online in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/jcu.20676

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Since its first reported application in 1990,¹ sonography has increasingly been used in the assessment of tennis elbow: to confirm diagnosis of the disorder, characterize tissue changes as it progresses or resolves, and monitor treatment effects in clinical trials. Sonography has provided information that could otherwise only be obtained through invasive surgical procedures or expensive and less convenient imaging modalities. However, its use in tendinopathy studies can be problematic. The quality of sonographic data is dependent on both the operator and the assessment protocol, and interpretation of images can be subjective.^{2–4}

Investigators using sonography in studies of tennis elbow have adopted quite different scanning and assessment protocols, making it difficult to compare and pool their findings.⁵

Consequently, concerns have been raised about the credibility of sonography in musculoskeletal research.^{5–7} These are particularly pertinent to tennis elbow studies, since investigations of its validity, reliability, and responsiveness to change for this particular application are scarce. In common with other assessment instruments, these measurement properties should be established before sonographic assessment is routinely incorporated into study protocols. The purpose of this paper is to review the literature concerning the use of sonography in tennis elbow research, with a view to enhancing practice. The potential benefits and limitations of sonography are outlined; available evidence on its measurement properties is presented, and its current use in tennis elbow research is critiqued. Issues for consideration in planning and reporting the use of sonography are discussed, and areas that require more detailed scrutiny by the research community are identified.

BENEFITS AND CHALLENGES OF SONOGRAPHY IN TENNIS ELBOW RESEARCH

Tennis elbow is a multifaceted disorder primarily affecting the common extensor tendon that connects several wrist and finger extensor muscles in the forearm to their origin on the lateral epicondyle of the humerus.^{8,9} Although its etiology is debated, it appears to be partly a result of inadequate healing following repeated mechanical microtrauma, caused by repetitive use of the extensor muscles.¹⁰ The principal tissue change occurring in the disorder is tendino-

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sis, degeneration of the tendon, typically characterized by some combination of the following: disruption of its collagen fibers, an increase in the proportion of ground substance in the extracellular matrix, microtears in the tendon substance, intratendinous calcification, or focal or diffuse changes in tendon thickness and hypervascularity.¹¹⁻¹³ Other structural features that may occur in association with these changes include cortical irregularities at the enthesis and damage to the ligaments and capsule at the radio-capitellar joint.^{14,15} Local and central changes in motor and sensory systems may also contribute to the complex of presenting signs and symptoms.¹⁶

Sonographic imaging is well suited to assessment of local tissue structures in tennis elbow. Tendons are easily visualized using sonography because of their high acoustic contrast with surrounding tissue.¹⁷ Their internal structure can be investigated because the endotendinous sheath surrounding collagen fibers reflects ultrasound enabling their arrangement and continuity to be visualized.¹⁸ Areas with abnormally high concentrations of ground substance preferentially absorb ultrasound and so appear hypoechoic, while calcifications and the cortical profile are highly reflective and so appear hyperechoic.¹⁹ These changes may all be observed with grayscale sonography. The use of color Doppler (CD) and power Doppler (PD) sonography can identify and quantify blood flow, enabling investigation of tendon vascularity.^{18,20}

Modalities such as MRI or radiography can identify some of these features and are superior for some applications, such as concurrent assessment of surrounding structures.²¹ However, neither can provide the same level of internal architectural detail as sonographic examination⁷ nor can they match it in terms of cost, portability, patient preference, and capacity for dynamic imaging,^{17,22} all of which may be important considerations in the research process. Once sonographic findings are correlated with histology, they can be used to make inferences about microanatomy and physiologic processes. Whereas histology requires a biopsy, normally provided during surgery, sonography has the advantage of being noninvasive. This means that all presentations of tennis elbow can be assessed, not only those for which surgery is indicated, a small proportion of those presenting with the condition.

On the other hand, sonography has a number of disadvantages. Many of these stem from its dependence on the skill of the operator, the influence of the imaging protocol, and the subjectivity involved in image interpretation. Operator tech-

nique will determine the quality of the acquired image, and 2 operators can produce markedly different images of the same tendon.⁷ Interpretation can also be problematic. A hypoechoic area may represent a tendon tear or a patch of tendinosis, or it could be a product of anisotropy, an artefact caused by oblique reflection of the ultrasound beam.²³ This is a common source of errors in the acquisition of accurate sonograms of tendons.²⁴ If images are saved for subsequent analysis by other investigators, which may be necessary in research, the advantages of "live" interpretation are lost. Because of such factors, less experienced imagers may produce more false positive and negative diagnoses of tendinopathy. Nevertheless even well-experienced readers may differ in their interpretation of the same image.¹⁵ These issues raise questions about the measurement properties of sonography, particularly in clinical trials where it is used to assess changes in the tendon.

MEASUREMENT PROPERTIES OF SONOGRAPHY FOR TENNIS ELBOW

A body of evidence has been accumulated regarding the validity, reliability, and responsiveness of sonographic evaluation with patellar, Achilles, and supraspinatus tendinopathies. Some of this is relevant to assessment of tennis elbow and is cited here, since they share many pathologic features.^{12,25,26} However, they cannot substitute for studies specifically relating to tennis elbow, which are presently scarce.

Validity

Histology is the gold standard for identification of structural changes in the tissue, and correlation of its findings with imaging data is required if sonography is to be used as a valid measure of tendinopathy. Connell et al compared grayscale and Doppler findings in 21 people with tennis elbow with histologic analysis of 8 biopsies taken during surgery.²⁷ Areas with focal hypoechoic and fibrillar disruption on sonography had a typical degenerative visual appearance at surgery. On histology, they demonstrated collagen fiber disorganization and degeneration and fibroblastic proliferation. Tears identified by sonography were also confirmed at surgery. In contrast to later studies, Doppler scans revealed no evidence of hypervascularity and none was reported on histology. Although a scale of sonographic change was used to grade severity, the authors do not

state whether this correlated with surgical or histologic findings.

In a study comparing grayscale sonographic and MRI findings in 11 cases of tennis elbow,²⁸ biopsies taken from a subsample of 4 patients demonstrated a correlation between decreased echogenicity and tendon thickening or "bowing" on sonography, and degenerative changes with angiofibroblastic change on histology. The severity of histologic change was found to correlate with imaging, although the authors do not provide supportive data on this point. This study concluded that MRI was superior in identifying pathologic changes, but the use of static sonographic images for interpretation, and the absence of Doppler imaging, may have influenced this finding. Image interpretation was carried out by two readers masked to clinical findings.

There appear to be no studies correlating Doppler sonography with histology in tennis elbow, or indeed any of the other tendinopathies. The modality has been shown to be a valid measure of vascularity and blood flow in other situations, however. PD is capable of quantitative estimation of blood flow in models of vascular tissue,^{29,30} and in a study of hip joint synovia⁶ it correlated well with vascularity as assessed on a histologic semi-quantitative scale. The paucity of Doppler correlational studies has significance for interpretation of blood flow observed in tendinopathy. Histologic studies of tennis elbow describe neovessels that are nonfunctional and blind-ended or with obliterated lumens.^{8,11} The hyperemia that is observed in Doppler imaging cannot be due to such vessels because no blood flows in them. In some cases it may be due to increased flow in existing blood vessels rather than the formation of new ones.³¹ Until correlation studies have been conducted, attributing sonographic signs of hyperemia to neovascularity is speculative.

The validity of sonography has also been assessed using clinical diagnostic criteria as the reference standard. In grayscale imaging, the presence of hypoechoic areas is a common finding with clinically diagnosed tennis elbow.^{27,32,33} However, this is not pathognomonic of the disorder. Indeed, no individual feature on grayscale or Doppler sonography is always seen in diagnosed cases of the disorder, and asymptomatic elbows may demonstrate sonographic abnormalities.^{32,33} Studies considering the diagnostic validity of grayscale sonography with tennis elbow have demonstrated sensitivities in the range of 36–82% and specificities between 72 and 100%.^{15,28,32,33} The ranges reflect differences between protocols

and raters. Performance can be improved when Doppler evidence of hyperemia is used in combination with grayscale imaging, giving sensitivities of 95–97% and specificities of 88–98%.^{33,34} Thus, sonography has very good diagnostic validity for tennis elbow and can exclude tendinopathy where diagnosis is uncertain. Since other disorders, such as radio-capitellar arthritis and radial neuropathy, may present with similar symptoms to tennis elbow,⁸ the differential diagnostic capability of sonography may be particularly helpful in confirming the presence of tendinopathy in clinical trials.

Although the evidence specifically relating to tennis elbow is limited, these validity studies suggest that grayscale and Doppler sonographic imaging are valid assessment instruments for the identification of the disorder and description of associated tissue changes.

Reliability

Evidence regarding the reliability of sonography in one application cannot necessarily be applied to another. This is because factors such as anatomic site, equipment settings, operator skill, as well as scanning and interpretation procedures, may have a significant impact on the images obtained and the data taken from them.^{35,36} Establishing the reliability of an assessment process can be a complex and resource-intensive task, and this may account for the fact that studies often resort to citing the years of experience of the investigators as the only indicator of reliability.^{33,37–39} While such information may enhance a study's credibility, reliability data are essential to give confidence in any conclusions reached. Nevertheless, a recent systematic review of studies using PD imaging to investigate musculoskeletal disorders found that reliability was addressed in only 17% of them.⁵

Test-retest, intrarater, or interrater reliability investigations may be required, depending on the context of investigation.⁴⁰ There are very few references to these properties in works relating specifically to tennis elbow. Levin and colleagues investigated inter- and intrarater reliability in a sonographic study of tennis elbow¹⁵: one experienced musculoskeletal sonographer assessed 22 patients with symptoms of tennis elbow and 10 asymptomatic volunteers, and a musculoskeletal radiologist stored representative images, which were subsequently interpreted by 3 other radiologists masked to the symptoms of those scanned. Interpretation of the same images was repeated at least 2 weeks later, to investigate intrarater reliability. The presence or absence of features

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such as tendon thickening, hypoechoic regions, and calcification was noted, but no dimensional measurements were made, and vascularity assessment by Doppler imaging was not attempted. Reliability, as measured by the intraclass correlation coefficient, was not high. Interrater reliability was lower than 0.3 for overall impression; the highest individual value was 0.49 for tendon thickening. The mean intrarater reliability was 0.61 across all findings, and as low as 0.31 for identification of hypoechoic regions (confidence intervals were not stated for these coefficients).

In another study, static grayscale images obtained from 11 symptomatic individuals were interpreted independently by 2 assessors twice, a week apart.²⁸ Consistency between sessions in identifying features of tendinopathy was only fair, with kappa values of 0.41 for one assessor and 0.53 for the other. These studies focused on the diagnosis of tendinopathy and did not use or assess severity rating scales. They demonstrate that general musculoskeletal sonographic experience and training does not guarantee interpretation reliability in a specific application. Assessment of live images, or of stored movie clips as opposed to still images, might improve matters, but this remains to be proven.

Studies concerned with other tendons have reported good to very good intra- and interrater reliability levels for identification of hypoechoic areas, and for measurements of tendon thickness.^{41,42} The discrepancy between their findings and those of Levin et al¹⁵ is striking. It may be that reproducible sonographic assessment of the common extensor tendon is more challenging than for some others. In a study investigating the reliability of thickness measurements made on a variety of asymptomatic tendons (but not including the common extensor tendon), very different reliability scores were obtained for different tendons.⁷ Reliability of dimensional measurements was also found to vary with the plane of scanning and whether they are for width, thickness, or cross-sectional area. Therefore proof of measurement reliability in one context should not be extrapolated to others. In this study,⁷ 2 examinations were carried at least a week apart, each done independently by 2 experienced musculoskeletal radiologists. This is one of the few investigations to address reliability by comparing data on the same tendon imaged on separate occasions, which can provide information on the uncertainties of longitudinal change.

Responsiveness

If sonography is used to measure differences in tendon structure within and between individuals and groups, its responsiveness needs to be established. Responsiveness is an indicator of an instrument's ability to detect change over time and may be considered in terms of minimal detectable difference (MDD) and minimal clinically important difference.⁴⁰ For longitudinal studies, the MDD can be calculated from the standard error of the measurement (SEM), obtained from test-retest reliability data.⁴³ The minimal clinically important difference—particularly important in clinical trials to establish whether any measured benefit is worthwhile—requires the sonographic scale to be validated against another, clinically meaningful measure.

Several studies have employed scales that differentiate between different levels of tendinopathy and vascularity in tennis elbow, and Table 1 summarizes these. Investigators have quantified variables individually or by an aggregate score. Various scales have been employed: categorical, using dichotomous or qualitative descriptors; ordinal and interval, with up to 11 possible values; and ratio measures in some cases. Scales with more levels may be able to distinguish smaller changes, and interval and ratio scales allow the application of more statistical operations and provide greater statistical power.⁴⁰ In the studies cited, most scales are based on subjective assessment; only those in the final column involve objective measurement.

None of the scales adopted in these studies appears to have been subjected to a reliability analysis, and their responsiveness to change is therefore unknown. A number of issues therefore arise:

- Test-retest reliability data from a study of asymptomatic tendons⁷ found that 95% confidence intervals in thickness measurements were typically greater than $\pm 20\%$. While the sample did not include common extensor tendons, the findings suggest that reporting thickness changes of less than 10% may not be meaningful.
- Scales that require a subjective choice between 11 possible levels of echogenicity or vascularity are in particular need of reliability assessment before they are used in preference to 2 or 3 point scales.

In fact, none of the scales employed in these studies can be used to draw definitive conclusions until data on their reliability and the minimum

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TABLE 1
Sonographic scales used in tennis elbow studies

→ Increasing number of points available on scale →			
Tendon thickness	<ul style="list-style-type: none"> • >30% difference in maximum compared with unaffected limb³² 	<ul style="list-style-type: none"> • Thickened compared with unaffected limb (1–3)³⁸ • Normal/enlarged/attenuated (>10% difference)²⁷ 	<ul style="list-style-type: none"> • Maximum thickness^{33,54} • Thickness at a defined point^{37,48}
Echogenicity	<ul style="list-style-type: none"> • Hypoechoic area or homogeneous^{33,38} • Hypoechoic, normal, or hyperechoic³² 	<ul style="list-style-type: none"> • Extent of hypoechoic area (<30%/30–70%/>70%)²⁷ • Extent of hypoechoic area (0–10: 0 = normal, 10 = changes throughout tendon)^{37,48} 	
Tears	<ul style="list-style-type: none"> • Presence or absence^{33,38} 		<ul style="list-style-type: none"> • Number^{37,48} • Size^{37,48}
Calcification	<ul style="list-style-type: none"> • Presence or absence^{32,38} 	<ul style="list-style-type: none"> • No obvious change, reduction, complete disappearance⁷³ 	
Bone changes	<ul style="list-style-type: none"> • Spur presence/absence^{33,49} 		
Vascularity	<ul style="list-style-type: none"> • Presence or absence^{49,84} 	<ul style="list-style-type: none"> • Number of vessels (0 = none, 1 = 1 or 2 small, 2 = several)³⁹ • Grade (0 = none, 1 = spotty, 2 = bar or strip shape)⁷³ • Number of visible vessels (0–10: 0 = none, 10 = 10 vessels or more)^{37,48} 	<ul style="list-style-type: none"> • Maximum color fraction (computer analysis)^{31,33}
Type of tendinopathy	<ul style="list-style-type: none"> • Enthesopathy, tendinosis, peritendinosis, bursitis^{1,32} 		
Aggregate measures	<ul style="list-style-type: none"> • Presence or absence of structural abnormalities^{32,39,49} 	<ul style="list-style-type: none"> • Normalized, improvement, no change²⁸ 	

change they can detect is available. Studies involving other tendons have used similar scales as outcome measures.^{44,45} Some have been subject to reliability analysis^{41,46} with encouraging results, but they cannot be used as proxies for studies relating specifically to tennis elbow. Figure 1 illustrates some of the difficulties in using measurement scales to rate and detect change in pathological features: indistinct tissue boundaries impede accurate thickness measurement and apparent changes in echogenicity can result from different positioning of the transducer.

The capacity of sonography to show clinically meaningful change in tennis elbow has been assessed by comparing sonographic and clinical findings in longitudinal studies. Sonographic changes over time may be readily apparent, and these may coincide with changes in clinical measures such as pain and function. In clinical trials, normalization of tendon thickness, echogenicity, and vascularity usually coincide with clinical improvement.^{31,37,38,47,48} Demonstrating correlations is problematic when MDD values are not known, but a recent trial using dichotomous scales for grayscale and CD imaging concluded that decreased blood flow was “related” to improvements in grip strength and pain scores 2

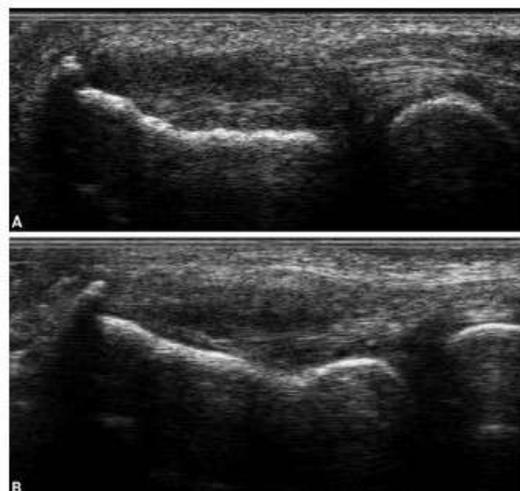


FIGURE 1. Longitudinal sonograms (A, B) of the same common extensor tendon, taken 1 week apart by same investigator and with identical settings. Cortical spurring, loss of fibrillar structure, and hypoechoic areas are seen in both images. Poor boundary definition and differences in cortical contour makes reliable tendon thickness measurements difficult, and hypoechoic areas appear different in extent.

years after treatment by intratendinous injection, but that grayscale changes were not.⁴⁹ Another group used CD imaging with computer-

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assisted quantification of vascularity and found parallel decreases in vascularity and pain over 2 weeks following treatment.³¹ No correlation test data were provided by either of these studies, however. In any case, the association between sonographic and clinical changes is only partial. Symptoms may resolve while tendons remain thickened, hypoechoic, and hypervascular,^{37,49} and normalization of sonographic appearance does not guarantee improvement in symptoms.³⁹ This is not surprising since tennis elbow involves features such as motor and sensory changes that are not apparent on sonography, and treatments that affect one aspect of the disorder may not influence another. Where differences in one scale do not correlate with those of another, this can give valuable information about different elements in the pathophysiological process.

Hence, responsiveness may more appropriately be gauged by correlation with histology rather than with clinical features. Existing correlational studies for tennis elbow tendinopathy have only considered dichotomous sonographic scales, and potentially more useful multipoint scales have yet to be validated in this way. Cross-sectional studies using biopsies obtained at surgery could at least test the capacity of sonographic scales to differentiate between different degrees of pathology. Longitudinal studies using animal models of tendinopathy may provide supplementary evidence.⁶⁰

There may be the potential to improve the responsiveness of some elements of sonographic assessment in tennis elbow. PD can detect much lower blood flow rates than CD, and its sensitivity is less affected by changes in probe angulation.²⁹ Even more sensitive modalities are available: laser Doppler flowmetry and contrast medium enhanced grayscale imaging have identified blood flow in normal Achilles and supraspinatus tendons,^{51,52} which would not be detectable by CD or PD.⁷ As sensitivity of Doppler equipment increases, the level of vascularity rather than its mere presence may be the more appropriate measure of tendinopathy.

Additional gray-scale techniques could also be adopted to enhance the measurement properties of sonography. A computer-based method of tissue border recognition has been used to overcome the subjectivity in visual identification of boundaries between the Achilles tendon and adjacent tissue, so improving the reliability of dimensional measurements.⁵³ The advent of imaging systems with frequencies in excess of 20 MHz provides the prospect of more detailed imaging of superficial tendons and hence

greater sensitivity to changes in tissue structures.⁵⁴ Higher frequency probes have been associated with improved reliability in musculoskeletal sonography.⁵⁵ Computerized grading of echotexture and fiber alignment, used in assessing equine tendinopathy,⁵⁶ might enable more objective assessment in human subjects. Recent work has suggested that sonography may also be used to distinguish different stages in the development of tendinopathy, which might have useful diagnostic and therapeutic implications. Calcification in the supraspinatus tendon has been classified morphologically into 4 formative and resorptive phases that may be identified by sonography, enabling the staging of calcification to be described.⁵⁷ Temporal changes in tendon thickness, echogenicity, and vascularity have been incorporated into a proposed progressive scale for patellar tendinopathy.⁵⁸ The applicability of these concepts to tennis elbow has yet to be explored.

SONOGRAPHIC ASSESSMENT PROTOCOLS

Since variations in practice can contribute to significant differences in data gathered and conclusions drawn, some degree of standardization is desirable. Efforts have been made to produce agreed standards and protocols for musculoskeletal sonographic evaluation,⁵⁹⁻⁶¹ but these focus on probe and limb positioning and do not address many of the other factors that can affect measurements. Reporting of protocols used in studies also varies substantially, leading to uncertainty about the techniques used. In this section, some of the issues that may affect the quality and reliability of sonography—and which should therefore be attended to in the planning and reporting of studies—are addressed.

Patient and probe positioning. Some investigators assess the elbow in extension with forearm neutral,^{17,62} while others have the elbow flexed to 90° and the forearm pronated.^{27,33} Sometimes the position is not stated at all. A panel of experts has suggested several standard assessment positions but elbow extension is not preferred over flexion.⁵⁹ Since stretching the tendon may compress blood vessels, a flexed elbow and neutral forearm may be preferable.⁶³ Certainly, adopting and reporting a standard position will give some reassurance of consistency. Increasing probe pressure has been found to reduce both blood flow and tendon thickness in pathologic common extensor tendons.⁶⁴ While it would be technically challenging to stand-

ardize probe pressure, a light and consistent approach using copious couplant gel may improve reliability.

Equipment settings. Sensitivity is influenced by settings such as gain, probe frequency, filtering, and pulse repetition rate.⁶⁵ Some tendinopathy studies have used identical values for all subjects to provide consistency,^{46,66} but this does not take into account body habitus, which may affect image quality and intensity. It may be preferable to optimize settings for each individual at baseline and replicate them at subsequent assessments. CD continues to be used for vascular imaging in recent tennis elbow studies,^{37,64,67} but PD's greater sensitivity suggests it may be preferable. As well as being less angle dependent, PD suffers less than CD from noise and aliasing (a sampling artifact that can result in vessels appearing discontinuous), although it can be more susceptible to flash artifact.⁶⁸

Exercise. Studies with Achilles and patellar tendons have shown that measured tendon blood flow can increase significantly with activity.^{69,70} Opposing conclusions have been drawn from these findings: that a standard warm-up period should be used to maximize measured vascularity,⁶⁹ or that 24 hours abstinence from intensive activity should be imposed.⁷⁰ In any case, prudence suggests that pre-assessment upper limb activity levels should be either controlled or recorded as a potential confounding factor.

Measurement reliability. Methods of measuring tendon dimensions vary considerably between tennis elbow studies: by maximum antero-posterior diameter, by thickness at a defined anatomic point, or by subjective comparison of overall thickness with the contralateral limb. The relative merits of each approach have yet to be explored, although, since activity may increase tendon thickness,⁷¹ bilateral comparisons as an indicator of pathology may not be valid. Taking a series of measurements along the length of a tendon—although rarely used—might provide useful information.⁵³ In any case, reliability could be increased by taking an average of several readings.

Where reliability studies are conducted, test-retest data from 2 assessments of the same tendon taken at different times will help establish the normal variability in measurements and hence the responsiveness of any scale used. A gap of about a week would minimize the potential for changes in tendon structure and for memory bias

by assessors.⁷ Where protocols include assessment of recorded images, it is not yet clear whether stills or movie clips are superior. A combination of the two may be best, with images of the contralateral limb available for comparisons of echogenicity.

CONCLUSION

The increased use of sonography as an assessment tool in tennis elbow studies indicates the growing recognition of its potential for both diagnosis and outcome measurement. While it cannot measure all facets of the disorder, it can provide valuable information about associated tissue changes. It may be particularly helpful in studies of the disorder's natural history, analogous to its use in arthritis monitoring.⁷² Correlational studies have confirmed the validity of sonography for identification of the degenerative changes that occur in tennis elbow. However, there is a dearth of relevant reliability and responsiveness studies, and questions remain about the scales of sonographic change adopted in studies. Variable standards in reporting sonographic assessment protocols—which can substantially affect the data collected—are also problematic. Until these deficiencies are addressed, the full potential of sonography's capability for assessing and following tennis elbow will remain elusive.

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