THE ACHILLES TENDON:

AN EVALUATION OF THE HEALING PROCESSES OCCURRING WITH CHRONIC PATHOLOGY

Using a Prospective Comparison study of Conservative Treatment Regimes & Micro-Current Application

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Submitted in Fulfilment of the Degree of Doctor of Philosophy

City University

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Submitted May 1998

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ACKNOWLEDGEMENTS

The author would like to thank the following people for their assistance with this study:

All the subjects who agreed to become involved in the study and saw it through to a conclusion.

Special thanks are paid to Dr D.Cooper, Professor E. Carson and in particular Professor D. Hill without whose guidance and immeasurable support this study would not have been possible.

Dr G. Papas, Consultant Radiologist and Head of Ultrasound, Dr C.Thomas, Consultant Radiologist and all the staff at Chase Farm Hospital NHS Trust.

Key Med for their loan of the ultrasound transducer.

Most of all I would like to thank my wife Catherine, for her enthusiasm, support and love and for tolerating my four year and continuing obsession with tendons. Finally I would like to dedicate this study to my two sons Elliot and Joseph.

Declaration

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ABSTRACT

Muscles enable the skeleton to move. Muscles are attached to bones via tendons. Inappropriate stress placed upon the muscular-skeletal system, for example sporting activities for which the subject is untrained, can result in injuries which may occur either in the muscle, muscle-tendinous junction or the tendon tissue itself. The resultant pathology can often result in loss of strength or pain in the area. The healing processes of tendon tissue are not well understood and the difficulty in the clinical management of pathology reflects this. Current treatment of this type of injury is dependent upon the severity of the injury, its site of occurrence and the practitioners preference of treatment modality.

The purpose of the study was to evaluate, following the application of micro-current for therapeutic purposes, the functional outcome In patients presenting with chronic pathology in the Achilles tendon in comparison with the current conservative management. A prospective comparison study was undertaken utilising a blocked randomisation method. Subjects were allocated to either group A and were exposed to current clinical management or group B the experimental micro-current regime. Classification and subsequent evaluation of pathology was assessed employing clinical assessment and tests; subjective assessment by the subject and assessment by diagnostic ultrasound. Subjects were assessed at three, six and twelve month intervals post entry into the study.

Forty eight subjects, twenty four in each group completed the study. A statistical analysis was performed, calculating the differences between the two groups and between each interval assessment. Categorical variables were compared between the two groups using the Chi-squared test. The Mann-Whitney test was performed to assess changes in ordinal variables. The Spearman rank correlation test was used to test for correlation between age and changes in the variables.

Statistically significant differences were found in favour of group B, the experimental group, in four out of the five clinical markers used. No difference was found between age or sex and the changes recorded.

It was concluded that the appropriate application of micro-current treatment to the Achilles tendon presenting with chronic pathology can make a significant contribution to the clinical management of the condition. This has the implication that a degenerative cycle promotes chronic pathology occurring in the Achilles tendon.

In order to narrow the gap between the clinical and experimental findings an examination of *in-vitro* applications was undertaken with laboratory work undertaken evaluating the effect of micro-current stimulation on 3T3 mouse and human tendon fibroblast proliferation. The results showed that the cells stimulated with 40μA proliferated at a greater rate than the non-stimulated control group. Stimulating the cells with 1μA suppressed activity with a suppression in proliferation..

PUBLICATIONS TO DATE FROM THIS THESIS

DIAGNOSTIC ULTRASOUND: THE APPEARANCE OF THE ACHILLES TENDON FOLLOWING SURGERY - Paper

Radiography (1996) **2**, 27-41

THE MANAGEMENT OF CHRONIC ACHILLES TENDON PATHOLOGY - A NEW APPROACH - Presentation

The Royal College of Surgeons of England in conjunction with

British Orthopaedic Sports Trauma Association

The Management of Sports Injuries: 25th - 26th April 1996

CHRONIC ACHILLES TENDON PATHOLOGY -

Round table discussion for educational tape

Smith & Nephew in Association with British Orthopaedic Association

Current Issues in Orthopaedics: 26th April 1996

CHRONIC PATELLA TENDON PATHOLOGY -

Round table discussion for educational tape

Smith & Nephew in Association with British Orthopaedic Association

Current Issues in Orthopaedics: 26th April 1996

ACHILLES TENDINOPATHY - Invited guest speaker

Royal College of Surgeons in conjunction with *BOSTA:*

The Management of Sports Injuries: April 7 1998

CHAPTER ONE

Introduction

1. Background to the study

Science and scientists have yet to reach agreement upon the aetiology of chronic tendon pathology. The pathophysiology of the tendon with chronic pathology and the healing processes involved are debated in the literature, particularly with reference to the Achilles tendon, for example, Blackman et al (1990), Galloway et al (1992), Clement et al (1984), Clancy (1990), Kvist et al (1988). Conservative management regimes have proved to be unreliable, with inconsistent results and a generally low level of success.

The use of electricity, electrical stimulation, and electromagnetic fields is not new in medicine. It is also well documented that electrical potentials are present in soft tissues and this has led to studies investigating changes in the biology of these tissues by externally imposing an electrical field or electrical current. There is experimental evidence to suggest that tendon repair can be affected by electrical stimulation of intensities at a micro-current level, for example Nessler & Mass (1985), Stanish (1984), Spielholz (1986).

To date few studies have attempted to look further than the effect of external electrical stimulation upon cell replication. The biological mechanism that results in an alteration in cell behaviour has not been addressed with the same vigour.

(In the text 'he' will be used when referring to the non-personal he, she or they)

In addition, despite many studies that have reported the augmentation of the healing processes in connective tissue, following micro current stimulation there have been no clinical studies which have demonstrated the efficacy of the technique for the treatment of tendon pathology in human subjects using a non-invasive, skin surface application.

To date animal models and *in-vitro* cell cultures, have been used to demonstrate the effectiveness of micro-current electrical stimulation.

It was against this background that the author undertook a series of experiments that aimed to:

examine the modification in cell behaviour induced by micro-current stimulation and, taking into account the difficulty in successfully treating the Achilles tendon with chronic pathology, the clinical potential of micro-current stimulation to augment the healing processes in the tendon tissue matrix.

This study was based upon the following general hypothesis:

Low amperage micro-current electrical stimulation will initiate an alteration in cell (fibroblast) behaviour and induce a modification in the healing processes involved in the Achilles tendon with chronic pathology.

The hypothesis was tested by a series of *in-vitro* experiments upon fibroblast cell cultures and an *in-vivo* study involving a clinical trial employing a prospective, randomised, blind comparison method. The efficacy of the experimental treatment *in-vivo* was to be evaluated against the present conservative management of the condition.

In order to start building a picture of the mechanism underlying the findings the study will address the following objectives:

With reference to the in-vitro studies:

1. Are rates of cell replication modified by the application of low amperage micro-current stimulation in comparison with a control group?

2. Do human cell lines behave in a same manner as those derived from animal specimens (this is particularly pertinent as many of the previous experiments reporting the augmentation of healing processes using micro-current have used animal models)?

3. Is there an apparent biological mechanism that suggests why the micro-current application induces an change in the rate and manner of cell replication and can this be related to the *in-vivo* study?

With reference to the in-vivo study:

4. Do patients exposed to the experimental micro-current treatment return to a normal functional outcome more quickly than those patients undergoing current conservative methods?

5. Is chronic pathology occurring in the Achilles tendon homogenous in its nature?

6. Is the experimental micro-current treatment more suited to a particular pathology?

7. Are present conservative treatment regimes applicable to the pathologies occurring in the Achilles tendon?

1.1. Design of the clinical studies

In order to advance the understanding concerning the processes involved in the modification of cell behaviour induced by the application of micro-current it was necessary to test the study hypothesis by dividing the study in to two parts, one involving the *in-vitro* cell cultures and the other the *in-vivo* clinical study. The results from each part could then be correlated with one another and a conclusion arrived at that may shed some light upon the "how and the why".

The *in-vitro* experiments involved two separate cell lines, 3T3 mouse fibroblast and fibroblasts harvested from cadaveric Achilles tendon. This enabled a comparison to be made between any modifications in behaviour noticed in an animal and a human cell based culture.

The *in-vivo* clinical study was slightly more complex for the following reasons. It was initially planned to carry out a comparison study examining the functional outcomes of two groups (group A control, group B experimental) of subjects presenting with similar clinical conditions. A block randomisation method was considered most appropriate in order to ensure that each group contained an equal number of subjects at the conclusion of the study.

In order to eliminate the placebo effect a blind method was planned. The device delivering the micro-current was arranged to make the same audible sound regardless of whether or not it was delivering the current. Therefore the subjects and the referring consultant would be unaware of whether the subject was receiving the new treatment or not. Only the person allocated to deliver the treatment would be aware of the treatment regime to which a given subject had been exposed.

The two groups would be managed in a similar clinical fashion. The control group, A, would continue their originally prescribed treatment and receive the placebo application. Group B, the experimental group, would continue their treatment and in addition have the new treatment. A comparison could then be drawn between the outcomes of the two groups. Protocols were drawn up for this methodology.

However, reports in the literature relating to the myriad of conservative methods, and the apparent non-discriminate selection of treatments utilised by different physicians and physiotherapists revealed the extent of the lack of consensus of opinion concerning the most effective, or least ineffective method, for the treatment of chronic Achilles tendon disorders. There appeared to be no empirical evidence to suggest that one treatment method should be used in preference to another. No evidence could be found of clinical trials that had been carried out to measure the effectiveness of the different methods. All the evidence to support the various treatments appeared to be purely anecdotal and, hence, there was no suitable basis for a clinical trial examining a new treatment regime.

To further complicate matters various authors, for example Williams (1986), claimed that some treatment methods employed by physicians and physiotherapists were not only ineffective but actually detrimental to the Achilles tendon presenting with pathology. For example, deep friction massage was believed to cause further aggravation to traumatised or immature tendon tissue. In addition he reported that from a group of one hundred subjects who had cortisone injected into the tendon, thirty percent later presented with a full rupture. For other treatment methods such as ultrasound and laser, there have been anecdotal claims of success, but only short term relief has been reported, Williams (1986).

It was evident therefore that the planned research methodology would have to be revised. If present treatment regimes do have a detrimental effect on the progress of the tendon then permitting subjects to receive the old treatment in addition to the new may not allow the new treatment regime to be judged on its own merits. For example, if a subject has a cortisone injection as part of his management and subsequently goes on to rupture the tendon, apportioning the reason for this complication would be impossible. The only suitable method to adopt would be to separate the two groups. Group A would undergo only the present conservative management and Group B would only undergo micro-current therapy. One treatment method could not then interfere with the progress of another.

Therfore, unfortunately, a placebo effect from the new and novel micro-current treatment could not be totally eliminated. However, this limited by the markers used to assess the staging of a given pathology. The progress of the subjects' tendons was monitored using essentially objective, measurable tests, so whilst the feeling of improvement, or not, was recorded, it was not the main unit of measurement.

1.2. The revised study design

The experimental hypothesis was tested employing a comparison, prospective, control, study utilising two groups, A and B, with blocked randomisation. Group A, the control group, would continue their prescribed treatment. Group B, the new treatment group, would only receive the new treatment regime. Functional outcomes would then be measured in the same way for both groups.

1.3. Suitable pathologies

In order to ensure that the study was comparing like with like it was important that both study groups contained subjects with similar pathological conditions. Obtaining an accurate clinical diagnosis for the Achilles tendon presenting with pathology is often difficult due to the inexact nature of the symptoms reported by the patient. The chronic tendonosis is often a cumulative condition, a result of multiple micro-traumas, which in isolation may be non-symptomatic. It may manifest itself it different ways. Pain and early morning stiffness are common early symptoms.

Patients will often not seek medical attention at this stage, or if they do, are prescribed an anti-inflammatory drug, for example Ibuprofen, by their general practitioner. If a referral is made to an orthopaedic consultant then generally conservative physiotherapy such as deep friction massage, ultrasound or laser will be used. If the problem continues then surgery may be considered to remove the damaged tissue.

For this study, subjects presenting with any pathology were given an initial consultation to clarify the pathology. Further explanation of this procedure is provided in the patient protocols, Chapter Three. Such is the chronic nature of many of the pathologies, that the majority of subjects have already undergone conservative methods of treatment which have been unsuccessful when they were referred for possible participation in the study. This had two implications.

Firstly, the consultation undertaken for the study occurred regardless of any previous consultations the subject may have had. Therefore, if a previous treatment regime had a detrimental effect on the tendon, then this was only recorded in respect of the current state of the tendon of the subject entering the study. It was also important that other treatment regimes did not interfere with the study. If a subject was to be included in the study he ceased whatever treatment he had received before the randomisation process occurs. In practice, patients were referred to the study when other treatments had been non-productive and they had ceased persevering with them. In conclusion, patients could enter the study with a past history of other treatments but not if they were presently undergoing them and, for reasons explained earlier in the text, subjects who have undergone a cortisone injection within the last six months were excluded from the study.

Secondly, it could be argued that the subjects included in the study had such chronic conditions that the new treatment regime was disadvantaged for it was not given the opportunity to be used by fresh patients.

This was true, but if the new treatment is to be productive in the environment where Achilles tendon injuries are common, in an active population, then it has to prove its worth in the most chronic of cases. Currently, the option for failed conservative treatment is surgery, which, in itself, is not always successful. Therefore, if the treatment regime could alleviate the need for surgical intervention then this would represent a step forward.

In summary, subjects who have undergone previous treatments were eligible for the study, assuming they had their management modified to the particular treatment group to suit which they were allocated.

It was clear, therefore, that if the new treatment regime yields successful results then it will have done so in the toughest of environments. To balance this, the subjects not allocated to the new treatment group and therefore continuing their current conservative regime would still provide a satisfactory comparison concerning the performance of the two treatment groups. The critical element of the study was therefore maintained.

A full explanation of criteria for subject inclusion is given in chapter three.

1.4. Randomisation

A blocked randomisation method was employed to ensure they there were equal numbers in each group, the control and the experimental group, at the conclusion of the study. Randomisation was undertaken by someone unconnected with the study. Details of subjects with a suitable pathology were forwarded to this person. The subject was then randomly allocated to a treatment group A or B. Details of the group allocation were forwarded to the research investigator who then contacted the subject.

Prior to randomisation, subjects were given a full explanation of the study and asked to sign to give their consent to inclusion in the study.

1.5. Clinical tests

In order to test the study hypothesis the functional outcome of the subjects following their prescribed treatment regime was evaluated using diagnostic ultrasound, isometric strength tests, dorsi and plantar flexion tests. In addition a more subjective measure was employed, which was not, perhaps, as comparable as the objective tests but nevertheless gave a good indication of the tendon(s) from a personal perspective. The clinical tests, subjective assessment and the ultrasound examination were carried out at three, six and twelve months post-inclusion into the study.

Achilles tendon trauma was not uncommon among athletes ranging from jogger to international standard. They commonly presented having been unable to train, either at all, or at the desired intensity due to the tendon "breaking down" with symptoms of pain, stiffness and lack of mobility. Subjective assessment was a valuable way of assessing the condition as they were stressing their tendon more than a sedentary subject and often on a daily basis. The subjects were encouraged to keep a record of their progress. They noted their level of pain and stiffness. In addition, if clinically appropriate, the subjects were given stretching exercises. They were requested to note to what level those could be performed. Prior to the commencement of the study a thorough preparation in ultrasound scanning and noting of the pathological appearance of the Achilles tendon was undertaken. This was achieved by reviewing the available relevant literature, scanning 'normal' volunteers and detailed examinations of tendons in cadavers.

1.6. Conclusion to the introduction

It could be argued that evidence based medicine will produce the most reliable results. However, obtaining the answers to some of the questions is often a long and arduous task particularly with regard to the modification of cell behaviour by external influences. The research methodology employed for this study which attempts to address the aims and the objectives was arrived at following a careful review of current practice and the literature available.

Consideration of all the influencing factors, some beyond control in the context of this study, resulted in a series of *in-vitro* and *in-vivo* experiments which, whilst not without flaws, aimed to produce a significant indication of the effect upon cell behaviour and relate this to the clinical potential of such a treatment regime and its medical use in the management of Achilles tendon pathology.

CHAPTER TWO

Literature Review

2. Introduction

In order to examine the mechanisms underlying the changes in cell behaviour induced by the application of micro-current stimulation it is relevant to examine the fundamental elements of human physiology and bio-chemistry relevant to tendon tissue. From this point it will enable the assessment of how a modification in behaviour may be related to the expected normal biological processes.

Hooke (1689), referenced in Nave & Nave (1985), observed through a crude microscope small empty chambers in the structure of cork. He named them cells, because they reminded him of the bare empty rooms of a monastery. Using sophisticated equipment more than a century later, biologists found that cells were not empty but filled with a viscous fluid that also contained chemical material that allowed them to live, grow and re-produce. They called this substance protoplasm, meaning the substance of life.

The German Biologists Schleiden and Schwann, proposed a cell theory in 1938, (Nave & Nave, 1985). They hypothesised that all living things are composed of cells. Virchow (1971) extended this theory with the idea that cells must arise from pre-existing cells.

The cell, the basic unit of any organism, exhibits all the characteristics of life, the ability to obtain food from its surrounding environment in order to sustain its metabolic processes.

There are two types of cell; I) prokaryotic type which is a simple cell having a rigid cell wall. It does not contain a nucleus and so does not have the ability to reproduce and II) Eucaryotic cells which make up most of the human body and which contain a nucleus enclosed within a nucleic membrane. They do not have a cell membrane in the same sense as the prokaryote, but they do have an extracellular matrix made up of many different carbohydrates and proteins.

The membranes compartmentalise and segregate cellular events, separate cells from one another and segregate organ functions. They mediate the regulation of cellular function by acting as selective barriers. Membranes localize specific enzyme systems and provide a semi-solid state in an otherwise aqueous solution.

Membranes are made up of proteins, lipids and carbohydrates which are attached in widely varying ratios depending upon cell function. Singer and Nicholson (1972) proposed the fluid-mosaic model describing the nature of the membrane structure. Diagrammatically they showed how proteins can move about in a phospholipid bilayer. The fluidity of the membrane depends upon the nature of the packing and interaction of the fatty acyl chains in membrane phospholipids.

External influence may also have an effect, for example an increase in temperature will increase fluidity as some of the trans c-c bonds rotate. It is stated that in more highly developed animals, cholesterol reduces membrane fluidity by preventing the movement of fatty acyl chains.

It would be inappropriate to chronicle all intracellular structures but an important one to mention is the eukaryotic cytoskeleton which provide strength and structure to the cells, controls intracellular movement and provides the fundamental mechanistic components needed for extracelluar movement. There are three types of fibres associated with the cytoskeleton, microfilaments, intermediate filaments and micro tubules.

The microfilaments are made of actin, the most abundant cellular protein, and associate with more than fifty proteins that allow them to perform their unique functions. The most common is myosin which is present in both muscle and non-muscle cells, and in association with actin and adenosine tri-phosphate, can produce a contractile force.

Intermediate filaments are made up of a diverse group of proteins all of which are long, rod-like molecules. There are five classes of intermediate filaments as stated by Davidson and Sittman (1994). The first, Vitentin, of particular pertinence to this study is found in fibroblasts, the cells that are present in the endotenon of the tendon. They produce collagen, the primary constituent of tendon tissue and they should proliferate in number at times of acute micro-trauma. Desmin is found in muscle cells.

Neuro-filaments and Glial fibrillar protein are found in nerve tissue and Cytokeratins are a diverse group made up of over thirty sub-types and are found in different types of epithelial tissue.

The primary function of intermediate filaments, as might be expected, is structural; playing a role in cell to cell attachment and in maintaining the contractile strength in muscle cells. Microtubules are the largest elements of the cytoskeleton and they are involved in extracellular and intracellular activity. Darnell, Lodish and Baltimore (1990) described how the micro tubules are made up of αß-tubulin dimers that polymerize in a head-to-tail array of thirteen proto-filaments. They state that the two ends of tubulin can be identified as a plus and a minus end. Although the dimers can assemble and disassemble at both ends it is reported that they do so at a faster rate at the plus end. Whether the disassembling can by manipulated by the external application of an electrical stimulus is not discussed but further literature in the text will explore this.

2.1. An Introduction to collagen

Collagen is a protein present throughout most of the animal kingdom and can be thought of as the scaffolding in mammalian tissue. Collagen itself is a glycoprotein and is unique among glycoproteins in that it contains no amino sugars and only two carbohydrate residues, glucose and galactose. Weiss and Jayson (1982) summarised that because of its structural function collagen is peculiarly resistant to attack by proteinases and other enzymes.

Only two, collagenase and bacterial collagenase, appear to have the ability to interfere with the unique triple helix configuration of the molecule. The bacterial collagenase has virtually no effect on other proteins, so it is useful in attempting to establish the collagenous nature of an isolated protein. Work in this area has been undertaken by Risteli et al. (1980) and Furuto & Miller (1981).

Early work on the chemistry of collagen was confined mainly to the glue and leather industry (Eastoe 1967). It was accepted that collagen, particularly tendon tissue swelled when immersed in acid solution. Zaccharides (1900), and later Nageotte (1927), who were the first to isolate rat tail collagen using cold dilute acetic acid, were early pioneers of the work. Nageotte was fortunate, for rat tail collagen is described as being peculiarly soluble in acetic acid where as human tendon is much more resistant. Important work was carried out in the 1930's and 1940's by Schmitt et al. (1942); Whycoff & Corey (1936) and Bear (1942), who extended the studies of Nageotte and demonstrated that when the solubilised collagen was dialysed against tap water or a salt solution, it precipitated as fibres indistinguishable from those seen in the original tendon by light microscopy.

Collagen's ability to reconstitute itself was the first evidence that it has the ability to assemble in fibrils in vitro. This work enabled the conclusion to be drawn in later work by Boedtker & Doty (1956) that native collagen in solution were composed of molecules containing three α-chains arranged in the triple helix configuration and behaving as rigid rods.

2.1.1. Collagen types

Six different types of collagen have been identified which exist either singularly or together in different proportions in the various connective tissues. Church et al.(1973), found that fibroblasts in culture have been shown to be capable of synthesising two different collagen types. Penttinen et al.(1980) believed that the ability of fibroblasts to synthesise these different types of collagen in rigidly controlled proportions indicates that the coding genes are simultaneously controlled, although the exact mechanism is unclear. Weiss and Jayson (1982) state that early work was performed on interstitial collagen, Type I, originating from tendon tissue, and therefore it was originally thought to be a single genetic species. However, later work on skin and cartilage by Miller and Matukas (1969) and by Miller et al.(1971), revealed the presence of additional α chains: to be known as Type II and III collagen. Tendon tissue contains predominantly Type I.

2.1.2. Chemical characteristics of collagen types

Old human tissue is difficult to solubilise, so much of the work has been carried out using young animals. Epstein (1974) explained how a limited pepsin digest is used to solubilise the collagen fibres. The product of the digestion can then be separated using a variety of methods; for example ion exchange chromatography (Bentz et al. 1978; Kresina & Miller 1979), or salt precipitation at acid pH (Rhodes & Miller 1978; Sage and Bornstein 1979) or at neutral pH (Epstein 1974).

Collagen is initially secreted into the extracellular matrix in the form of procollagen. It is exported from the cell in the form of a non-fibrillar, but structured, aggregate, (Trelstad & Hayashi 1979). In this current study it is believed that this is a significant factor and its relevance will be highlighted when discussing the pathological stages in the traumatised or chronic tendon. Byers et al.(1974) and Timpl et al.(1975), commented that a neutral salts solutions of collagen extracted from young tissue which represents newly synthesised protein, often contain some unprocessed procollagen α chains.

2.2. Macro and microscopic appearance of the tendon

The study is based upon the chronic pathology occurring in the Achilles tendon often following repeated bouts of micro trauma. It is useful to highlight the *in-vivo* and *in-vitro* work that has been carried out to date for it will clarify how these studies have influenced this present investigation.

In the adult tendon the tensile strength is derived from the fascia of the collagenous fibrils which outweigh the cells and other connective tissue components by a factor of more than four to one, (Davidson and Sittman 1994). It would appear that because of the simplicity of the structure, composition and function of the collagenous matrix, the tendon should afford the easiest correlations between molecular structure and physiological function. However, this does not appear to be the case.

Davidson and Sittman (1994) stated that there remains unanswered questions ranging from the supramolecular organisation to the disposition of the intermolecular cross-linking upon which the strength of the tendon depends. Few experiments have been reported that define the turnover of tendon collagen, and, although the fibrils within a tendon show a range of diameter that changes with age and disease, little is known about the molecular aspects of fibril growth or replacement following trauma or wounding. This is confirmed and will be elucidated further when examining the relevant studies on the pathological sequences affecting the tendon.

2.2.1 Basic anatomy

Elliot (1965) reviewed tendon anatomy describing the bundles of fine filaments in which sparse cells are embedded, all within a sheath of connective tissue. The connective sheath, the paratenon, contains the bundles of fibres wrapped in cylinders of a continuous, loose connective tissue (the endotenon), in which run fine vessels and nerves to the inner mass of the tendon. Columns of flattened cells, fibroblasts, lie in the endotenon and, in part, in the sheath. Microscopically these appear star-like as they send long lamellipodia through the fascia of the fibrils. In adults, the tendon has a sparse capillary blood supply which reflects the large content of the non-metabolizing extracellular tissue. To eliminate friction some tendons are contained within a collagenous sheath. The Achilles tendon is not so contained.

2.2.2. Growth, turnover and repair

As collagenous tissue matures the percentage of water is reduced and it develops acid resistant cross-links. Parry et al.(1978) reported that under repeated stress a tendon will hypertrophy. As these changes occur there is a general increase in the diameter of the fibrils, although in some tendons a bimodal or trimodal distribution of fibril diameter occurs.

It is hypothesised that the increase in size can be attributed to the accretion of collagen to each fibril by the progressive addition of individual molecules or filaments secreted by the fibroblasts. Trelstad & Hayashi (1979) suggested that the collagen fibrils are virtually spun from secreting fibroblasts, like silk from a spider.

The fine filaments are known as collagen fibrils. In the bundles they are arranged to generate a coherent, wavy pattern so that the packed mass of them in the fibre, under zero stress, appears iridescent. Kastelic et al (1978) reported that this crimping, and the iridescence, disappears reversibly with minor stretching of the fibrillar bundle. This is an important point to consider when imaging of the tendon is undertaken (Chapman-Jones 1996).

The mechanisms of fibril growth are not fully understood and the processes involved in tissue repair are equally cloudy. Macro or micro fibrillar rupture of the tendon tissue matrix is a common injury, particularly in sport and such injuries have been categorised as overuse injuries by many authors, for example Hunter & Poole (1987). Healing is thought to follow an embryonic pattern with cell infiltration and the laying down of first, fine, poorly orientated fibrils. Peacock & van Winkle (1976), summarised that the fibroblasts are not resident but activated from the superficial connective tissue of the tendon; thus a torn tendon within a sheath does not completely heal. Through the area they invade these cells secrete newer, finer fibrils which later increase in diameter and orientate themselves as the cell population decreases and there is a restoration of the original structure (Greenlee & Pike 1971).

Peacock (1967), although dated, wrote a relevant review article on collagen formation and structure. Peacock describes the different collagen formations for different types of wound healing. Fyfe & Stanish (1992) reviewed the three phases of tendon healing as described by Enwemeka (1989); Peacock (1965); Salamon & Hamori (1966) and Steiner (1982). They are:

1. Cellular reaction to injury:

The inflammation period lasts five to seven days (Enwemeka 1989). An important point to highlight is that the tendon is unable to synthesise collagen, however, other cells from the epitenon or extracellular matrix develop from pluripotential cells into fibroblasts (Salamon & Hamori 1966; Steiner 1982).

Collagen is produced from well developed large stellate fibroblasts that have matured with time. As the collagen matures, the fibroblasts decrease in size and number; are called fibrocytes, and become polarised parallel to the tendon.

By the fifth day post-injury, in the area of tendon injury, there are patches of fibrin, blood clots, exuded plasma and white blood cells. By the seventh day, the collagen fibrils are in a state of disarray in the extra cellular compartment. There are numerous fibroblasts with increased rough endoplasmic reticulum, vesicles and granules. There is increased ground substance and occasionally well organised patches of fibrils.

2. Fibrous protein and collagen synthesis:

During this period there is an increasing vascularity and a relative paucity of inflammatory cells (monocytes, lymphocytes and mast cells) by day twelve. The fibroblasts increase in number and shape, manifesting an abundance of Golgi complexes, free ribosomes and rough endoplasmic reticulum.

By day twenty one post-injury the fibrils of immature collagen coalesce into bundles.

3. Scar and remodelling phase:

This process is continuing throughout life. Peacock (1967) states this process to be most pronounced at seventeen to twenty eight days, as evidenced by the increased extractable saline from collagen. It was therefore believed to be weaker than normal collagen. From day fourteen to forty two post-injury, collagen synthesis equals collagen degradation, therefore the total amount of collagen was stable.

Fyfe and Stanish (1992) reported that longitudinal tension helps to increase the extractable saline from the collagen and, therefore, would aid remodelling. This explains their paper on the use of eccentric training and stretching in the treatment and prevention of tendon injuries reviewed later in the text.

Peacock believed that aggressive early motion initially gives a good range of motion, but this decreases with time as dense fibrous cicatrix forms. In contrast Enwemeka (1989), reported that mechanical stresses applied to tendons on days five to seven yield a stronger tendon than if applied in days two to four post-injury.

Clancy (1990); Kannus & Jozsa (1991); Perugia, Ippolitito & Postacchini (1976) and Puddu et al.(1976) discussed the evidence that distinguishes the pathological findings between the acute traumatic inflammatory response and the more insidious process of chronic tendon degeneration. There is still no hard clinical or experimental evidence to resolve this issue but it is important to attempt to distinguish between them in order to explain the mechanisms of a therapeutic treatment. Some studies have attempted to do so, for example Leadbetter (1990) and Williams (1986).

2.3. Tendon injury, inflammation, repair and degeneration

Leadbetter (1992) described the overuse injury as a failure of the cell matrix to adapt to sudden or accumulative overload. Teitz (1989), highlighted that injuries are divided into acute and chronic patterns according to the rate of onset and the mechanism. Acute injuries are typified by a sudden crisis, whilst chronic injury is characterized by slow, insidious onset, implying an antecedent sub-threshold spectrum of structural damage. Chronic injury may last months or even years. Leadbetter (1990), produced a schematic diagram that illustrated the sports induced inflammation response. It summarises the complexity of the processes.

Degeneration in the tissue was described in Leadbetter's text as a change in tissue from a higher to a lower or less functional active form. The weakened structure is then more vulnerable to dynamic or cyclic overload. Rubin & Faber (1988), stated that a predominant source of degeneration is cell atrophy, which is the decrease in the size and/or function in response to a presence or lack of, an environmental signal. One prescribed treatment of tendon pain, immobilisation, has been described as a predominant cause of cell atrophy (Fox et al. 1979; Gamble 1988; Rubin & Faber 1988; Woo et al. 1975).

Acute tissue loss or damage results in regeneration, fibre productive response and repair by scar tissue or a combination of both (Hunt & Dunphy 1979; Jennings & Hunt 1992).

The literature contained many reviews of the biochemical and cellular processes that occur following the disruption of the tissue matrix. These included; Adzick & Longaker (1992); Arnheim (1989); Booher & Thibodeau (1989); Christie (1991); Clark & Henson (1988); Clement et al. (1984); DiSabstino (1979); Fox, Lotz & Carson (1979); Gallin, Goldstein & Snyderman (1988); Holmes et al. (1991); Hunt & Dunphy (1979); Jennings & Hunt (1992); Madden & Arem (1991); Oakes (1982); Rubin & Faber (1988); Uhthoff & Sarker (1991) and Sporn & Roberts (1989). The processes are highlighted later in the discussion section of the study when an explanation is sought for the effect of micro-current on the chronically traumatised tendon.

Once thought to be biologically inert, tendons are best appreciated as a heterogenic group of structures with variations in cell character, collagen orientation, collagen cross-linking, vascularity, configuration load pattern, biomechanical profile, shape and the presence, or not, of a synovial sheath (Leadbetter 1992). The study of tendon injury is the study and understanding of cell injury and its matrix milieu as an expression of pre-existing capacity to adapt to such injury on the part of the injured or intact cell (Rubin & Faber 1988).

The fact remains that even with the extensive work that has been carried out in this area there is still a mystery surrounding what stimulates repair following an injury, and when a normal physiological state has returned what ends the repair process.

Becker (1985) proposed a theory following extensive studies on the limb regenerating properties exhibited by the Salamander. He proposed that the body has a micro-current circulatory system which provides intercellular communication through electromagnetic signalling.

Becker documented that the body presents a positive polarity along the central axis and a negative polarity along the peripheral structures. He believed this polarity was reversed during hypnosis, anaesthesia and following injury which creates a positive potential at the site of trauma.

Becker speculated that the reversal of polarity set up a current of injury that is conducted by means of direct micro-current signals passed along the Schwann and Glial cell sheaths that surround neurons. This current then initiates and signals the beginning of the tissue repair and regeneration process.

This work undertaken by Becker and documented in the book "The Body Electric", was the impetus for much of the subsequent work involving micro-current therapy.

Nordenstrom (1967), in a similar vein, described the body's tissue in terms of biologic batteries, believing that an electrical potential difference exists in the body which is created by a separation of electrically charged ions. He states that the electrical energy may be tapped once this circuit is closed. In his book "Bioelectricity", he describes the activation of these biological semi-conductor circuits following muscular activity and soft-tissue injuries, both of which cause a build-up of positively charged ions.

Researchers utilising the theory that the body works at a micro-current level have undertaken many scientific studies to evaluate the use of applied micro-current. It is certainly worth reviewing the literature that documents studies on Bioelectricity.

2.4. The living cell as an electrical source

Bioelectricity refers to electrical phenomena in living tissue. It has been known for a long time that a small electric current is generated in tissue and that the conduction of electrical impulses is important in the functioning of nerve tissue (Nave & Nave 1985). Nave & Nave commented that the use of the word *cell* to refer to a small battery and to the functioning unit of living tissue is somewhat appropriate, since the living cell has the ability to generate a small voltage. The membrane of the living cell can maintain a voltage difference between the inside and the outside of the cell.

Langley (1971) and Strong (1970), stated that when a living cell is in its normal or rest state it retains a voltage of about 70-90 millivolts between the inside and the outside of the cell. The inside of the cell is negative with respect to the outside. The voltage across the cell membrane is described as the membrane potential or rest potential of the cell. The origin of the voltage is due to the behaviour of the electrolytes potassium, sodium and chloride. The salts potassium chloride (KCl) and sodium chloride (NaCl) are dissociated in solution and the resultant charged K±, Na± and Cl= ions constitute mobile charge carriers.

The electrolytes vary in concentration within and outside the cell and their movements are governed by several factors; diffusion, the permeability of the membrane towards the particular ion and the tendency for like charged ions to repel one another. The rest potential is maintained by controlling the concentration gradients of the electrolytes. The membrane normally withstands a strong electrochemical gradient tending to push Na+ into the cell. This influx causes an electrical change known as depolarization and the reinstatement of the rest potential is described as re-polarisation. The process only takes milliseconds and produces an electrical pulse commonly known as the action potential. The action potential of cells are thought to be the basic communication and control mechanism of the body.

Another element vital to life, calcium, that makes use of these ion channels, and relevant to this study, is laid down in abnormal quantities in the tendon with chronic pathology. The body contains about 1100grams total body calcium of which ninety percent is found in the skeleton.

In its free ionized state in body fluids it is a vital messenger necessary for blood coagulation, muscle contraction and nerve function. The free calcium concentration in the cytoplasm is maintained at about 100 nmol/l compared with the interstitial fluid level of about 1,200,000 nmol/l, so there is a marked inwardly directed concentration and electrical gradient. In the context of this study it is believed that this is an important point to consider when discussing the presence of calcium in post-traumatic cases.

Calcium enters the cell through two kinds of channels; voltage-gated and ligand channels, activated by hormones. Ganong (1993) also suggests that there may also be a channel activated by a mechanical stretch.

Many calcium binding proteins have been described and perhaps the one worth highlighting for this study is Troponin which is involved in the contraction of skeletal muscle. Troponin C binds to calcium and in conjunction with tropomysin mediates the regulation of contraction.

This area will be further investigated in the discussion section of the thesis in relation to the post-trauma calcium deposits found in the chronic tendon.

2.5. The use of electrical stimulation in medicine

The concept of electricity as a therapeutic tool or as an aid to healing is not a new idea. Early documentation reports that in 1757 Dr. Benjamin Franklin wrote that the administration of electric shocks to his neighbour's frozen shoulder produced good results.

The diverse applications of electrical treatments are due to the variety of physiological levels at which it is said to be effective. The range of voltage and current utilised has a direct bearing upon the applications.

One of the oldest forms and perhaps the easiest to evaluate is electrical stimulation. It is believed that all electrical stimulation is neurological whether sensory, motor or proprioceptive, since it is the neurofibrils within the muscle tissue which are the true communicators of the stimulation current to the muscle cells. There are now differing forms of stimulation: neuromuscular, electrical muscle, functional and transcutaneous stimulation as discussed by Khan (1991).

The physiological effects or response to electro muscular stimulation are reported as relaxation of muscle spasm, controlled contraction of muscles, production of endorphines, circulatory and reticulo-endothelial enhancement and increased fibre recruitment , although these effects are not based upon scientific research data. In fact, although it may be felt that the science has come a long way since the days of Galvani there is little scientific data available that demonstrates the efficacy of the treatment regimes currently offered.

2.6. Micro-current

The term micro-current refers to an electric current at a strength of less than 1 milli-amp. It is important to explain how the application of micro-current differs from the other uses of electricity in medicine. Micro-current is believed to work on a different physiological level. The research data available utilising animal studies highlights how its application may be applicable to human use.

Picker (1987) put forward the argument that micro-amperage current is better at enhancing cellular physiology processes than current of greater amplitude. The acronym M.E.N.S (micro-current electrical neuromuscular stimulation) is used in connection with the application but this does not reflect the fact that the current is insufficient to stimulate or excite motor nerves.

The voltage at which the current is driven will to an extent determine its application. Constant current generators used in equipment ensure that only the minimum voltage is used to deliver a given current independent of varying tissue resistance.

2.6.1. Research with micro-current

Although Williams and Berger (1975) demonstrated that bone and tendon have similar electrical properties, experience with this current study supports the view of Stanish and Gunnlaugson(1988), that there is a paucity of literature on the electrical stimulation of tendon and ligament healing. Stanish stated that since the piezo-electrical effect is thought to be mediated by collagen, tissue largely composed of this protein would respond even more dramatically than bone for which electrical stimulation is an accepted clinical method, (Spadaro 1977).

Owoeye, Spielholz and Nelson (1987) evaluated the application of pulsed direct current on the healing of rat tendons. Electrical stimulation, with a current of 75μA, was applied daily, via implanted electrodes, for a period of fourteen days. The authors stated that the intensity was chosen arbitrarily. The authors also commented that "despite employing a high voltage direct current it was believed that high voltage was not delivered to the tissue". The level of the voltage was not stated. The authors supported this statement by reporting the evidence that the electrical stimulation appeared to be painless since the animals "dozed" throughout its application.

The references to the specific levels and type of electrical stimulation in this paper, and others in the field of study, are at best a little vague and at times confusing. The authors state that the pulse rate and the current were arbitrarily chosen at 10/sec and 75μA. The time between the onset of the first and second spike was 100μseconds±5. There was no reference to the voltage used.

Following the two week period of stimulation the animals were anaesthetized, the skin sutures were removed and the Achilles tendon was exposed. The electrodes were removed and the healing tendon was freed from the underlying tissue and then transected at the osseo-tendinous junction distally and the musculo-tendinous junction proximally. Healing was assessed by measuring the tension in grams required to re-break the surgical site.

Testing the tendons using load-to-breaking measurements, the authors found that the group treated with the direct current electrical stimulation withstood significantly greater loads than did either the group which healed with no electrical intervention.

Other study's including Carley & Weinapel (1985); Wheeler, Wolcott & Morris (1971) and Wolcott, Wheeler, Hardwick & Rowley (1969) have reported variations in the potential augmentation of soft-tissue healing when either a positive or negative current is used produced by a rectified alternating current.

Whether the healing effects were due to tissue regeneration, i.e collagen formation, or consistent with the view of Osborne and Holmquest (1944) that the anodal current has a coagulating effect on protein and tissue hardening was discussed. However, the authors believed that as so little current was used this latter effect would be of no significance.

Nessler and Mass (1985) used *in-vitro* experiments on whole tendon cultures. Deep flexor tendons of rabbits were excised, transected, repaired and grown in a cellular culture medium for a period of seven to forty two days.
The cultures were exposed to a continuous direct current of 7μA at a voltage range of 1.3V - 1.5 V and then compared with control groups. The electrical device consisted of a 1.4 volt mercury battery and a 150 kohm resistor in series. The voltage level across the electrodes was not mentioned.

The resistor was connected to the positive lead of a snap-on battery adaptor, and a 0.75mm diameter stainless steel wire was soldered to the resistor to act as the anode. The anode and cathode were placed 4cm apart. If the distance was reduced brown discolouration of the tissue was noticed. This was presumably because the amount of tissue the current passed through and the subsequent resistance was reduced.

Throughout the experiment the current delivered remained constant for all the stimulated tendons, with an average circuit resistance of 200 kohms and battery potentials ranging from 1.3 volts to 1.5 volts. From these figures the current delivered can be calculated to be in the region of 7μA.

Histological sections showed that intrinsic tendo-blastic repair may be enhanced by electrical stimulation. The control tendon sections maintained a normally organised collagen matrix, whereas the stimulated group showed scattered areas with loss of organisation. In addition the stimulated group displayed a greater proliferation of collagen fibrils.

It has been reported for several years that electric current and electromagnetic fields exerts a stimulating effect on living cells. The work is diverse in its nature ranging from enhanced osteogenesis, reported by Bassett, Pawluk and Becker (1964); Brighton, Black and Pollack (1979); Brighton et al (1981) and Lavine et al.(1972), to the regeneration of frog limbs and the healing of ligaments in rabbits.

The mechanisms involved have not been fully elucidated, although authors have reported that they may differ with different modes of electrical stimulation.

Borgens (1982) examined the role of naturally produced electric current in vertebrate regeneration and healing. Frank et al.(1983) and Goodman (1983), examined the effects of electromagnetic and pulsed electromagnetic fields on ligament healing in rabbits and cellular transcription, respectively.

Stanish (1985), discussed how the piezoelectric effect of bone, tendon and ligament responds to mechanical stress by producing an electric current, probably due to the re-orientation of dipoles in the polypeptide units of the collagen molecule which mediates cellular effects. He speculates that the application of an externally applied current will produce the same effects.

Stanish undertook a study to examine the effect of direct current on surgically repaired dog patellar tendon. The experimental group had an electrode wrapped around the patella tendon which was connected to a constant current (20μA) electrical stimulator (Osteostim, Telectronics Ltd). N.B. No further details of the device were supplied in the paper. The stimulated group demonstrated increased tensile strength although all the tendons appeared similar in size on visual inspection. This suggests a qualitative change in the newly formed tissue. Although this application was used as an adjunct to surgery the possibilities for non-surgical application in chronic tendonitis were highlighted.

Following this, Stanish et al (1985) undertook a second clinical study consisting of seventy cases of anterior cruciate ligament reconstruction using an ilio-tibial band over the top surgical technique. An electrode supplying electrical stimulation was wrapped around the graft. The electrical device used to supply the stimulation was the Osteostim HS12 electrical stimulator (Teletronics Ltd). It consisted of a power source of two silver oxide alkaline zinc cells of 105µA capacity. The solid state circuitry delivered a constant 20µA regardless of the changes in the tissue resistance over a range of 0 to 100kohms. Stanish stated that although it is impossible to test the healed ligaments mechanically, visual inspection showed a larger cross-sectional area. Butler et al (1978) found that there was a correlation with cross-sectional area and functional tensile strength.

There was no explanation in the paper as to why a constant current was used as opposed to a pulsed current or stimulation being applied for a set period during a twenty four hour span. Certainly other studies quoted have suggested the micro-current stimulation is used to "kick start" and, consequently, accelerate the body's own healing process.

Particularly pertinent to this study is another work of Stanish (1988) using a similar technique for the treatment of the ruptured Achilles tendon. He claimed that when surgery was augmented with the electrical stimulation patients returned to full activity within six weeks. This compared with the conventional clinical management where a time of three to six months would be more realistic for a successful outcome.

The power source was two silver oxide alkaline zinc cells that, akin to his previous work, delivered a constant current of 20μA. The electrodes were wrapped around the exposed tendon. A control group was used that only had the electrodes implanted with no power source. No external types of stimulation were used in the study. Twenty such repairs were undertaken and immediate motion was undertaken following surgery.

Stanish cited his earlier work (Stanish, Valient, Bonen & Belcastro, 1982) with animal experiments to demonstrate that early motion alone, without electrical stimulation, would provide only half the strength of the tendon that was stressed with early motion and electrical stimulation. The positive effect of early motion in the healing of flexor tendon lacerations had also been shown by Gelberman et al.(1983).

Studies undertaken by Cheng, Van Hoof, Bocky et al (1982) demonstrated the effect of direct current on rat skin in terms of increased A.T.P generation, protein synthesis and membrane transport. The current was produced by a transistorised current source supplied by two 9-volt batteries (Duracell, Malory, England) and potentiometrically regulated. An operational amplifier assured that each required current was kept constant. The total resistance of the skin was estimated as a function of the varying electric current applied using a four -point measurement technique as reported by Sansen and De Dijcker (1976). The resistance of dry skin was initially high, 100kohms, but decreased linearly with the applied current up to 50μA.

At higher currents the resistance levelled off at 10 kohms to the point at which tissue destruction occurred. When the skin was submerged in Krebs Ringer bicarbonate buffer, pH 7.4, the resistance decreased considerably. Pertinent to other studies using skin *in-vivo*, this study reported that at low current, below 50μA, the current through the skin was about one sixth of that through the buffer. At currents exceeding 50μA, however, the current through the skin was limited to about 6μA, whereas the current through the skin in the buffer kept rising as a function of the applied current. These findings are not too surprising as skin is known to provide considerable resistance to current flow(Bruner;1967). The latest study utilising the animal model is currently being undertaken in the orthopaedic department at Yale University. The study is utilising non-invasive electrical stimulation and evaluating its effect on the healing of the Achilles tendon lacerations on rabbits.

The technique used is in contrast to the work by Stanish. Stimulation is carried out for fifteen minutes daily, which is a variation from the constant stimulation used by Stanish. Direct contact electrodes are replaced by surface electrodes delivering an alternating current of 40μA at a frequency of 2 Hz. No further details were supplied. Tendon healing was measured by magnetic resonance imaging. Additionally, the tendons are evaluated for actual size and for tensile strength - measured by an Instrometer loaded to failure at a speed of 2 cm/minute. Histological studies are also undertaken to examine the collagen fibrillar matrix.

It is interesting to note that the information presented in the final proposal for the above work references two animal studies, Stanish et al (1985) and Frank et al (1983), but infuriatingly and consistent with all other clinical studies cites no reasoning or justification for the selection of the level and intensity of stimulation given. Rather it follows a similar pattern to previous work and theories.

It must be postulated, however, that continuous stimulation and part stimulation are likely to introduce large variables to the consistency of the studies.

2.6.2. Micro-current, fibroblast & collagen activity

Alvarez et al.(1983) studied the effects of direct current supplied by silver-coated electrodes on dermal and epidermal wound healing.

The effects of electrical stimuli on tissue and the influence on the complex electrical systems of cells have been documented, and this particular study of Alvarez et al examined dermal collagen production and DNA content. Early studies undertaken by Young (1966) examined electrical impulse therapy as an aid to wound healing. Alvarez et al. used Yorkshire pigs. Each pig acted as its own control. The wounds were divided into three, no electrode (control), a silver electrode but with no electrical stimulation (placebo) and one with a silver electrode that delivered a current of between 50-300μA. The electrical device was a self-contained, battery operated source of a constant current. The generator was equipped with a voltage limiter which kept the voltage below 0.9 volts. A liquid crystal digital display provided information of current output (μA). The batteries used were standard 9 volt (Duracell, Malory, England).

A cable with a 5-pin connector on one end and electrode connectors on the other connected the electrode and the generator. The contact electrode (anode) was fabricated of high purity nylon coated with silver, the return electrode (cathode) was a pre-gelled surgical grounding pad. The current intensity declined linearly from 300μA upon initial connection to 50μA at the conclusion of the twenty four hour treatment. It was unclear from the paper if this was planned or how it was achieved.

To evaluate the wound healing of the three groups, tissue was excised daily for a period of seven days and each section incubated in 0.25% trypsin for twelve hours to allow separation of the dermis from the epidermis. The epidermal sheet was then examined microscopically for epidermal migration as described by Eaglstein and Mertz (1978). The researchers observed that the wound exposed to electrical stimulation showed significantly accelerated epidermal resurfacing in partial-thickness wounds when compared to the control and placebo groups. The mechanisms of the action remained unexplained.

The increase in the collagen synthetic capacity in the dermis of the direct current treated group was attributed to an augmentation of collagen producing cells. Alvarez et al.(1983) speculated that the increase in the number of cells at the wound site could be the result of proliferation and/or chemico-attraction. Bassett (1968) observed that cultured fibroblasts subjected to an electrical field proliferated more rapidly (20% increase in DNA) compared with non-stimulated controls.

With reference to fibroblastic activity, the cells responsible for the production of collagen, Bourguignon and Bourguignon (1987), examined electrical stimulation of protein and DNA synthesis in human fibroblasts.

The interest in the effects of electric current and electromagnetic fields on biological systems have been studied previously. With regard to cell cultures Yang et al.(1984) have observed cell shape changes and cytoskeleton reorganisation in mouse fibroblasts exposed to a low intensity direct current.

Bourguignon and Bourguignon also based their study on reports on the effect of different types of electrical stimulation on macro molecular synthesis by cells in culture. Several of these studies have already been cited in this text. The authors of the studies include Cheng et al.(1982); Harrington & Becker (1973); Aro et al (1984) and Korenstein et al. (1984).

Bourguignon and Bourguignon's study examined the effects of "high voltage pulsed galvanic stimulation" on normal diploid human fibroblasts in culture. The stimulator used in this study was the EGS Model 100-2 (Electro-Med Health Industries). The authors reported that the electrical waveform used consisted of a monophasic, twin-spike pulses (reason for twin pulses unknown), that had a fixed pulse duration of 100μseconds. Voltages ranging from 0-300 volts, with pulse rates of 60-120 pulses/second was applied to the cell cultures. Because the electrodes used were rectangular (2.5 x1.5 cm) and covered each end of a chamber the electric field and current were essentially homogenous throughout the chamber.

The fibroblasts were grown on Millepore filters. The filters were suspended in a growth medium contained within a plastic tank. At one end of the tank the filters were placed adjacent to the negative electrode, a filter was placed in the middle and the third filter placed at the positive electrode. The time averaged current that flowed through the chamber filled with growth medium at the maximum settings of 300 volts and 120 pulses per second was measured with a volt/Ohm meter (Radio Shack, Tandy Co. Fort Worth, Texas) and was found to be 50μA. No mention in the text was made of the resistance of the electrical device. However, applying the principles of Ohm's law there must have been considerable resistance (6,000 kohms) in the circuitary. Protein and DNA synthesis were monitored following stimulation using radioactively labelled precursors. Summarising the results of this study, the rates of protein and DNA synthesis were significantly increased, by up to 160%. The maximum rate of synthesis was obtained using a current of 50μA at voltages of 50V and 75V. However, as the voltages increased further the effect diminished and it was found that voltages greater than 250V are inhibitory for both protein and DNA synthesis. This was not the only work undertaken by these authors within this area of scientific study. Electrical stimulation using similar parameters was used to initiate lymphocyte activation via a transmembrane signalling process. Hormone receptor exposure, as evidenced by insulin binding, as well as DNA synthesis in mouse splenic T-lymphocytes were both increased maximally at approximately 50 volts, beyond which point the enhancement returned towards the baseline, levelling off at about 100 volts.

The effect of electrical stimulation was also used in relation to investigating intracellular calcium influx. The results showed that there was a significant increase in calcium ion influx beginning within the first minute of stimulation. Bourguignon and Bourguignon speculated that cell membranes' potentials modified by an applied electrical field "could trigger the gating of voltage-sensitive calcium channels or activate membrane-associated enzyme(s) involved in the regulation of calcium uptake".

It was suggested that the electrical stimulation causes certain plasma proteins to cluster and form calcium ion channels and thus induce the influx of calcium ions.

Picker (1987), discussed, in a letter in Clinical Management in Physical Therapy, Bourguignon's work and also cited three other studies, (Thuren et al; 1987; Tsong and Astumian, 1986, and Valleton and Selegney, 1987), describing the activation of different membrane associated enzymes by electric fields.

Picker concluded:

> *I am most eager to see such research continue, particularly with the fifty percent duty cycle micro-current units specifically designed to deliver low-volt pulsed micro-ampere stimulation.*

2.6.3. Micro-current: The behaviour of the connective tissue matrix

The role of electrical potentials in mediating cell function and cell to cell communication has led to studies that have investigated the changes in the biological functions of cells and cell structures by externally imposing an electric field or electric current. For example, cell-specific effects, accelerated tissue formation and healing, have been noted following electric field exposure on the cells involved in wound repair (Lee et al, 1993). Modified interactions between cells due to the altering of the signal transduction mechanisms of cell membranes, are areas where experimental evidence has highlighted potential clinical applications, although the mechanism of the altered action are unclear. *In-vitro* studies, for example Nessler and Mass (1985), Cleary et al (1988), Stanish (1984), Owoeye, Spielholz and Neilson (1987), have suggested that the processes involved in tendon repair can be augmented by the application of a direct electric current at a micro-current intensity. This is supported by experimental evidence with fibroblast cell cultures that have demonstrated enhanced protein and DNA synthesis following micro-current stimulation in comparison with non-stimulated control cultures, (Cheng et al, 1982; Bourguignon & Bourguignon 1987; Fujita et al, 1992).

However, there is conflicting evidence from other studies, Bassett et al, (1964), Brighton et al (1979), Frank et al (1983), and Akai et al, (1988) found that electrical stimulation enhanced healing of the medial collateral and patellar ligaments of the knee in rabbits, while Norrie (1975) reported no observable effects.

2.6.4. Micro-current therapy: Investigating the mechanism of its action

Establishing the biological mechanisms underlying the cited studies is a task no previous author has managed to achieve. Stanish et al (1985), who undertook a number of significant studies, *in-vivo* and *in-vitro,* evaluating tendon healing and the application of micro-current electrical stimulation commented that " a distinct gap exists between our laboratory experiments and the conclusion that our clinical success is entirely due to electrical stimulation. Our research team is attempting to narrow this gap with continued *in-vivo* and laboratory experiments".

Arthroscopic examinations and biopsies allowed the research team to evaluate tissue samples from anterior cruciate ligament that had been electrically stimulated. They reported mature, organised collagen and re-vascularisation.

With reference to *in-vitro* research there are two scientifically accepted approaches aimed at assisting the understanding of the complicated systems of the connective tissue matrix. One is the biochemical approach of isolating and purifying all the different kinds of molecules, determining their structure and investigating their interactions in solution.

The second is to measure the bulk mechanical properties of the tissue. Mechanical wear and tear and biological degradation will influence the mechanical properties of the tissue matrix in tendons. The laboratory based studies approach the mechanics of the application by the first method and investigate if the alteration of fibroblast activity described by authors such as, Fujita et al (1992), Stanish et al (1985) can be reinforced.

Investigating the cellular response to electrical stimulation in laboratory based experiments for this study concentrated upon evaluating the behaviour of the 3T3 mouse fibroblasts and tenocyte cells derived from both human tendon specimens. This was done in order to compare the biological response from two different cell types. This may, in turn, assist in relating the findings from the cited animal studies into a human context.

2.6.5. Micro-current and fibroblast activity

Fibroblasts through their ability to become motile and contractile are thought to influence the evolution of various pathological processes, for example wound healing,(Gabbiani et al ;1972).

It is reported that under certain conditions fibroblasts, for example the myo-fibroblast, can progressively assume ultrastructure, chemical, immunological and functional characteristics similar to that of smooth muscle.

It is suggested that this intermediate type cell could be responsible for the contraction of connective tissue *in-vivo,* a process that is beneficial to wound closure, but harmful in other situations, for example the formation of adhesions within the paratenon.

Fujita et al (1992) examined the effects of constant direct current electrical stimulation upon the reparative processes in flexor tendons cultured *in-vitro.* Following a period of incubation the non-stimulated control tendons were found to be covered with fibroblastic surface cells, thought to have originated from the epitenon. In contrast, the tendons subjected to low amperage stimulation, below 1μA, had no proliferation of the epitenon cells in the surface layer but the tenocytes still remained viable. The results indicated that the electrical current had suppressed adhesion causing synovial proliferation in the epitenon and whilst not affecting the activity of collagen production in the tenocytes. Controversially, they reported that at a current of 6μA tenocytes were damaged. This contradicts reports from other studies. The electrical devices used in this study was assembled using two 15-volt batteries and an operational amplifier. The electric current was regulated by potentiometer. This device varies the resistance in the circuit and maintains a pre-set level of current between zero and 10 μA.

The promotion of collagen synthesis was reported in an earlier paper by Nessler and Mass (1985). Employing a similar procedure to Fujita et al, whole deep flexor tendons from rabbits were used to assess the effect of electrical current on healing *in-vitro.* Histologic sections showed that intrinsic tenoblastic repair may be enhanced with electrical stimulation *in-vitro* with protein synthesis being up to 255% greater in the stimulated group.

2.6.6. Recent studies: Suggestions for a possible mechanism Induced by micro-current stimulation.

It is pertinent to cite and report in some detail a study, (Chapman-Jones 1997), that was conducted after the clinical part of this study, but adds to the knowledge base concerning the modification of cell behaviour induced by the application of micro-current stimulation. The aim of the study was to examine the ultrastructural effects of direct micro-current electrical stimulation upon the intrinsic healing of the Achilles tendon. The electrical device used in this study was assembled by the Medical Electronics department, University of Kent. A square wave generator produced a modified wave form at a pulse rate that could be pre-set from 1 pulse to 10 pulses per second. The electric current was regulated by a constant current source which contained a series of resistors which changed the voltage in response to a change in the tissue resistance. This ensured that the current level was maintained at its pre-set level. The device used a 12-volt battery (Duracell, Malory, England). A battery test facility indicated when they needed changing.

The study used Achilles tendons that were harvested under sterile conditions, from cadaveric specimens with no previous medical history of Achilles tendon pathology. The tendons were divided longitudinally, dissecting along the fibrillar bundles, to produce narrow strips of tendon tissue approximately 2-3cm in length. These sections were divided arbitrarily into three groups. One group acted as a control and two acted as experimental groups. The control group was labelled A, the experimental groups were divided into group B and C.

The tendons in the experimental groups were subjected to continuous direct current electrical stimulation for 48 hours at currents of 40μA and 1μA and at a pulse rate of 10 hertz. Voltage and tissue resistance was not monitored during the experimental period for fear of bacterial contamination of the samples. However, in pre-test experiments driving the current through different mediums confirmed the efficacy and reliability of the constant current source generator.

During the experimental period the tendons were kept in Dulbecco's modified medium, changed every three days, at a temperature of 37°C in an atmosphere with 5% carbon dioxide and a humidity level of 100%. To deliver the electric current a stainless steel electrode was inserted into the end of each tissue segment.

In order to assess the changes in the tendon tissue, following the incubation period, the specimens were stained and fixed and subjected to electron microscopy at four different levels of magnification, x1200, x3000, x15,000, x40,000. The authors evaluated changes by making a visual comparison of cell proliferation and distribution between the control group and the treatment groups.

The authors reported some difficulties in obtaining the specimens from the cadavers. Before embarking on the study they were unsure as to how long after the patient's death the tendons would remain viable.

It was thought that more reliable results would be obtained if the tendon could be taken from patients of less than forty years old, as tendon tissue is known to degenerate with age. It was also felt to be important to match the tendon sections harvested from different subjects. Evidently this proved to be difficult. It was reported that when a suitable specimen was available the Coroner's clearance to take the appropriate sections did not come within forty eight hours of the patients death. This resulted in a compromise and Achilles tendon sections were taken from only three different patients.

Tendon sections were taken from patients two and three for the main study and from patient one for a pilot study. The sections were then allocated to the experimental groups with a minimum of two tendon sections from different patients in each group.

Electron microscopy on the sections was conducted in a blind fashion with the examiner being provided with the sections in identical bottles containing the fixative solution. Therefore the pathologist undertaking the evaluation was unaware of which sections had been subjected to which intervention.

The results of the electron microscopy were presented in photographic format showing the electron micrographs. Each experimental group had two samples for analysis with four different levels of magnification.

The Group A specimens, that acted as the control group and received no intervention, showed appearances close to the normal post-mortem appearance.

There were inactive fibroblasts (tenocytes) and some evidence of degeneration in the nucleus and the cytoplasm.

Group B specimens, the group that contained the tendon sections electrically stimulated with 1μA micro-current showed similar findings to the control group with inactive tenocytes. In this group there was a greater degree of poor preservation of collagen and tenocytes. Separation of collagen fibrils was demonstrated. The section taken from the younger patient was less degenerate than the section from the older one.

The results reported in group C are the most relevant to this current clinical study. The tendon sections electrically stimulated with 40μA micro-current were remarkably different to the other tendon sections. There was disruption of the mature formed compact tendon collagen with an increased number of active fibroblasts which appeared to have acquired the cytoplasmic organelles to synthesise new protein, which they did in abundance. However, there was no evidence that this newly synthesised protein was forming itself into mature collagen fibrils at the stage of analysis.

The electron micrograph, magnification x 40,000, demonstrated the tenocyte nucleus and the cytoplasm. The detail of cytoplasm revealed an active tenocyte with numerous polyribosomes and some rough endoplasmic reticulum. They reported fine fibrillar structures between the fragments of mature banded collagen. The researchers believed this was suggestive of synthesised pro-collagen.

The results of this study suggest that the changes seen can only be explained by an alteration of the genetic information contained in the tenocyte nucleus. It appears that the rate of mitosis is being modified. Whether this is due to a genetic modification or a change in the chemical environment is unclear. However, collating all the relevant information together from the cited and the current study may allow reasons to be deduced for the changes noted. This will form the basis for the discussion for this thesis.

2.7. The choice of the Achilles tendon

The Achilles tendon was chosen for this and previous studies primarily because clinically it is so difficult to successfully treat when it is subjected to trauma or pathology. In addition it is anatomically unique in that, unlike other tendons it is not contained within a synovial sheath. Whether this is the reason for its biological behaviour can only be the subject of speculation.

The significance of the Achilles tendon can be traced to the mythological Greek warrior Achilles who, after being dipped in the Styx river by his mother Thetis, was rendered invulnerable except for his heel. The legend states that later in battle, in the Trojan war, Achilles died after being wounded in the heel by Paris.

Achilles tendon traumas were first documented in the medical literature as long ago as the 16th century, (Tripp, 1970). Yet there still remains no consensus of opinion as to how best to treat the tendon whether from full ruptures to chronic pathology.

It is reasonable to state that one of the few points of agreement is that Achilles tendon disorders are a nemesis both to the athlete and to the physician. This is perhaps epitomised by Clement et al.(1984) who states that different treatment strategies may be required for seemingly identical symptoms in two individuals. One such individual may respond in a matter of days while another may require a prolonged convalescence.

Many studies have been undertaken to evaluate the efficacy of one treatment in relation to another for acute ruptures of the Achilles tendon. Clement et al.(1984); Lennox et al.(1980); Denstead & Roaas (1979); Kvist & Kvist (1980); Leadbetter et al. (1992); Williams (1984); Carden et al.(1987) are examples of such work. The diversity of opinion in these studies highlights the problem that faces the clinician presented with a patient who has a ruptured Achilles tendon. These citations may be appropriate, for it is believed that a complete rupture may be preceded by low grade micro-trauma that weakens the tissue matrix. Therefore, a patient presenting with a complete rupture may well have an underlying chronic pathology. There are no studies that have adequately evaluated the efficacy of one treatment in relation to another for chronic pathology.

2.7.1. Pathophysiology

It is believed that pathologies affecting the Achilles tendon progress through well defined stages which have been described in the literature of many studies. Searching the studies in chronological order it would appear that the original exponents of such theories are Puddu et al.(1976).

Galloway, Jokl & Dayton (1992), review the literature, (e.g. Blackman et al. 1990; Clancy, Neidhart & Brand, 1976; Kvist et al. 1988; Nelen et al. 1989) that builds on the initial Puddu et al. theories. Overuse injuries to the Achilles tendon manifest initially as inflammation in the surrounding paratenon, and is referred to as *paratenonitis.* Surgical and necropsy findings in these cases have demonstrated thickening and oedema of the fatty areolar tissue of the paratenon, with widespread fat necrosis and connective tissue proliferation.

Kvist et al.(1988) reported increased vascular permeability and the presence of immature scar tissue, fibronectin and fibrinogen, in the areas of proliferating connective tissue within the paratenon in chronic pathology. Teitz (1989), examined overuse injuries and concluded that the thickening of the paratenon impairs the gliding function of the endotenon, thereby intensifies the inflammatory stimuli. Histological studies, (Kvist et al. 1988), of tissue from patients with chronic Achilles tendon paratenonitis, have demonstrated evidence of collagen breakdown and a decrease in anaerobic metabolic enzyme activity. If the inciting stimuli are removed, paratenonitis is usually self-limiting and can heal without consequence but unfortunately, scarring of the paratenon and structural disruption to the tendon tissue itself can occur.

Tendinosis denotes degenerative change within the tendon substance, the endotenon. A popular theory of tendon overuse injury is that it is the inability of the tendon to resist repetitively applied loads results in micro-tearing. These changes most commonly present within the tendon mid-substance and have been described by many authors, notably Clancy et al (1976); James, Bates & Ostering (1978); Nelen, Martens & Burssens (1989) and Teitz (1989).

Blackman, Boquist, Friden et al.(1990) added a significant amount of data to the clinical evidence of tendon degeneration. Using an experimental model, involving rabbits that were exposed to electrically stimulated eccentric and concentric contractions, degenerative changes, inflammation, increased capillary ingrowth and fibrosis in the paratenon were revealed. The changes were seen in the animals following a six week regime of overload that simulated a typical exercise programme.

When the tendons were examined histologically, areas of tendon injury demonstrated focal proliferations of poorly organised scar tissue. In similar studies Kvist et al.(1987); Nelen, Martins & Burssens (1989); and Teitz (1989) report that collagen breakdown products which arise from the site of injury can initiate an inflammatory response, predisposing further tendon degradation through the release of proteolytic enzymes by inflammatory cells.

Puddu et al.(1976), noted that ischaemic changes within the tendon mid-substance may precede structural disruption. Vascular thrombosis is a predominant histologic finding in surgical specimens from patients with tendinitis and a decreased pH in the areas of involvement reflects tissue hypoxia.

2.7.1.1. Predisposing factors

Kvist & Jarvinen (1982) stated that among their sports clinic patients the overload injuries account for about fifty percent, and their sequelae about twenty percent, of all reasons for consultations. About forty percent of the stress injuries were different cases of tendinitis.

The reported aetiological factors causing overuse injuries can be divided as follows:

1. Real factors: various forms of overstrain
2. Provoking factors: poor equipment, anatomical misalignment
3. Complicating factors: environment i.e. temperature

Kvist and Jarvinen described the basic feature of the overuse injury as an inflammation of the cell membranes leading to direct communication between intra-and extra cellular space. The subsequent release of different mediators of inflammation is followed by the development of pain and oedema. This will then lead to impairment of circulation and disturbance of cell metabolism.

The aetiology of acute and chronic paratenonitis can be varied but morphological alterations appear similar, a fibrinoid exudation in the oedematous paratenon with new connective tissue and capillaries, an increase of neutral and acid mucopolysaccharide and an increase in connective tissue cells.

Kvist, a supporter of surgical intervention for chronic tendonitis, confirms that there is no known biological reason why there is a loss of symptoms after surgery. He expands the theory that the tendon exists in a hypoxic state when chronically inflamed. Because anaerobic glycolysis is so prevalent in energy metabolism of chronic tendonitis, the accumulation of lactate in the inflamed tissue is increased during times of strain. This, combined with the release of vaso-active amines, leads to the intense pain during exercise.

2.7.2. Current clinical management

Many retrospective studies have been undertaken to evaluate the efficacy of the various treatment regimes to which the chronic Achilles tendon has been exposed. It is worth reviewing a selection of these studies although they all present with similar findings and often quote the work of each other.

Clement et al.(1984), examined 109 cases over a two year period. Patients who exhibited a total rupture were excluded from the study. Runners who had Achilles tendinitis with peritendinitis were included. Peritendinitis, refers to inflammation of the paratenon and tendinitis, inferring devitalization and disruption of tendon fascicles due to repetitive micro-trauma of overuse. Most runners presented with symptoms of gradual pain and swelling.

Clinical examination was undertaken which revealed focal tenderness and frequent crepitus. The examination involved using a goniometer which measures the alignment of the tibia, heel and forefoot. Patients were then classified into various groups: mild, moderate and severe degrees of varus alignment. *Varus alignment*, describes a notable degree of tibial varum and subtalar and /or forefoot varus, in the non-weight bearing position as described by James & James (1984). Surprisingly no imaging was used.

It is worth reproducing the treatment plan devised by Clement et al. as it is typical of the myriad of regimes that patients will often undertake in the search to find successful relief from pain and functional disability.

Rehabilitation of	Control of	Control of
gastronemius/soleus muscle-tendon unit. ↓ 1.flexibility exercises - e.g. Calf Raisers and Stretching 2. ultrasound (20)	inflammation and pain ↓ 1.ice massage (82) 2.modified rest (78) 3.oral anti-inflammatory medication (61)	Biomechanical parameters. ↓ 1.orthotic devices(62) 2.heel lifts(29) 3.change of running shoe (18)

Table 2.1 The treatment plan: Clement et al.(1984).

The brackets denote the number of patients receiving specific treatments.

Patients who had undergone a treatment regime that had not produced results were then exposed to another.

As the patients were exposed to more than one treatment regime it would be difficult to evaluate objectively the efficacy of one treatment in comparison with another, or to attribute a change in the patient's symptoms to a particular therapeutic treatment. This study will be considered further in the discussion section of this study, but the methodology employed by Clement et al is questionable for this reason.

Williams (1984) reviewed the same study and concluded that the role of podiatry in the management of Achillodynia has been energetically promoted by a number of authors, James et al.(1978); Smart et al.(1980) & Subotnick (1977), and there was some evidence that the provision of suitable orthoses reduced symptoms.

It was felt this was due to shoe realignment rather than any biomechanical change in the foot. It may be that in these cases the relief of symptoms follows more the provision of an effective heel raise.

The conservative management of chronic Achilles pathology and pain is often unrewarding, Mach & Behounek (1966) commented. Twenty years later Williams (1984) reported the same story; that various forms of treatment have been recommended, none of which stand the test of controlled clinical trials.

Rest is often prescribed as an initial course of clinical management. Symptoms will diminish and over a sufficiently long period of time tendinitis and focal degeneration may gradually resolve. However, conditions such as chronic fibrotic peritendinitis recur with resumption of activity due to the tightness of the paratenon. Unfortunately, for most sufferers of Achilles tendon pain, rest is the last thing they want since the patient's lifestyle and sporting aspirations demand physical activity. Williams (1967) wrote in an earlier paper that gradual transitions in training may well help to reduce the stresses imposed on the tendon.

Schmidt (1968) and Wise (1977) state that various forms of physiotherapy have had their vogue. Transverse friction is extremely painful and its effect is felt by these authors to be a counter irritant. They even postulate that the patient may suggest he is feeling better to avoid a repetition of the treatment.
This current study follows up this point and it will be discussed later in the thesis.

Ultrasonic and interferential therapy also have their supporters and excellent claims have been reported. However, the evidence in support of these claims is essentially anecdotal and clinical experience shows that the efficacy of these forms of treatment is not regularly reproducible, (Williams 1984). Williams concludes he believes that apparent cures may well be no more than a reflection of the capricious nature of the clinical condition rather than a direct response to any particular form of treatment.

There have been many strong words used in reference to the use of local steroid injected on to the tendon. Although there is evidence that a normal tendon cannot be damaged by intratendonous injection (Matthews et al. 1974; Phelps et al, 1974), all the clinical and some experimental evidence (Balasubramaniam & Prathap, 1972; Krahl & Langhoff, 1971; Kennedy, Baxter & Willis, 1976 and Unverferth & Olix, 1973), makes it clear that where there is injury or pathology in the tendon, local steroid injected, whether into the tendon itself or around the paratenon, may precipitate rupture.

Further studies by Ismail et al.(1969); Lee (1957) and Visser (1980) confirm this and Skeoch (1981) and Jacobs et al (1978) make the link between steroid injection and Achilles tendon partial and full rupture.

There are many supporters of surgical intervention for the Achilles tendon with chronic pathology and pain, and most of them are surgeons. In a study of fifty eight partial ruptures, Denstead and Roaas (1979) claimed that forty-six patients indicated they were pleased with their results, eight felt their results were satisfactory and three were dissatisfied. One patient died. Thirty seven of the forty four patients that engaged in competitive sports pre-operatively returned successfully to the activity.

The post-operative survey time ranged from eight months to seven years and the patients were only followed up by postal questionnaire. No follow-up clinical examination or imaging was undertaken.

Lennox et al.(1980) in a study of forty one patients for Achilles tendon injuries reviewed the results of the operative treatment. They examined patients who had suffered ruptured tendons and, although the present study is examining the efficacy of micro-current application on the chronic tendon, useful parallels with it may be drawn. The authors came to the conclusion, later to be reiterated by Carden et al.(1987), that surgical intervention is optimum for ruptures of less than seventy two hours whilst post seventy hours they should be treated conservatively.

Kvist and Kvist (1980) are also exponents of surgical intervention.
They comment that the non-surgical treatment of chronic peritendinitis, as generally practised, is far from satisfactory, with only occasional success but even then recurrence of symptoms is common. They do conclude that surgery does not preclude recurrence, but this has been uncommon. However, they also concede that this may be because the patients have learnt how to avoid the predisposing factors. Partial ruptures have been mistakenly treated as paratenonitis. However, Kvist and Kvist believe that these patient's benefited from the operation. Again, consistent with other studies the patients were not imaged before or after the surgical procedure and the degree of objective assessment was limited.

Fyfe & Stanish (1992) comment that the treatment of tendon injuries has long been, and still is, disputed. With more people involved in physical activity, especially at the non-professional, recreational level, there is an increased incidence of tendon injuries. The consideration of not only the tendon but also the entire muscle-tendon-bone unit is highlighted by Fyfe and Stanish.

The debate concerning whether to immobilise or exercise following injury and the effect of each on the macroscopic and microscopic structure of the tendon, muscle and bone is raised.

The paper by Fyfe and Stanish (1992) provides an understanding of the optimal treatment for chronic tendinitis based upon their experiences. They examined the use of eccentric training and stretching in the treatment and prevention of tendon injuries.

The rationale behind their study is based upon the documented stages of healing the tendon goes through as described by Peacock (1967). The eccentric exercises are based on three parameters, length, load and speed (Stanish, Rubinovich and Curwin, 1986).

Length or stretching helps to increase the length of the muscle-tendon unit and therefore reduces the strain with joint movement. Increasing the load to the myotendon unit results in increased tensile strength, whilst an increase in the speed of contraction also increases the force.

Three forms of muscle-tendon contraction are discussed:

* concentric - the muscle resists an applied force which results in the muscle-tendon unit shortening. This is designated positive work.

* isometric - the muscle resists an applied force and the muscle tendon unit length remains constant. This is designated no work.

* eccentric - muscle resists an applied force but the muscle-tendon unit lengthens. This is designated negative work.

Petersen (1960), found that the maximum tension in eccentric contraction was twenty to thirty per cent higher than in isometric contraction. Fyfe and Stanish highlight work undertaken by Darcus & Salter (1955) who showed that thirty maximum isometric contractions per day over twenty five days demonstrated an increase in isometric strength. They concluded that the type and duration of exercise is important.

Examining the collagen content in rabbit tendons, Viidik (1969) found it increased in the trained rabbits compared with the untrained group and the trained group also exhibited a greater maximum load potential.

The influence of exercise on the metabolism of collagen was further investigated by Heikkinen and Vvori (1972). It was discovered that a graduated exercise programme increased, and physical inactivity decreased, the metabolism of collagen.

Komi and Burskirk (1972) undertook a similar study, but as an interesting new approach they conditioned subjects for seven weeks to concentric, eccentric or no exercise and compared the results. They concluded that the concentric group showed a greater increase in the concentric maximum tension. On a percentage basis the eccentric group showed the greatest increase in maximum tension across all exercises. However it did take the eccentric group a longer time, (6 weeks), to reach the maximal isometric tension relative to the concentric group, (2 weeks). Muscle soreness was also reported in the eccentric group which was not a complication reported in the other groups.

Komi and Viitasalo (1977) found that in both eccentric and concentric exercises there is an increased load, increased blood lactate, and decreased muscle glycogen. Komi concluded that an appropriate exercise programme should commence with concentric exercises and progress to eccentric.

Fyfe & Stanish (1992) suggested that the time when maximum load is placed on the tendon is during the eccentric force. This is the time when the athlete is most likely to experience symptoms for their condition. The exercise programme was therefore designed to strengthen the tendon so that it may be placed under greater stresses.

The programme is as follows:

1. Stretch - hold a static stretch for fifteen seconds, and repeat three to five times.

2. Eccentric exercises - progress from slow on days one and two, to moderate on days three to five and on to fast on days six and seven.

3. Stretch statically as in phase one

4. Apply ice for five to ten minutes to reduce swelling and moderate pain.

It does not appear, however, that the exercise programme has been exposed to the rigours of a controlled trial other than that of Curwin and Stanish's original study in 1984 so its efficacy is unclear.

Curwin and Stanish reported on two hundred patients having chronic Achilles peritendinitis for an average duration of eighteen months. The patients performed an eccentric exercise protocol once a day for six weeks. Eighty seven per-cent exhibited either a complete recovery from, or a marked reduction, in functional impairment at the sixteen months follow-up. Two per-cent were worse and nine per cent unchanged.

Curwin and Stanish (1984), feels that the presence of severe scarring, caused by long term pathology, reduces the chance of successful conservative treatment.

Certainly the reported success rate of eighty seven per-cent is remarkable taking into account the comments of other authors on the problems of successfully treating the Achilles tendon presenting with chronic pathology. The question must be raised, if these results could be replicated, why this eccentric exercise programme has not become the treatment of choice and why there are still so many people searching for relief from their Achilles tendon symptoms?

Relevant to the clinical aspect of this present study, a point worth highlighting is that this, like many of the studies previously highlighted, does not employ imaging as an objective measurement of the progress of the tendon's healing. An example of an available, suitable, low cost imaging modality that was utilised for the present study is diagnostic sonography.

2.8. Diagnostic sonography of the Achilles tendon

2.8.1. Introduction

Howry published the first sonographic, static B-mode scan of a leg as early as 1965. Since then the advance in high quality real-time scanners has made ultrasound a suitable modality for imaging the musculoskeletal system. Fornage (1986a&b); Wilson (1988); Laine (1984) and Kaplan et al.(1989), are the leading authors who have documented the areas of the muscular skeletal system that are suitable for imaging using diagnostic ultrasound.

The advent of magnetic resonance imaging has slightly changed the goal posts somewhat with regard to the imaging of the musculoskeletal system as it has the ability to differentiate between soft-tissue structures that only exhibit a slight variation in density. The choice of ultrasound for the imaging of the Achilles tendon in this study is fully explained in the research methodology section, Chapter Three.

Several authors, O'Reilly & Massouh (1993); Maffulli et al.(1987); Fornage (1986a), and Matheson et al (1988) have documented the use of diagnostic ultrasound to investigate pathology occurring in the Achilles tendon, with similar conclusions. Improved image quality has enabled both the confirmation of a diagnosis, and in addition, the identification of alterations in normal tendon anatomy and its anatomo-pathological stage.

Williams (1986), advocates the use of soft-tissue radiography as an aid to clinical diagnosis, and reiterated this in 1995 at a presentation given at the National Sports Medicine Institute, London, but this must be contested.

Its relative insensitivity to differentiate between subtle pathologies makes its value limited to calcaneal impingement on the tendon, gross pathology, dense calcification or a substantial degree of paratenonitis.

2.8.2. The physical basis of ultrasound and the equipment used

The transducer, or probe, used in diagnostic ultrasound has the ability to transmit sound waves and then collect the resulting reflected sound waves so providing a pictorial representation of their journey through the body part under examination.

High frequency sound waves transmitted through soft-tissues such as muscle and fat are reflected by a boundary, where there is a change in tissue density or texture. So, for example, it is possible to identify easily the bundles of collagen fibres of a tendon contained within the tendon sheath, providing there are no more superficial high density structures such as bone.

Fluid transmits sound with little reflection and attenuation. Tissue/air and tissue/bone interfaces reflect a large proportion of the sound therefore transmission is effectively blocked.

2.8.2.1. Transducer type & frequency

A linear array transducer that produces parallel beams of sound, provides a good quality image in the near field, (the part of the image closest to the transducer). This makes it particularly suitable for evaluating superficial soft-tissue structures. Sector scanners produce a narrower near field and poorer resolution in this part of the image. Consistent with all ultrasound examinations, the skill of the operator is essential to the production of high quality diagnostic images, (Fornage, 1986 b).

High frequencies of sound are associated with improved spatial resolution but also with increased attenuation of the ultrasound beam. Currently probes of 3.5MHz to 10MHz are commercially available. Generally the higher the frequency the more superficial the application and the narrower the field of view.

Fornage (1986 a) states that most muscle examinations are performed using a 5MHz probe, and the evaluation of superficial tendons usually requires the use of a 7.5 MHz probe. The 7.5MHz and 10MHz probes are needed for the evaluation of the distal extremities and very superficial structures.

The use of a water stand-off placed between the area of interest and the transducer allows better visualisation of superficial structures. In an earlier paper (1984), Fornage et al describe in detail the experiments they conducted with water stand-offs using various items from water filled latex gloves to more developed systems.

2.8.3. Scanning technique

The need for orthogonal views applies to ultrasound examinations of superficial soft-tissue structures. Fornage (1986 a) states that the combination of longitudinal and transverse scans allows:

> *"a) more accurate identification of the structures to be evaluated,*
>
> *b) differential diagnosis between vessels and a minute fluid collection,*
>
> *c) preoperative three-dimensional localization of lesions, in particular foreign bodies and the determination of the volume of lesions".*

A standard technique for scanning the Achilles tendon is documented by all the previous authors mentioned, (Fornage, 1987; O'Reilly and Massouh, 1993; Matheson et al, 1988). Patients must be prone on the scanning couch with their feet hanging over the end of the table or resting on a bolster so the feet can be freely plantar- and dorsi-flexed during the examination. The tendon is relatively small and the examination technique must be meticulous to avoid artifacts. The major pitfall consists of false hypo-echogenicity resulting from an oblique ultrasound beam. Longitudinal and transverse real-time scans are performed.

It is imperative to ensure that the surface of the probe is placed parallel to the tendon. Fornage (1986a,b) and Kaplan et al.(1989) document that obliquity of the beam in relation to the tendon can result in an artificial hypoechogenic pattern, mimicking pathology. Fornage (1986a,b and 1987), has written several separate articles on this subject alone.

Longitudinal scans: - The fibrillar structure of the tendon provides longitudinally oriented parallel interfaces. The tendon's echotexture is best demonstrated with the ultrasound beam perpendicular to the fibrillar structure.

When there is obliquity of the beam an artifactually hypoechoic tendon that has a similar appearance to pathology may be visualised.

Fornage confirms that artefact occurs when there is an oblique anatomical course of the tendon in relation to the skin, at the point of the tendon's physiological curvature; or when there is improper placement of the probe when using a stand-off. The advent of water stand-offs that are incorporated within the probe reduces this problem.

Transverse sections: These enable an accurate assessment of the tendon's size and establish any degree of tendon thickening, although there are difficulties. With transverse scans obliquity of even a few degrees will result in a falsely hypoechoic cross-section because of beam scattering. Tendonitis is characterised by a thickened and hypoechoic tendon, therefore awareness of false hypoechogenicity is crucial in the sonographic evaluation of tendon disease, particularly in sports medicine, (Fornage, 1987).

Other operator dependent problems documented by the same author are in relation to the measurement of the Achilles tendon. The Achilles tendon is flattened antero-posteriorly, hence the greatest diameter of the oval transverse section is oriented obliquely both medially and anteriorly. This results in over-estimation of its thickness on strictly sagittal scans.

The thickness is most accurately measured on transverse scans.

The transverse scan also help to determine the correct placement of the longitudinal scan plane for obtaining a true mid-sagittal sonogram of the tendon. This orientation of the Achilles tendon also affects the measurement of its thickness on plain lateral radiographs. To enable an evaluation of functional anatomy the patients are also scanned whilst in dorsi-flexion and plantar-flexion. This provides valuable information about the tendon's response during movement.

2.8.4. Normal ultrasound appearance

The normal appearance of the Achilles tendon on ultrasound is ribbon-like and hypoechogenic, being delineated by two thin regular echogenic bands, the peritenon. The normal range of Achilles tendon thickness is 4-9mm, described by Matheson et al.(1988). O'Reilly and Massouh (1993) reiterated these findings. Anterior to the tendon at the os-calcis is the triangular area of adipose tissue, Kager's triangle, which is less echogenic than the tendon itself.

Anterior to the tendon at its superior end, lies the soleus muscle, the flexor hallucis longus, digitorum longus and the posterior tibial tendon.

Fornage (1987) stated that normal tendons do not vary significantly in echogenicity but the surrounding tissue, particularly fat, may show significant topographic as well as individual variations. Tendons are slightly more echogenic than adjacent fat.

The transverse section demonstrates the tendon's oval shape, having a greater medio-lateral diameter than antero-posterior.

In a recent article, "High resolution ultrasound anatomy of normal Achilles tendon", Bertolotto et al.(1995) evaluated the normal appearance of the Achilles tendon at increasing frequencies, 10 MHz and 15MHz, examined *in-vitro* and *in-vivo*. The increased spatial resolution provided by the high frequency probes allows an accurate ultrasound description of the superficial structures. The aim of the work was two-fold, to correlate the ultrasound appearance at increasing frequencies of ultrasound in order to characterise further the normal inner echotexture, and to correlate the ultrasound findings with the gross anatomy of the tendon.

Two tendinous portions were detected by the presence of an internal acoustic interface which had different appearances. These were classified as Type I & II, which showed continuous lines of increased thickness and greater reflectivity than adjacent fibrils, and Type III where there is displacement of the distal portion of the well insonated sector of the tendon body.

When, on transverse scans of the tendon, no intratendonous linear increased reflectivity was visible, the two portions of the tendon were identified through the converging courses of the bundles of collagen fibrils.

Different echogenicity allowed the detection of intratendonous portions on axial sections. It was noted that, although the normal Achilles tendon is commonly regarded as a uniform structure using conventional ultrasound, the use of high resolution probes allows identification of its constituent portions. Bertolotto et al believe that this may be useful in avoiding the misdiagnosis of pathological findings.

2.8.5. Sonographic appearance of pathology

The sonographic appearance of pathology in the Achilles tendon has been documented by several authors, Fornage (1986a,b); Maffulli et al (1987); Kaplan (1989); Maffulli, Dymond and Regine (1990) and O'Reilly and Massouh (1993), each one repeating what the preceding had written. This section will document the consensus opinion.

When inflammation of the peritenon occurs there is a fluid accumulation, firstly in the retro-calcaneal bursa, with subsequent migration in a cephalad direction around the tendon itself.

Maffulli et al.(1987) described pathology from a clinical point of view using Puddu et al.'s (1976) classification. Briefly, there is a distinction between inflammation of the tendon tissue itself, the endotenon and the surrounding sheath - the paratenon. Tendinitis may be diffuse or nodular and will be demonstrated on ultrasound imaging as small echogenic areas within the tendon.

Small dense echoes with posterior shadowing correspond to calcification within the tendon while degeneration is evident as sonolucent areas. Acute Achilles tendon ruptures appear as focal lucencies in the tendon.

2.8.5.1 Ultrasound appearance post surgery

Chapman-Jones (1996) described the post-operative appearance of the Achilles tendon following surgery for chronic pathology.

Post-operatively the tendon may appear oedematous and thus be demonstrated as enlarged. Sonography should therefore, not be used until this has stabilised.

With reference to the ruptured Achilles tendon Maffulli, Dymond and Regine (1990) report that the repaired tendon is increased in size, but tends to become smaller over time without, however, returning to its original thickness. They go on to report that the ultrasonic characteristics tend to return to normal: the borders of the tendon are indistinct two weeks after surgery but become more regular after some months, and the suture line is not sonographically recognizable a few months after surgery.

2.8.6. Diagnostic ultrasound: conclusion

Real-time sonography of the Achilles tendon has been recommended as a useful first-line imaging technique. Imaging of anatomy with pathology or post-surgical changes is difficult for as has been stated, the appearances can be diverse. Diagnostic ultrasound can, however, make a significant contribution to the post-surgical assessment of the Achilles tendon.

With reference to other imaging techniques, computed tomography is of limited value because direct sagittal reformations lack the clarity necessary to accurately evaluate Achilles injuries, (Maffulli, Dymond and Regine 1990). Magnetic resonance imaging is becoming more common and has the advantage of soft-tissue discrimination, and the ability to evaluate adjacent soft-tissue and bony structures in relation to one another. However, currently ultrasound does have the distinct advantage of greater availability and the ability to easily perform dynamic examinations. It is also of relatively low cost. The use of sonography for this study is appropriate for the anatomy involved and is justified by the current literature.

CHAPTER THREE

Research Methodology

3. Introduction

The aim of this study in its entirety was to examine the modification in cell behaviour induced by direct micro-current electrical stimulation. In order to achieve this the study was divided into two distinct parts. The main part of the study, in terms of time and resources, was an *in-vivo* study involving a clinical trial employing a prospective, randomised, comparison method. This trial was based upon evidence from previous *in-vitro* and *in-vivo* experiments which has suggested that direct current electrical stimulation at a micro-current level may augment the soft-tissue healing processes.

The second aspect of the study was a series of *in-vitro* experiments on fibroblasts cell cultures. These were conducted in order to clarify some of the explanations of results provided from previous in-vivo experiments. The research methods used for these two aspects of the study were very different and will be outlined separately.

3.1. The In-vitro experiments

The *in-vitro* experiments involved two separate cell cultures. The first was 3T3 mouse fibroblasts derived from intra abdominal organs, the second used tenocytes derived from human cadaveric Achilles tendon specimens. The biochemical products of the 3T3 cells may be different from the behaviour and biochemical products of human tenocytes. The mouse fibroblasts were experimented on first for they were readily available and relatively inexpensive. In addition the author hypothesised that any alteration in their behaviour may be act as a marker for changes noted in subsequent cells harvested from other tissue. With reference to the behaviour change of specific cell types induced by the application of micro-current there is currently no evidence to suggest that behaviour modification is cell specific. However, using two different cell types will answer that question.

The experimental method outlined was derived from a standard cell culturing technique for this type of study as reportd by Pentinnen et al (1980)

3.1.1. Growth medium preparation

Prior to the tendon tissue and cell study the growth medium was prepared. 500ml of medium was prepared using 50ml Dulbecco's minimum essential medium (Life Technologies, Paisley, Scotland), 360ml sterile distilled water, 50ml newborn bovine serum (heat incubated), 25ml sodium bicarbonate; 7.5% mmol. concentration, 5ml L.glutamine; 200mmol. concentration; 2ml penicillin/streptomycin and 10ml sodium pyruvate. Prior to preparing the cell culture the medium was warmed to a temperature of 37 °C.

3.1.2. 3T3 Cell study method

Cell cultures: The cells cultured were MC3T3 mouse fibroblasts derived from abdominal organs. Prior to the cells being cultured the growth medium was prepared.

A vial containing 3T3 cells, P56 (passaged 56 times), was removed from the liquid nitrogen store and warmed in a water bath to a temperature of 37 °C.

The following procedure was carried out under sterile conditions in a Walker safety cabinet.

Washing the freezing solution from the cells. With a 3ml Pasteur pipette medium was added dropwise to the cells. The two were mixed using the pipette. The cells and the medium were introduced into a 50ml universal containing 5ml of medium. The capped universal was placed in the centrifuge, which was balanced with a universal containing water of equal weight and size, and spun for 5 minutes at a speed of 1200 revolutions per minute (rpm). Following this the universal was returned to the cabinet.

The medium was removed leaving the cell pellet at the base of the universal. 1ml of fresh medium was added to the pellet and this was mixed using a Pasteur pipette. A further 4ml of medium was added to the universal and the contents were spun for a further 5 minutes at 1200 rpm. The medium was removed using a 5ml pipette leaving the cell pellet at the base of the universal. 1ml of fresh medium was added.

Cell culturing The cells were grown in a 25ml tissue culture treated sterile flask(Falcon, Becton Dickinson Co. New York, USA). 5ml of pre-warmed (37°C) medium was added to the flask. The prepared cell solution was added to the flask. The flask was viewed under a microscope (screened) to check the cells were present. The flask was labelled with the researchers name, the date and the appropriate passage (P) number. The flask was loosely capped and incubated at 37°C, 5%CO_2 at 100% humidity. The culture was screened each day to check for infection. At day three the cells were confluent.

Passaging the cells

The cells grown in the 25cm flask, when confluent, were passaged after release with 1 X trypsin-hepes solution.

Mixing the trypsin-hepes solution (under sterile conditions).

1ml of hepes buffered solution was mixed with 100ml of phosphate buffered solution (pbs). 0.02 grams of trypsin was added to a 5ml universal. 1 ml of the hepes/pbs solution was added dropwise to trypsin and mixed using a Pasteur pipette. This mixed solution was added to the remaining hepes/pbs solution. This was mixed and equally divided into five 50ml universals using a 20ml syringe and filter. The universals were labelled with a name, date and trypsin/hepes solution and four of the universals placed in a freezer. The remaining universal containing the trypsin/hepes solution was used to passage the cells.

The flask containing the confluent cell culture and the growth medium was taken to the sterile cabinet. The excess medium was removed using a 5ml pipette. To wash the cell layer, 5ml of sterile phosphate buffered solution was added to the flask. After this was removed 2ml of trypsin/Hepes solution was added and left incubated for 10 minutes. An examination under a microscope revealed that the cells were motile. On returning to the sterile cabinet, 5ml of clean growth medium was added to the flask. Using a sterile 5ml cell scraper (Falcon), the cells were loosened from the inside of the flask ensuring that all the corners are covered.

The medium containing the fibroblasts was collected using a 5ml pipette and put in a sterile 50ml universal. The flask was washed with a further 5ml of fresh medium to collect any remaining fibroblasts. This was added to the universal. The universal was capped and centrifuged as previously practised at a speed of 1200 rpm for 5 minutes. Once spun down the medium was removed leaving a cell pellet at the base of the universal.

Cell number and viability

The number of cells was determined by haemocytometer counts and viability by the trypan blue dye exclusion assay (0.4%, >85% saline). The procedure was undertaken in the sterile cabinet. The cell pellet was washed with 1 ml of growth medium. 50 µlitre of the cell pellet medium was taken and put into a sterile yellow tip. An equal amount, 50 µlitre of trypan blue dye exclusion was added to the yellow tip.

The haemocytometer was swabbed with alcohol and the glass cover slip was placed over the counting grid. The trypan blue and cell mixture was injected under the side of the cover slip. The number of cells contained on the haemocytometer 5x5 square grid was then obtained by viewing the haemocytometer under a light microscope by manually counting the number of fibroblast cells present on each square counting from left to right. Dead cells are distinguished since they take up the blue stain.

The following calculation was then undertaken to determine the number of cells. The number of cells counted are multiplied by two, (x2 because of equal dilution of cells in growth medium to trypan blue). In order to obtain the cell number per ml it is necessary to multiply the µl number by 1000.

Experimental Cultures

Once cell density had been established in a confluent culture the fibroblasts were added to a six-well (3.5cm diameter, Falcon, Becton Dickinson Co.) plate containing 10ml of fresh growth medium at a density of $3x10^3$ cm^2, per well. For experimental purposes two six-well plates were used in order that each experiment may be replicated in triplicate.

Therefore for two experimental groups and a control group nine wells were used.

Electrical stimulation

The electrical device used in the previously cited study, (Chapman-Jones, 1997) was available and used to supply the electrical stimulation for the *in-vitro* experiments. A circuit diagram is contained in Appendix One.

The cells in three of the wells were left with no intervention and acted as the control groups. In order to mirror the study by Fujita et al. (1992), which reported a supression in cell proliferation, the cells in three of the wells were exposed to a 6 hour continuous period of micro-current electrical stimulation with a current of 1μA. The cells in the other three wells received the same level of electrical stimulation, a current of 40μA, as the *in-vivo* study. Consistency and standardisation of current levels reaching the cells in regardless of alterations in resistance for both studies was an important factor. An explanation of how this was achieved is given on page 121.

The current was delivered via sterile, high quality, stainless steel needles that acted as electrodes inserted in the lid of the well plate so they protruded into the growth medium (see Fig. 3.1).

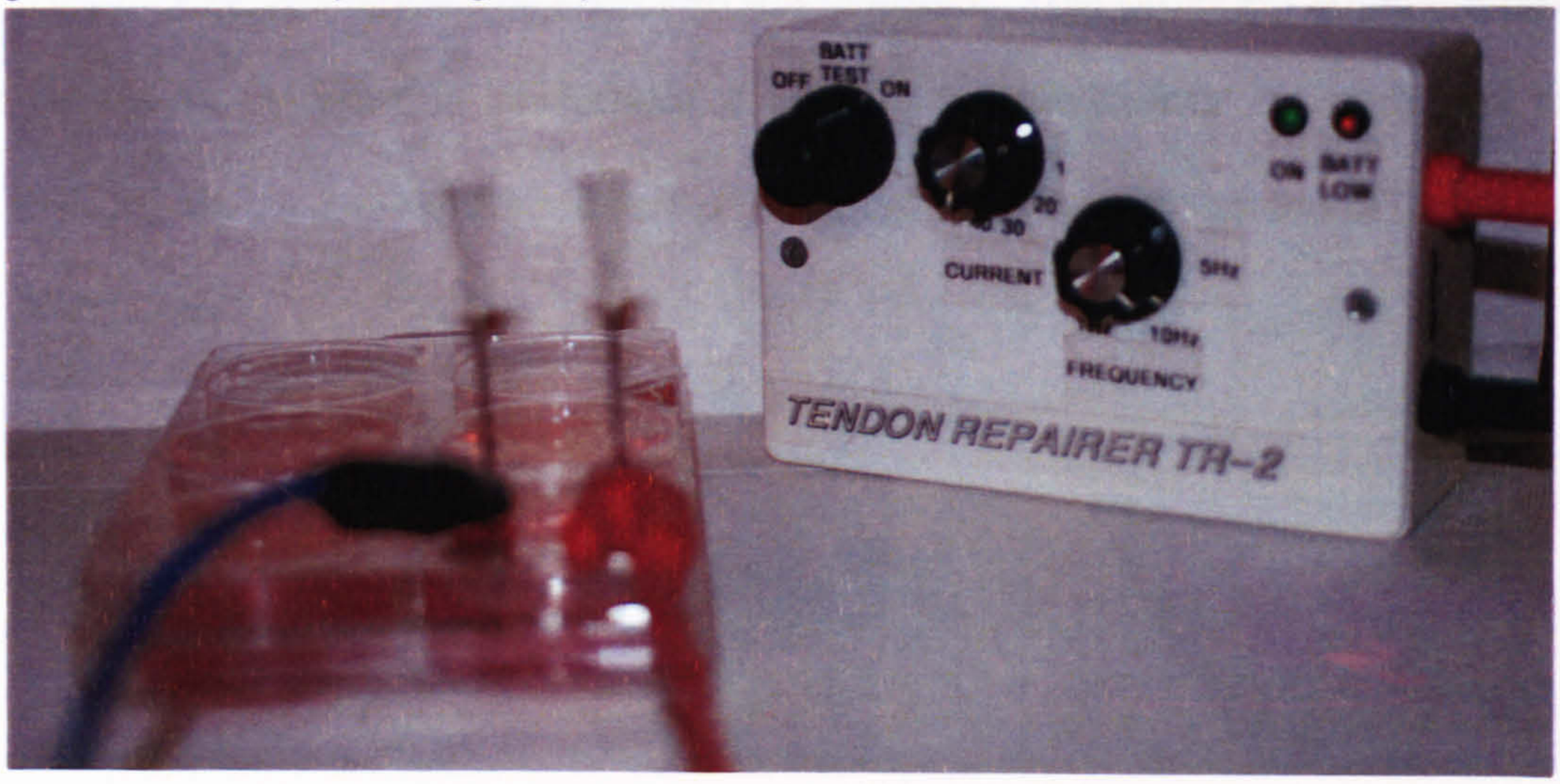

Fig. 3.1 Cells receiving the electrical stimulation

Measurement of fibroblast activity

Following the period of stimulation the cells were incubated in growth medium at 37°C. The number of cells per well was determined by haemocytometer counts and cell viability by the trypan blue exclusion assay at intervals after plating. This was undertaken at 1,3 and 7 days.

3.1.3. Human tenocyte cell study method

An Achilles tendons was harvested, under sterile conditions, from a cadaver with no known previous medical history of Achilles tendon disorders or current infectious disease. This policy was adopted in order that the behaviour of normal tendon tissue could be evaluated. A longitudinal strip of tendon within the paratenon, approximately 2cm in length, was harvested from the mid-section of the Achilles tendon. The section was placed into a sterile pot containing Dulbecco's modified medium. With a little agitation of the pot the cut ends of the tendon segment spilled the cells into the medium. This provided sufficient cells to culture in order to undertake a series of experiments to compare the behaviour of the tendon fibroblasts with the behaviour of the 3T3 mouse fibroblasts.

The following procedure was carried out under sterile conditions in a Walker safety cabinet. The cells and the medium were introduced into a 50ml universal container. The capped universal was placed in the centrifuge, which was balanced with a universal containing water of equal weight and size, and spun for 5 minutes at a speed of 1200 revolutions per minute (rpm). Following this the universal was returned to the cabinet. The medium was removed leaving the cell pellet at the base of the universal. 1ml of fresh medium was added to the pellet and this was mixed using a Pasteur pipette.

Cell number and viability

In the same manner as for the previous experiment the cell number was determined by haemocytometer counts and viability by the trypan blue dye exclusion assay (0.4%, >85% saline). The procedure was undertaken in the sterile cabinet.

The cell pellet was washed with 1 ml of growth medium. 50 µlitre of the cell pellet medium was taken and put into a sterile yellow tip.

An equal amount, 50µlitre of trypan blue dye exclusion was added to the yellow tip. The haemocytometer was swabbed with alcohol and the glass cover slip was placed over the counting grid. The trypan blue and cell mixture was injected under the side of the cover slip.

The number of cells contained on the haemocytometer 5x5 square grid was then obtained by viewing the haemocytometer under a light microscope by manually counting the number of fibroblast cells present on each square counting from left to right. Dead cells are distinguished since they take up the blue stain. The following calculation was then undertaken to determine the cell number.

The number of cells counted are multiplied by two, (x2 because of an equal dilution of cells in the growth medium to trypan blue). In order to obtain the cell number per ml it is necessary to multiply the µl number by 1000.

Experimental cell cultures

The cells were grown in a 3.5cm tissue culture treated sterile six well plate (Falcon, Becton Dickinson Co. New York, USA). 10ml of pre-warmed (37°C) medium was added to each well. The prepared cell solution was added to each well to a density of $3x10^3$ cm^2, per well. The well plates were viewed under a microscope (screened) to check the cells were present. The cultures were labelled with a the researchers name, the date and the appropriate passage (P) number.

The cell cultures were incubated at 37°C, 5%CO_2 at 100% humidity. The culture was screened each day to check for infection.

Electrical stimulation

The electrical device used was the same as the previously described experiment. The cells in three of the wells were left with no intervention and acted as the control groups. The cells in the other three wells were exposed to a 6 hour continuous period of micro-current electrical stimulation at a current of 40μA. The current was delivered via sterile, high quality, stainless steel wires that acted as electrodes inserted in the lid of the well plate so they protruded into the growth medium.

Measurement of fibroblast activity

Following the period of stimulation the cells were incubated in growth medium at 37°C. The number of cells per well was determined by haemocytometer counts and cell viability by the trypan blue exclusion assay at intervals after plating. This was conducted at 1,3 and 7 days.

3.2. Addendum: An extra In-vitro experiment

This following experiment was conducted as a result of opportunity rather than design and was concluded before a conclusive result was obtained due to circumstances beyond the author's control. However, it is believed that it was a useful potential area of study to pursue particularly in the context of understanding why the application of micro-current has the effect of augmenting wound healing.

Laboratory study undertaken

The purpose of the laboratory based experiments undertaken for this study was to isolate a collagen gel cell culture and determine if electrical stimulation had any effect upon its contraction and fibrillar formation compared with a non-stimulated control group. The method used was derived form the a previous study reported by Eastwood et al. (1994).

3.2.1. Methodology

The collagen gel was prepared by mixing 4 ml of native acid soluble type 1, rat tail collagen with 0.5 ml of 10 X Dulbecco's modified Eagles medium, DMEM. (Life technologies, Paisley, Scotland). A balanced pH was achieved by drop-wise addition of NaOH.

Cell preparation was undertaken using type 1 collagen that were prepared by the clostridial collagenase treatment of samples obtained directly from the operating theatre. A cell suspension in 0.5ml of DMEM, with 10% fetal calf serum plus 1% glutamine and 1% streptomycin/penicillin buffered with 25mM Hepes was produced. This was added to the neutralised collagen solution, which had a concentration of 1mg/ml. The cell culture medium was then poured into a tissue cultured treated, 3.5cm diameter, six dish well plate, (Falcon, Becton Dickinson Co. New York USA). This allowed four wells for stimulation and two wells to act as a control.

Stainless steel wire electrodes were used to apply the current to the gels. The wire was hooked over the edge of each plate separately, the end of each wire protruded into the culture medium. Once in place a lid was secured to the well plate.

The gels were placed in a 100% humidity incubator at 37°C perfused with 5% carbon dioxide in air. Initially the electrical stimulation parameters were set with a view to determine if a pattern emerged by using high and low levels of current and frequency. These experiments were carried out using the same electrical device as the *in-vivo* study. The device was able to deliver an alternating or direct current with the facility to modify the waveform. For this set of experiments an direct positive current was used with a square wave form. A constant current generator ensured that the current selected was maintained regardless of any change in the resistance of the tissue, electrodes or growth medium.

The following levels were set:

Plate sample No.	Stimulation parameters
1	40μA, 10 pulses/sec
2	40μA, 400 pulses/sec
3	400μA, 400 pulses/sec
4	400μA, 10 pulses/sec
5	control with electrodes
6	control and no electrodes

The duration of stimulation was the only factor that would initially be changed.

Analysis of contraction

Gel contraction kinetics were analysed following the period of stimulation after 3, 6, 12 and 24 hours by measuring the gel diameter.

3.3. The clinical study

3.3.1 Aims and objectives

Aim: The aim of the clinical, *in-vivo*, study was to investigate if patients with Achilles tendon pathology, exposed to the experimental micro-current treatment returned to a better functional outcome than those patients undergoing current conservative methods measured by greater reduction in pain and stiffness.

Objectives: The study aimed to answer the following three specific objectives:

1. Is there a difference in the time that a change or cessation in symptoms is noticed in the two treatment groups?
2. When comparing the two treatment groups, is there a difference in the resultant functional outcome related to a resumption of the patients activity pre-symptom(s)?
3. Is diagnostic ultrasound sensitive and specific to the clinical symptoms reported in Achilles tendon pathology?

3.3.2. Subject Selection

Two main factors determined the method of patient selection.

1. Subjects with a suitable clinical condition were required
2. The number of subjects needed to meet the statistical criteria.

In general, patients with Achilles tendon problems present to their general practitioner (G.P). The clinical management of these patients, the subsequent clinical management route, and the time taken on that route, appear to be diverse, unquantifiable and dependent upon the individual G. P.

The flow chart below highlights the possible pathway(s) taken
(for a National Health Service patient)

Acute Tendon Injury

↓

Sent home ← Accident & Emergency Department → Referred to G.P

↓

Referred to Orthopaedic Department

↓

Surgery/Conservative Physiotherapy

↓

Condition clears up or becomes Chronic

Chronic Tendon Injury

↓

Advice and/or rest ← G.P → anti-inflammatory drugs

Refers and requests physiotherapy

↓

Orthopaedic or Rheumatology clinic

↓

Surgery/Conservative Physiotherapy

↓

Discharged with (or without) improvement

↓

Patient seeks alternative treatment or lives with the condition

The clinical management using conservative methods of physiotherapy can include deep friction massage, laser therapy, ultrasound treatment, interferential electro-therapy, general massage and stretching. Information obtained for this study demonstrates that the order and combinations of delivery of these treatments appear to have no formalised pattern or rationale. It is quite feasible that two patients with a similar clinical condition attending different physiotherapists will follow quite different programmes of clinical management.

Obtaining subjects with appropriate conditions would require the co-operation of the medical staff involved with the patients at one of the stages of the patients' clinical pathway. Such direct access was not available for this study and, regardless of the evidence of studies highlighted in the literature, there was a degree of scepticism from physicians regarding the proposed new treatment regime utilising micro-current.

An interesting point to note, however, which perhaps highlights the inconsistent results that present treatment regimes offer, is that when patients, particularly patients involved with sporting activities, were informed of the research programme, they actively requested to be involved. This resulted in the recruitment of possible subjects for screening becoming easier as the study progressed.

Having identified the referral source of the subjects it was important to ensure that the number of subjects available would furnish the study sufficiently. The anticipated difficulties in obtaining a steady stream of potentially suitable subjects was partially overcome by accessing subjects directly. An open letter was placed in two national athletic publications requesting anyone with a chronic Achilles tendon condition to contact the author of the study. Potential subjects then underwent an initial screening consultation in the same way as the subjects coming from a direct referral source. Once a suitable subject had been identified their clinician or general practitioner was contacted and the procedure then followed was consistent with the direct referral subjects.

The response was very good, although many subjects were unsuitable for inclusion in the study for reasons such as geographical location.

However, it did indicate the extent to which Achilles tendon injuries affect athletes and the myriad of treatments used in an attempt to cure them.

In summary, for subjects to be included in the study, they must present with a minimum of a three month history of one, or a combination of, Achilles tendon pain, stiffness and function impairment. In reality this almost certainly happened by default as it took patients at least three months to work their way through the referral system.

Patients with an acute total rupture were excluded from the study since the clinical nature of the condition required immediate treatment and it would be difficult to guarantee availability at the time of these injuries, additionally, the serious nature of the condition would make it highly unlikely to obtain enough referrals from this group to be able to draw a significant conclusion as to the worth of the new treatment.

3.2.3. Study design

The human body is a complex organism and its functioning is far from understood. For this reason it is often difficult to predict the outcome of a new treatment regime, or indeed, a current one, particularly if its documented clinical efficacy is based upon anecdotal evidence. This makes it necessary that the new method of treatment is evaluated in direct comparison with the existing one.

A brief explanation of the reasoning behind the chosen study design is required. This clinical study has the firm objective of establishing the efficacy of one form of clinical management of chronic pathology of the Achilles tendon in comparison with another. The two clinical management regimes must run concurrently with each other, with all subjects following the same criteria for selection, randomisation and monitoring.

The essential consideration for any proposed new treatment is whether the new treatment demonstrates greater efficacy than the standard treatment for the given clinical conditions. It would be unacceptable to stop the standard form of treatment in preference to a new form without justification.

In order to test the micro-current application to the strongest scientific rigour the author believed it was important to eliminate the placebo effect. It was planned, therefore, to utilise a double blind method. As the new treatment does not induce any sensation on delivery it was possible to give the impression to the patient that they were receiving the new treatment when in fact they were not. The micro-current machine used in the study was set up to produce the same audible sound regardless of whether it was delivering current or not.

Three groups were planned, A - a control group receiving the standard treatment only, B - a group receiving the standard treatment and thinking they were receiving micro-current. C - a group receiving the standard treatment and micro-current. This satisfied the various ethics committees which approved the study to be undertaken in their hospitals as no group had their standard treatment withdrawn.

On the face of it this was a sound scientific design. The standard treatment alone could be evaluated through group A; group B would measure the placebo effect on the patients being given the new treatment method and C would be able to evaluate the efficacy of micro-current with the standard treatment.

There were, though, major technical flaws with this design. Firstly, the micro-current application was not being evaluated as a single treatment so it could not be assessed for its own worth. Secondly, and the most important factor that dictated a revised study design, was that the literature had reviewed some studies, (Clement et al 1984; Kvist et al. 1988; Williams 1984; Schmidt 1986; Wise 1968), that showed that not only were some of the standard treatments ineffective but, actually detrimental to the tendon presenting with pathology so causing further aggravation to traumatised or immature tendon tissue. An example of such a treatment noted earlier in this study (page 21), is deep friction massage, a treatment in common use. It was also suggested that such is the harsh nature of the deep friction treatment that patients may indicate they are feeling better to avoid repetition of it.

In an attempt to quantify this suggestion, a small study was undertaken to evaluate this treatment using diagnostic ultrasound as the objective measure. The results of this small study will be discussed in the discussion section of this thesis, but it is relevant and pertinent to outline briefly the finding at this point. Patients were scanned using diagnostic ultrasound before and after deep friction massage treatment. In all cases examined, (n = 10), the patients returned with intense pain after treatment and with sonographic findings that showed the paratenon swollen with fluid, consistent with an inflammatory response.

Repeated ultrasound and laser treatment of chronic Achilles tendon pathology also has its critics and there is an almost universal condemnation of the use of steroids injected into the tendon. This latter treatment is still used by some clinicians, particularly it would appear, in sportsmen/women seeking an early return to competition following injury.

The lack of consensus about the efficacy of current treatment regimes and the controversy surrounding some of them made it evident that a study design that involved mixing the standard and new treatment regimes would be inappropriate. For this reason, it was concluded that the only suitable method by which the proposed new treatment regime could be properly evaluated and would yield significant results, would be one which separated the two groups.

However, this meant that the placebo effect could not be eliminated, for it was deemed unethical to have a group where the standard treatment was stopped to be replaced with no treatment, i.e subjects of the group believing they were receiving micro-current when in fact they were receiving nothing. It was also felt that objective testing would help to evaluate the current treatment regimes, perhaps more accurately than they had been previously.

It is of interest to establish how standard treatments stand up to the rigours of a randomised study and information concerning their efficacy may be of as much significance to the management of chronic Achilles tendon pathology as information about the efficacy of the new treatment.

For the reasons stated above a *prospective, randomised, parallel study was selected as the most appropriate of study design.*

3.3.4. Randomisation of the subjects

With forty eight subjects involved in the study it was essential that equal numbers of subjects were allocated to each group but with a completely random distribution. To ensure this a balanced, or restricted, randomisation method was employed. The two groups, the standard treatment group and the new treatment group were allocated the prefix A and B. The allocation procedure was organised in such a way that equal numbers were allocated to group A and group B for the forty eight subjects.

The method employed was to use successive blocks of four patients. Firstly all the combinations of A and B are generated with equal numbers of A and B; they are:

1 AABB	4 BBAA
2 ABAB	5 BAAB
3 ABBA	6 BABA

These combinations were then allocated the numbers one to six as above.

The numbers 1 to 6 were then scrambled by a simple computer programme to give the sequence 654131342611. As forty eight subjects were required the first twelve digits chosen gave the completely randomised selection for the trial. The balance of subjects allocated to group A and B is therefore maintained throughout the study.

The pattern of randomisation was as follows:

BABA, BAAB, BBAA, AABB, ABBA, AABB,

ABBA, BBAA, ABAB, BABA, AABB, AABB.

In considering patients for inclusion in the study, it was important that they had undergone a clinical examination by their consultant or General Practitioner, and as a result, had received a diagnosis indicating chronic Achilles tendon pathology. Often, however, clinical examination was found to be brief and for this reason, regardless of the route of referral, all subjects were required to undergo a standardised further clinical baseline assessment undertaken by the researcher. An essential point about the randomisation is that the pattern of randomisation was drawn up prior to the commencement of the study and the group allocation was held by a person unconnected with the study.

When a patient fulfilled the clinical criteria for inclusion in the study, following clinical assessment, information concerning the group allocation for that subject was then sought. In this way there could be no choosing "light pathologies" for one group and not another so avoiding prejudice or bias to a particular group or outcome.

Where patients who were referred for inclusion in the study had undergone previous treatment that had been unsuccessful, or they were continuing with that treatment, they were required to stop it for a minimum period of a month.

Subsequently they were required to have another clinical assessment and only then if they met the clinical criteria for the study were they allocated to a group. This step was essential to ensure that the standard treatment prescribed by their consultant or general practitioner would not,

1. - influence the efficacy of the new treatment, or

2. - produce a result which could be attributed mistakenly to the micro-current treatment, if they were allocated to group B.

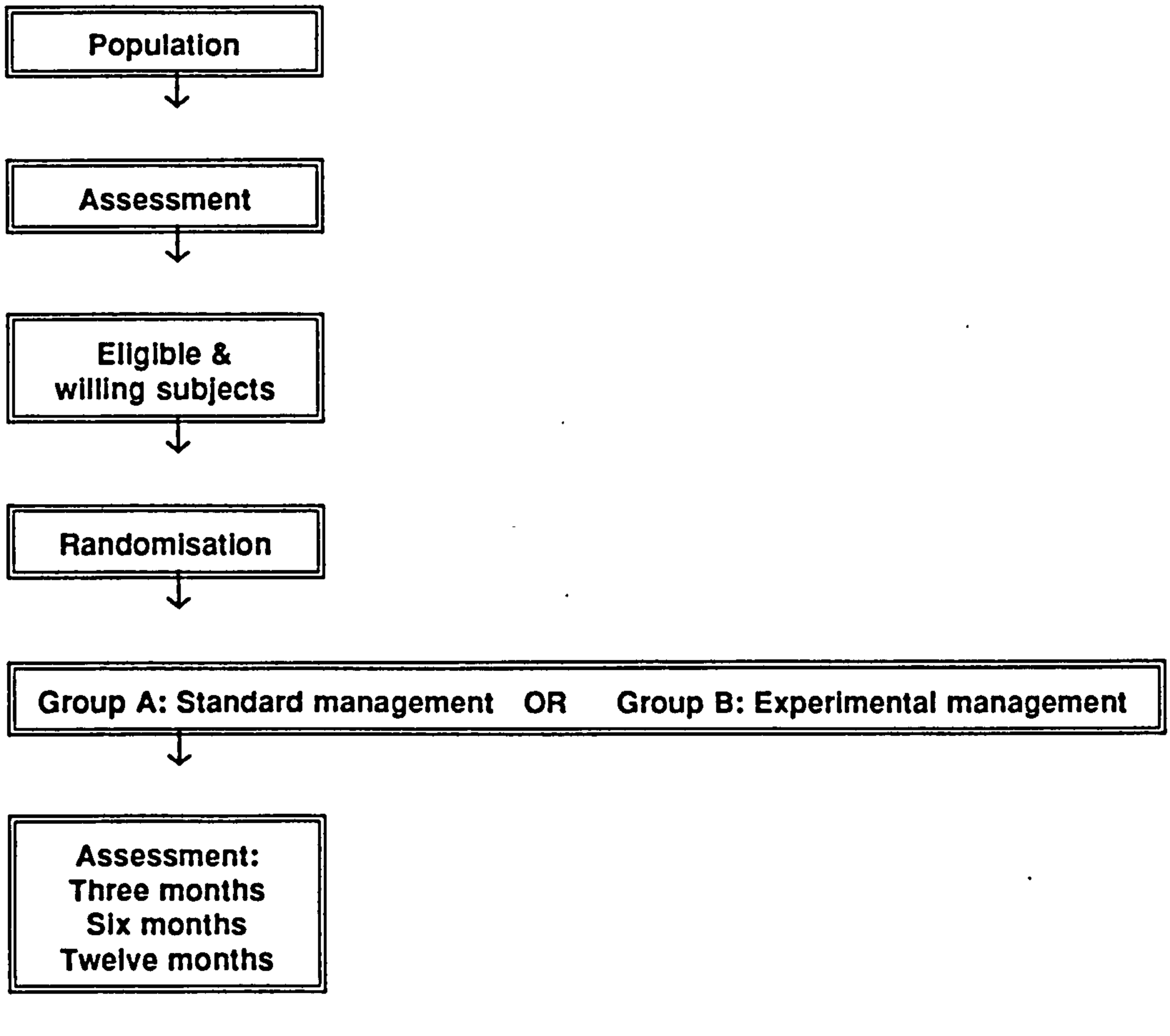

Fig.3.2 - A Flow Diagram: Patient Pathways

3.3.5. Apparatus and procedure

The subjects allocated to group A underwent the current clinical management prescribed by their clinician for the treatment of the Achilles tendon presenting with chronic pathology. As the distribution of these treatment methods varies from clinician to clinician it was difficult to predict in advance the particular clinical pathway an individual would follow. The preliminary research undertaken prior to the commencement of the study had suggested that there was no clear clinical rationale behind the various treatment plans.

Indeed, it was apparent that a subject may be exposed to several different therapies depending upon the attending physiotherapist and certainly friction massage, ultrasound and laser therapy appeared to be the most common treatments.

Separating group A subjects into various sub-sections of the different standard treatment regimes was totally impractical for this study. The numbers of patients required to make the study statistically valid would have been vast and most importantly there could have been no guarantee that subjects would have been exposed to only one treatment modality for the entire period that an individual participates in the study such is the difference of opinion concerning the efficacy of the standard treatment available.

In the light of the literature in which the efficacy of all the current treatment methods are questioned, it was concluded that little problem was posed for the study by the fact that not all subjects in group A would be receiving the same treatment. Therefore, it was felt valid to evaluate and compare the outcomes of the new treatment regime, to be given to group B subjects, with outcomes from group A taking their various methods clinical management together. Group B, the micro-current group, were all to be exposed to the same treatment parameters and establishing the appropriate level, duration and type of micro-current to be used was, perhaps, the most difficult aspect of the study.

There is a general consensus of opinion, as highlighted by Picker (1987), that a low level of current tended towards a better acceleration of collagen production than did a higher level of current. However, there was no empirical evidence available that gave a definitive and finite value, although a positive current was certainly reported consistently as being better for treating soft-tissue.

The rationale behind parameter selection for the micro-current treatment that forms the basis of this study was drawn from the current literature. However, it is fair to state that due to any lack of consensus the parameters used are not put forward as necessarily the optimum choice. The outcome of these current studies, however, may shed a little more light on this.

The electrical device used to deliver the micro-current treatment, in this study, is a computer controlled, solid state unit, with a touch screen control panel. It was manufactured and supplied by Face and Body Perfector Ltd (Burnham, England). It was possible to alter the following parameters on the unit:

- **Current**: A range of 1-500μA
- **Wave shape**:Sine, Rectangular, Square and Ramp
- **Duration**: Minute intervals. Range 1 minute to 120 minutes.
- **Frequency**: A range of 0.5-500Hz
- **Polarity**: Alternating, or rectified to positive or negative direct current
- **Power Supply**:Battery or Mains supply

The device has a constant current generator. This has a negative feedback mechanism which monitors the resistance to the flow of current so ensuring that the average pre-set current will be delivered in a homogenous manner regardless of differences in the subcutaneous fat levels in the skin. Therefore following the principle of Ohm's law all subjects received the same current regardless of their age (which affects skin thickness) or skin condition by the device altering the voltage as the resistance changed. The skin normally offers a large resistance to electric current and this is further affected by moisture.

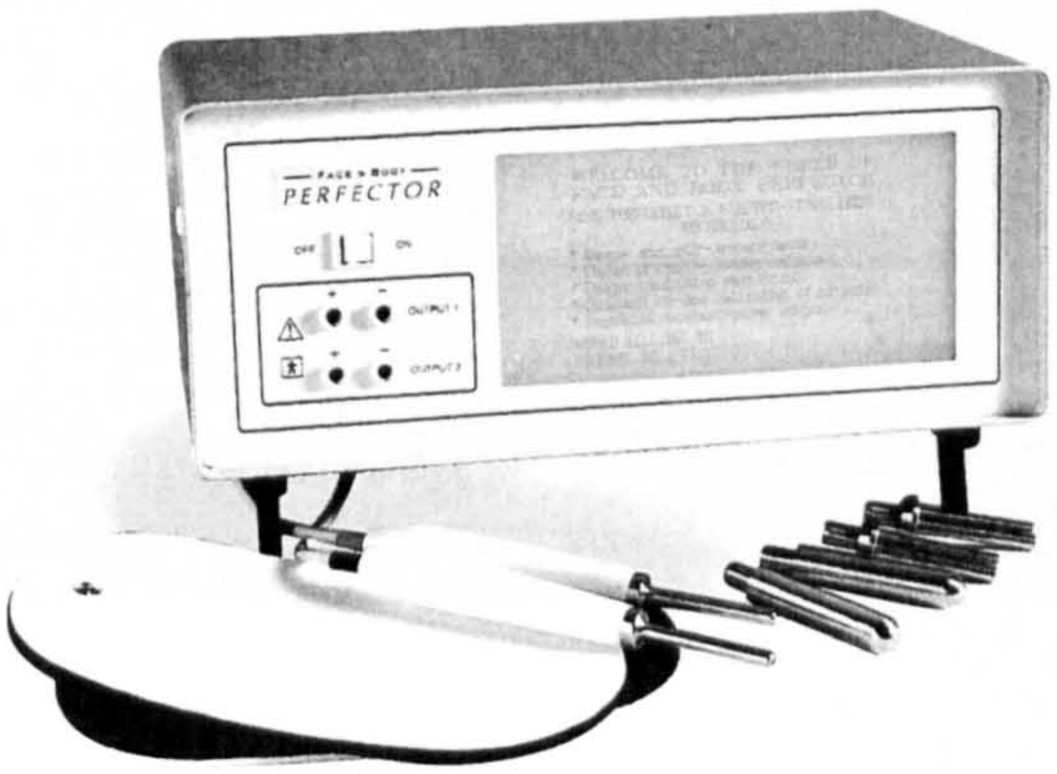

Fig.3.3. The micro-current device used for the study

For example, the electrical resistance from one hand to another can vary from over 1,000,000 ohms (Ω) for very dry skin to less than 1000 Ω for wet skin.

In summary group B subject's treatment regime was as follows: -

Daily electrical stimulation to the Achilles tendon was applied via two skin surface stainless steel electrodes containing an integral coupling gel which ensured a good contact between the electrode and the skin. One electrode was placed on the medial side of the tendon and the other on the lateral side adjacent to the area of the pathology. This was determined by the clinical and ultrasound investigation. Figure 3.4. shows the palpation of tendon nodule prior to the placement of the electrode. The following electrical parameters were used: A rectified alternating current of 40μA modified to a square wave form, positive current pulsed at a rate of at 10 per second for a period of fourteen days. Subjects were treated for half an hour per day.

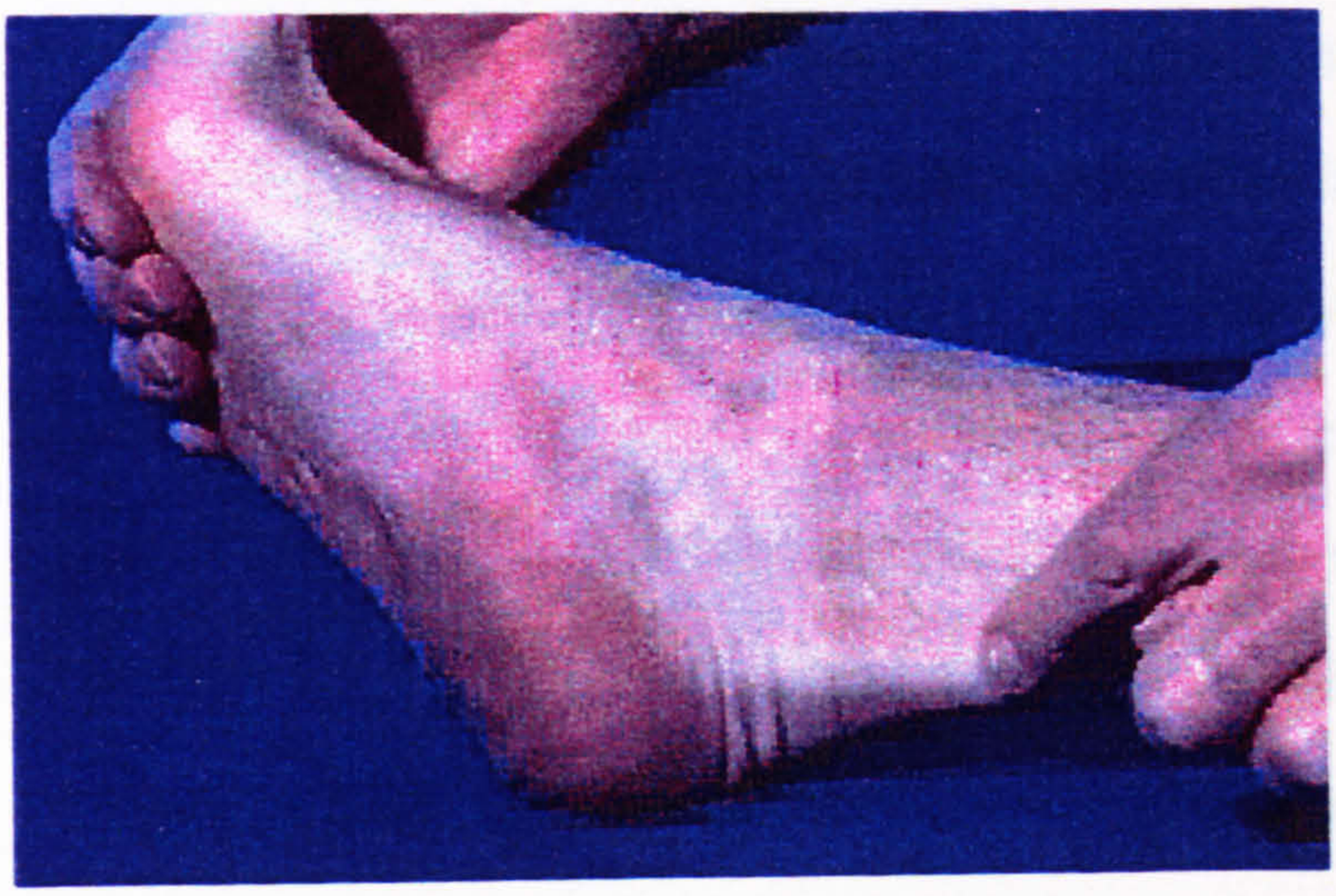

Fig 3.4. Site of electrodes on the skin surface of Achilles tendon

3.3.6. Clinical assessment

In addition to the baseline clinical examination undertaken as subjects entered the study, a series of objective clinical tests were undertaken. Objective clinical tests are an essential component of the study, both to evaluate the efficacy of the treatments and to assess the subjects' clinical conditions on presentation. Diagnostic ultrasound imaging, isometric strength tests and dorsi-plantar and plantar-flexion assessments were undertaken. In addition, a more subjective measure was used, the subjects' own assessment of their problem (questionnaire in Appendix Four). This utilised indicators such as levels of discomfort/pain, noticeable functional disability, and duration of the problem.

In some studies, for example Kainberger et al.(1990), patients are grouped depending upon the duration of their symptoms into those with a history lasting, two months or less, three to twelve months and more than a year.

This was not undertaken for this study. The criterion for subject inclusion was that they must have had their symptoms for a minimum of three months. By this time the injury would be past the sub-acute, post-inflammation stage so helping to ensure that the study was not misled by temporary, minor, acute, one-off, conditions. Such is the documented difficulty that the chronic tendon presents to the clinician, it may be claimed with confidence that once insidious pathology has affected the tendon it makes little tangible difference to the clinical management whether the condition is six months or six years old. Certainly there is no clinical evidence that contradicts this point of view.

It was anticipated that in reality by the time the patients were referred for inclusion in the study their symptoms will have been evident for a minimum of six months duration. It should also be mentioned that, in many cases, patients put forward for the study have had other therapies that were unsuccessful.

Upon presentation for entry into this study patients' symptoms were consistent with one of the categories below:

* **Excellent:** A full range of movement through the Achilles tendon comparable with the contra-lateral side. For the athletes - can run at full competitive speed, distance and can undertake their accumulative weekly training regime with no significant symptoms.

* **Good:** Can train at pre-injury levels with only intermittent or mild discomfort, and dorsi-flexion of the affected Achilles tendon is within 5° of the contra-lateral side.

For bi-lateral cases a dorsi-flexion of at least 20°.

* **Fair :** The patient is asymptomatic or mildly symptomatic in relation to activities of daily living. For athletes there is discomfort that does not allow a return to pre-injury activity, in terms of speed and distance, and this has dictate cessation of competition.

* **Poor :** The patient is symptomatic during activities of daily living and is unable to perform daily activities without discomfort, for example, driving or walking upstairs.

The patients would not present with a good or excellent value of the criterion at the initial assessment, but the same criteria were used when monitoring their progress.

In order to undertake statistical analysis of the general assessment each classification was allocated a numerical score as follows: -

Poor - 1 Fair - 3 Good - 5 Excellent - 7

The rationale for employing several different objective tests together with a subjective examination by the patients clinician and a subjective assessment by the subject themselves was to ensure that their diagnosis of the type of chronic Achilles tendon was as accurate as possible.

In addition, some valuable information concerning the worth of these assessment tools in relation to patients' symptoms was obtained.

3.3.7. Diagnostic ultrasound assessment

The value of sonography as an aid to the clinical diagnosis of the Achilles tendon presenting with pathology has already been documented in the review of previous studies. It is important to explain at this juncture how the results of the sonographic data obtained will assist in evaluating the efficacy of the treatment regimes.

Ultrasound is used both for establishing the initial diagnosis and also for monitoring the progress of the tendon's pathology. As previously stated, many studies have evaluated the accuracy of sonography of the Achilles tendon presenting with pathology.

However, two studies are of particular value to this current study; Kainburger et al.(1990) and O'Reilly & Massouh (1993).

It is important from a clinical perspective to state the various forms of Achilles tendon pathology and to correlate these with sonographic findings. The work of Clancy (1990) and Puddu et al (1976) is particular helpful and the following classification of pathology was used as a guide for this current study:

* **Tenalgia:** A painful tendon, without evidence of alteration in the tendon itself

* **Paratenonitis:** Inflammation of the highly vascular paratenon, often accompanied by fluid around the tendon.

* **Paratenonitis with tendinosis:** Paratenon inflammation associated with intra tendinous degeneration.

* **Tendinosis:** Intra tendinous degeneration due to atrophy (age, micro-trauma, vascular compromise etc.) The is a non inflammatory condition.

* **Tendinitis:** Symptomatic degeneration of the tendon with vascular disruption and an inflammatory response. May present as acute, sub-acute or chronic.

* **Enthesopathy:** Pathological involvement at the osseous end of the tendon, often involving the fibrocartilaginous transitional area with vessels coming from the bone and the periosteum. As described by Perugia et al.(1976).

Peritendonitis is an old term used to describe a combination of paratenonitis and tenonitis. Tendinitis is also known as tendinosis.

3.3.8. Statistical Methods

3.3.8.1. Study size calculation

The appropriate number of patients that it was necessary to recruit to the study was dependent on four components.

Response to the standard treatment

As a comparison study was to be undertaken it was important to postulate the response rate of the subjects to the standard therapy, i.e the response rate of the control group. The value of this response is denoted by π_1 to distinguish it from the value that was to be obtained from the new treatment group denoted as π_2.

Postulating the response for the control group was difficult for there are no studies available which adequately demonstrate that the standard treatment regimes are reproducible clinically. Williams (1984), goes so far as to state that such is the capricious nature of chronic Achilles tendon pathology that any response to healing may be no more a reflection of the treatment than of the condition itself.

If, in anticipating the response to standard treatment, the figure denoting the number of subjects responding is set too high then a greater number of subjects than is necessary will be required to demonstrate any potential difference between the two treatments. Conversely, if set too low, the study size may be too small to highlight a difference should one exist. For this study the response rate for the standard treatment was postulated at thirty per cent.

This figure was obtained by gaining anecdotal opinions for practitioners in current clinical practice.

The anticipated benefit of the new treatment

It was also important to postulate the response rate in patients receiving the new treatment programme. This is denoted by π_2. It was also important that this was postulated such that the response rate for the new treatment group would be better than for the control therapy otherwise no benefit would be derived from the study.

For this study, where the human application of this treatment was new the response rate remains an unknown factor. However, the study was planned so that if the new treatment gives an advantage this can be detected. Based upon animal and different, but similar, human applications for comparison the response rate for the new treatment group was postulated as seventy per cent. Thus the anticipated benefit of the new treatment, σ, was calculated:

$$\sigma = \pi_2 - \pi_1$$

Once the study is completed and the results from both groups are known the response to the conservative treatment becomes known as p_1 and the response rate to the new treatment as p_2. It was anticipated that π_1 would be similar to p_1 figures and π_2 similar to p_2..

Significance level

Statistical analysis is concerned not only with summarising data but also with investigating relationships, (Campbell &.Machin, 1993). This study is based on the theory that the new micro-current treatment is more effective in the treatment of chronic Achilles tendon pathology than present standard treatments. This forms the study hypothesis.

In most circumstances, however, it impossible to prove, beyond doubt, a study hypothesis. Accordingly statistical analysis techniques provide a more logical approach for disproving rather than proving an hypothesis. This is known as the null hypothesis and therefore the probability of detecting a significant difference when treatments are equally as effective is set at apparently the arbitrary level of 5% (0.05).

Campbell & Machin, in the publication Medical Statistics, argue against the rigid use of significance tests. They discourage the use of statements such as "the null hypophysis is rejected when $p< 0.05$" or, "worse, we accept the null hypothesis $p > 0.05$". The basic rationale behind the null hypothesis is it is easier to disprove a theory rather than to prove one.

3.3.8.2. Study size

Taking into account the factors outlined in the preceding section, the sample size was calculated to detect an improvement in the proportion of subjects recovering, e.g. a response rate of 30% recovering with the standard treatment compared with 70% response rate for the new treatment. The power of the test was set at 80% with a 2-sided significance level of 5%.

The figure was calculated using the method of Pocock & Stuart (1983).

$$n = \frac{p1x(100-p1) + p2x(100-p2)}{(p2-p1)^2} \times f(\alpha\beta)$$

Where f(0.05,0.2) = 7.9

$$n = \frac{30(70) + 70(30)}{(70-30)^2} \times 7.9$$

$$n = \frac{2100 + 2100}{1600} \times 7.9$$

$$n = 2.625 \times 7.9 = 20.73$$

Therefore to detect an improvement from 30% to 70% the study requires a minimum of:

N = 42 subjects → 21 in each group. To ensure an even randomisation and to allow for some leeway in the postulated response rates the study size was rounded up to 48 subjects, with twenty four in each group.

3.3.8.3. Methods of data analysis

In order to evaluate the response rate of the group A subjects to the standard treatment and the response rate of the group B subjects to the new treatment regime it was necessary to expose the data to the rigours of appropriate statistical tests. This enabled a value judgement to be made concerning the statistical significance of the response rate of the subjects in the two groups to the different treatment regime.

Categorial variables, for example sex, were compared between the two treatment groups using the chi-squared test. The unpaired t-test will be used to compare the ages in the two treatment groups.

After calculating the difference between interval one and the subsequent interval assessments the Mann-Whitney U test was performed to assess changes in the ordinal marker variables such as Achilles tendon pain, stiffness and the general assessment. The un-paired t-test could have been used to assess the continuous deflection variables, but for consistency the Mann-Whitney U test will be used throughout. As long as the scores are an accurate reflection of the ordering, the actual values would have had little or no effect on the final outcome. The scores were necessary because there were several variables involved in assessing an individual's progress and it was important that any improvement or worsening of the patient's pathology was accurately reflected in the data analysis.

In order to make a fair comparison between the different symptoms of the subjects a scoring system was devised. This was not taken from any previous study for none came to light that fulfilled the desired criteria, although there are similar scoring mechanisms discussed in the 35-point shoulder rating scale (Ellman, Hankerge & Bayer 1995) and in the assessment of elbow trauma response by Harrie & Verhaar (1995). The scoring system devised for this study may appear rather complex but it was necessary to produce a method that discriminated between different, although similar, cases while not getting bogged down in complicated formulae.

The variables that occur with a positive diagnosis of Achilles tendon pathology have been identified as discomfort and/or pain, decreased flexibility, loss of strength and additionally there are the diagnostic ultrasound findings.

It was decided to separate the ultrasound data from the other variables, to enable the modality to be evaluated against the other methods of clinical assessment. To make the scoring system clear each one of the parameters, pain, stiffness and ultrasound will be discussed.

Pain: The level and frequency of pain or discomfort a subject suffers from is a good indicator of the severity of their pathology. The pain scale was set as follows:

Subjects level and duration of pain/discomfort	Score
Totally non-symptomatic	0
Pain with exercise, ceases when activity stops	25
Pain with exercise, gives prolonged symptoms	50
Pain with daily living activities, ie driving, walking	75
Total pain	100

Table 3.1 - Pain scoring system

In addition subjects are asked to indicate, on a 1-10 scale, the severity of their pain/discomfort, where one is a very mild discomfort and ten is likened to having red hot burning tongs put on their tendon, this is how some patients have described the intensity of their pain.

0----1----2----3----4----5----6----7----8----9----10

No pain Red hot tongs

Linking this rating to the Table above enabled a greater degree of discrimination. For example, if a patient, reports pain with exercise which ceases soon after accords with a score of 25 on the pain table. During the exercise the pain is quite severe and subject X reports a score of 7. Overall then the subject will score, on the pain scale, a total of 32 (25 + 7).

Using this scoring method, an evaluation of treatment may be made even if a subject is not non-symptomatic following treatment. For example, if the subject, Y, entered the study exhibiting pain on exercise that gave prolonged symptoms and with a pain rating of 6 then the initial score for subject Y is 56 (50+6). If following treatment subject Y reports only mild discomfort with exercise they would score 26 (25+1), a considerable improvement.

These scores can also be correlated with the stiffness/flexibility score and the ultrasound findings to produce a complete picture of the subjects' progression. For example, does a subject with a significant level of pain or stiffness demonstrate the appropriate appearances on ultrasound?.

Flexibility: This is simpler to classify and is illustrated in the table below.

Tendons flexibility	Score
No stiffness	0
Stiffness post-exercise	5
Morning stiffness	5
Loss of dorsi/plantar flexion of more than 5°	5

Table 3.2 - Flexibility scoring system

The scores used in order to attribute a numerical value for the flexibility or stiffness are less than the pain scales due to the fact that the symptoms of stiffness are less severe. If subjects have two or more of the flexibility categories, which is likely for more severe cases, then the scores are added together. As a subject progresses through the study flexibility may be numerically compared from one interval to another. Additionally the flexibility score may be added to the pain score. For example, subject X, previously mentioned (pain score of 32), may only notice stiffness post-exercise, they would then need to add five to their score, giving a score of 37. If in addition they suffered from morning stiffness they would add 10 to their pain total, resulting in a pain score of 42.

Justification of the use of the pain, stiffness and general assessment scoring method

The important aspect of a measurement scheme is that measures, with a reasonable degree of accuracy, what is designed to measure and that there is an adequate degree of discrimination between one criterion and the next. The pain and stiffness score was designed specifically to provide this degree of discrimination for the clinical condition under examination. An example can best demonstrate the reason for the large numerical gap, 0, 25, 50, 75, 100, chosen between each marker.

Assume that patient, X, presents with an initial pain score of 57, he has pain with exercise which gives prolonged symptoms at a subjective pain score of 7.

If following his treatment he reports that he still gets pain, but it is at a reduced level of 4, and it ceases when activity stops, he will then have a score of 29, 25+4. It is clear that an improvement has been made.

However, if the existing numerical values for each marker of 0, 25, 50, 75, 100, were changed to contiguous numbers 0,1,2,3,4, the following could occur. Patient X would have scored 9 at initial assessment, 2+7. Following his improvement his score would have been 5, 1+4. It would then not be possible to discriminate between the condition suffered by patient X from another patient, Y, who also scored 5 , 4 (total daily pain) at a level of 1 whose condition, from a clinical perspective, could be considered more severe because the tendon is giving symptoms with little or no aggravation. In addition patient X would present with a condition that the assessment scheme told us was worse than patient Y.

The stiffness score was based upon the same principle. The accumulative scoring mechanism means that the more severe the condition the higher the score. Before the scoring system was devised anecdotal evidence provided the author with sufficient information to suggest that a sufferer of Achilles tendon pathology, for example would not have loss of dorsi/ plantar flexion without having an accompanying degree of stiffness.

The numerical values applied to the general assessment (GA) scores allowed the author to undertake a statistical correlation analysis, primarily between GA and the ultrasound findings. However, it was a useful tool to assess the validity of the scores applied to the pain, stiffness, GA, and the ultrasound findings.

Strength: The strength of the gastrocnemius/soleus muscle unit transmitted through the Achilles tendon was assessed using a static isometric plantar-flexion test Figure 3.5. The foot plate of the boot was linked to a strain gauge which produced a numerical read-out when the foot was plantar-flexed against the plate. All patients conducted the test in a seated position with the leg under test in a horizontal position. This eliminated the effect of gravity.

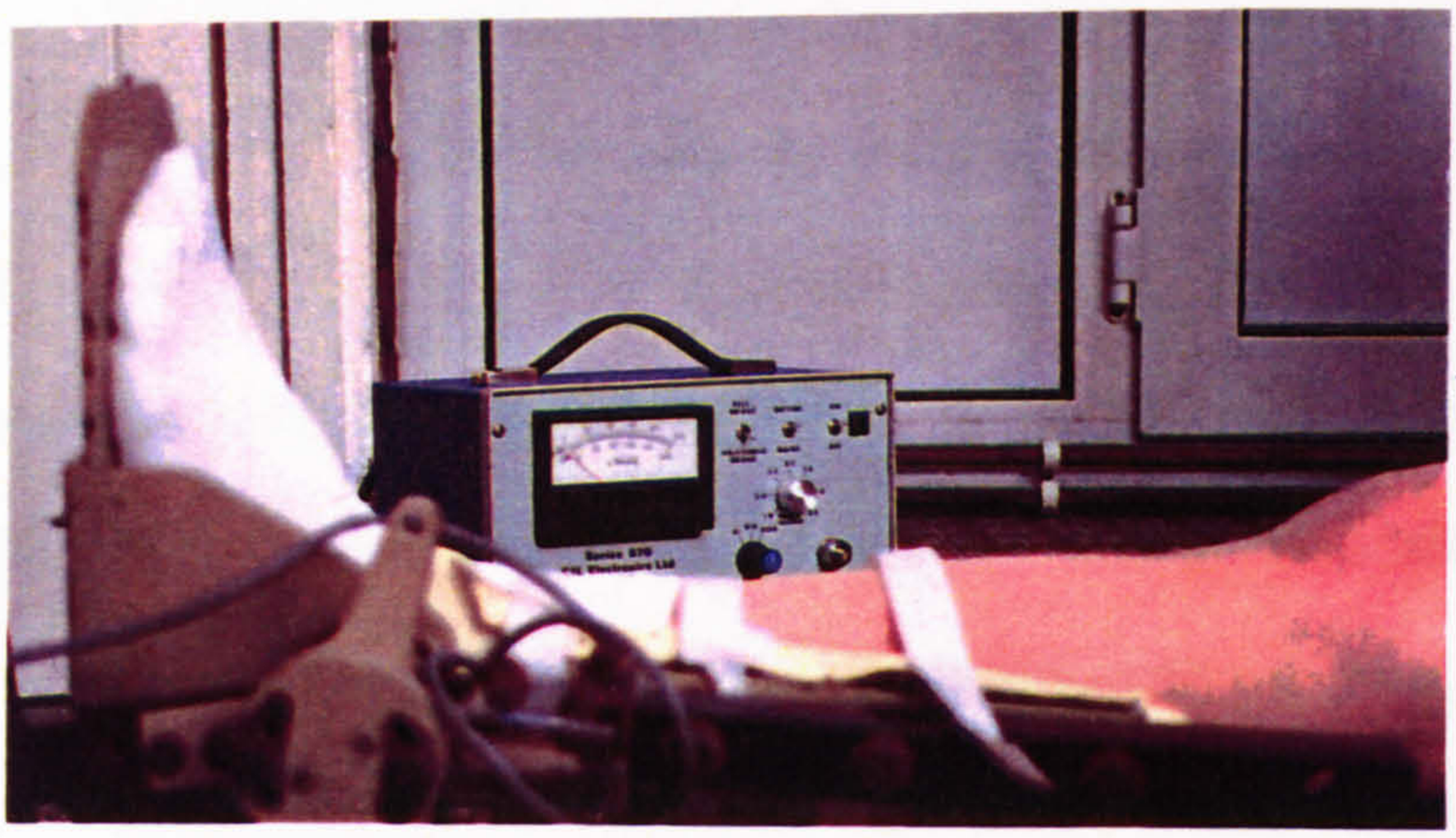

Fig.3.5. Isometric plantar-flexion test device

Three attempts were conducted for each test and the best score recorded. Isometric testing was used because there is little or no shortening of the muscle unit and therefore this would produce a static uniformity of pressure in addition it eliminates different strength patterns produced at different angles of contraction. However, the strength test was not included in the scoring criteria, although it was used to assess the patient's clinical condition. Pre-study assessment demonstrated that many subject's presented with bi-lateral Achilles tendon pathology, therefore no individual measure of normal strength could be made for it was not possible to use the contra-lateral side to evaluate tendon strength or an improvement in tendon strength.

It also proved to be the case that many athletes continue to train and compete with symptoms and could produce a relatively normal set of tendon strength results despite often quite severe pathology; perhaps athletes are used to performing under painful conditions. Taking these factors together it was concluded that whilst tendon strength is a useful adjunct to clinical assessment, it was too unreliable as an objective measurement.

Other strength tests to assess the integrity of the musculo-tendinous unit could have been employed, for example isokinetic. However, there is not a study available which defines which test is the most appropriate to evaluate the functional ability of the Achilles tendon itself. In addition, this study was conducted on a fixed budget and the resources were not available to embark upon the evaluation of such devices or to employ more than one method of strength testing.

Ultrasound: The clinical classification of chronic Achilles tendon pathology has been stated previously. The clinical assessment markers such as pain, stiffness and the general assessment were correlated with ultrasound findings. In order to do this the following findings have been highlighted; paratenonitis, tenonitis, tenonitis with paratenonitis, degenerative change, post-surgical mal-alignment, enlarged tendon, rupture - grade 1-4 and calcification.

The Spearman Rank correlation test was undertaken to examine if the results of the clinical and subjective assessments correlated with the diagnostic ultrasound findings. The test was applied to evaluate for a relationship between the findings on ultrasound and tendon stiffness. The application of appropriate tests for measurement in medicine is discussed by Bland and Altman (1986), Altman and Bland (1985) and Atkinson (1995). It was only possible to do this by allocating a numerical score to each of the findings listed above and placing them in a rank order.

The rank order was allocated in degrees of the severity of the pathology. They are as follows:

Score	Ultrasound Finding
0	Normal
1	Paratenonitis
2	Tendon Enlargement up to 4mm
3	Enlargement 4-6mm
4	Enlargement 6-8mm
5	Enlargement 8-10mm
6	Enlargement 10mm +
7	Degenerative Changes including calcification
8	Tendinosis including partial ruptures
9	Tendinosis with Paratenonitis

The limitation of such an arbitrary scoring system was appreciated for it was difficult to categorise findings in a logical order. The changes demonstrated may be seen in isolation or in combination with another. There was though no model available in the literature which could be adequately applied to this study.

It was decided that for a two sided analysis, comparing the general assessment scores with the ultrasound results would give an indication of the agreement of the two methods of assessment. The general assessment score encompassed the data from other tests, for example pain and stiffness.

Therefore, if a subject provided a high pain and stiffness score they will have a lower general assessment score indicating a poor tendon.

Conversely the reverse should be true. For a more detailed analysis a comparison was also undertaken to compare individual markers, Achilles tendon pain and stiffness, with the ultrasound findings. This would demonstrate if all four markers displayed a similar degree of discrimination.

CHAPTER FOUR

Results

4. Introduction

The results from the three separate strands of the study are reported in the same order as the research methodology was presented.

4.1. 3T3 fibroblast cell experiment

The mean of the cell counts of the three wells for each experimental group was calculated. The cell count on the fibroblasts that received no electrical stimulation, the control group, was used as the base line measurement. In addition an analysis of the growth pattern for each group was conducted.

4.1.1. The control group

Trypan blue exclusion studies revealed that during the seven day period cell viability was 98%; the growth medium was changed once during this period. There was a lag phase in the growth pattern with a 2.8-fold increase measured at day 3, the biggest proliferation was noted at 3-5 days with a 18.6 fold increase from day 1. Between days 5 and 7 a decrease in cell proliferation was noted. The number of cells per cm^2 increased to a maximum cell density of $1.96x10^5$ per cm^2. Tables 4.1 and 4.2 demonstrate the cell growth pattern over the duration of the experiment in comparison with the other two experimental groups.

4.1.2. Cell cultures stimulated with 1μA of electrical stimulation

Similar to the control group the viability of cells was in the range of 96-98% using trypan blue exclusion studies. However, whilst the majority of the cells remained viable there was a large reduction in their proliferation in comparison to the unstimulated control group. The lag phase noted at 24 hours in the control group continued up to the end point of evaluation at day seven.

At day 3 the cell number was half that of the control group, $4.0x10^3$ to $8.3x10^3$ per cm^2. From day 1 to day 7 there was only a 11-fold increase in cell proliferation. This compares to 66.6-fold increase in the control group.

Despite the down regulation in cell proliferation the pattern of growth over the 7 day period was consistent with the control group. Table 4.2 demonstrates the rates of cell proliferation over the seven day period in comparison with the control group and the fibroblasts stimulated with 40μA.

4.1.3. Cell cultures stimulated with 40μA of electrical stimulation

The cell cultures stimulated with 40μA did not show such a lag of proliferation like the other two groups. The cell cultures became confluent within three days From this point cell density continued to increase and showed a greater proliferation than the other two groups to a density of $2.2X10^6$ per cm^2. From day 1 to 3 cell density increased by 4.4-fold, this compares with 2.8-fold and 1.3-fold increase in the control group and the 1μA group respectively. The total increase to day 7 was 733-fold.

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Tables 4.1 and 4.2 show, in tabular form, the cell proliferation over the duration of the experiment.

Experimental Group	*Cell Number: Mean±S.D per well/ plate cm²*			
	Day 1	**Day 3**	**Day 5**	**Day 7**
Control	$3x10^3$	$8.3x10^3$ S.D±$.96x10^3$	$5.6x10^4$ S.D±$1.4x10^4$	$2x10^5$ S.D±$.5x10^5$
1µA	$3x10^3$	$4x10^3$ S.D±$.44x10^3$	$1.5x10^4$ S.D±$1.4x10^4$	$3.3x10^4$ S.D±$.89x10^4$
40µA	$3x10^3$	$13.3x10^3$ S.D±$.3x10^3$	$1.2x10^5$ S.D±$.3x10^5$	$2.2x10^6$ S.D±.68x10

Table 4.1 Cell growth from plating to day seven.

Experimental Group	*Cell proliferation*				*Total Increase X*
	Increase x Day 1-3	*Increase x Day 1-5*	*Increase x Day 3-5*	*Increase x Day 5-7*	*Days 1-7*
Control	2.8	18.6	6.7	3.6	66.6
1µA	1.3	5	3.8	2.2	11
40µA	4.4	40	9	18	733

Table 4.2 Cell proliferation in each well

The cell number increased 733-fold which resulted in a ring of cell and protein visible in the well plate. The difference in appearance is clearly highlighted in the photograph of the well plates, Fig.4.1 below.

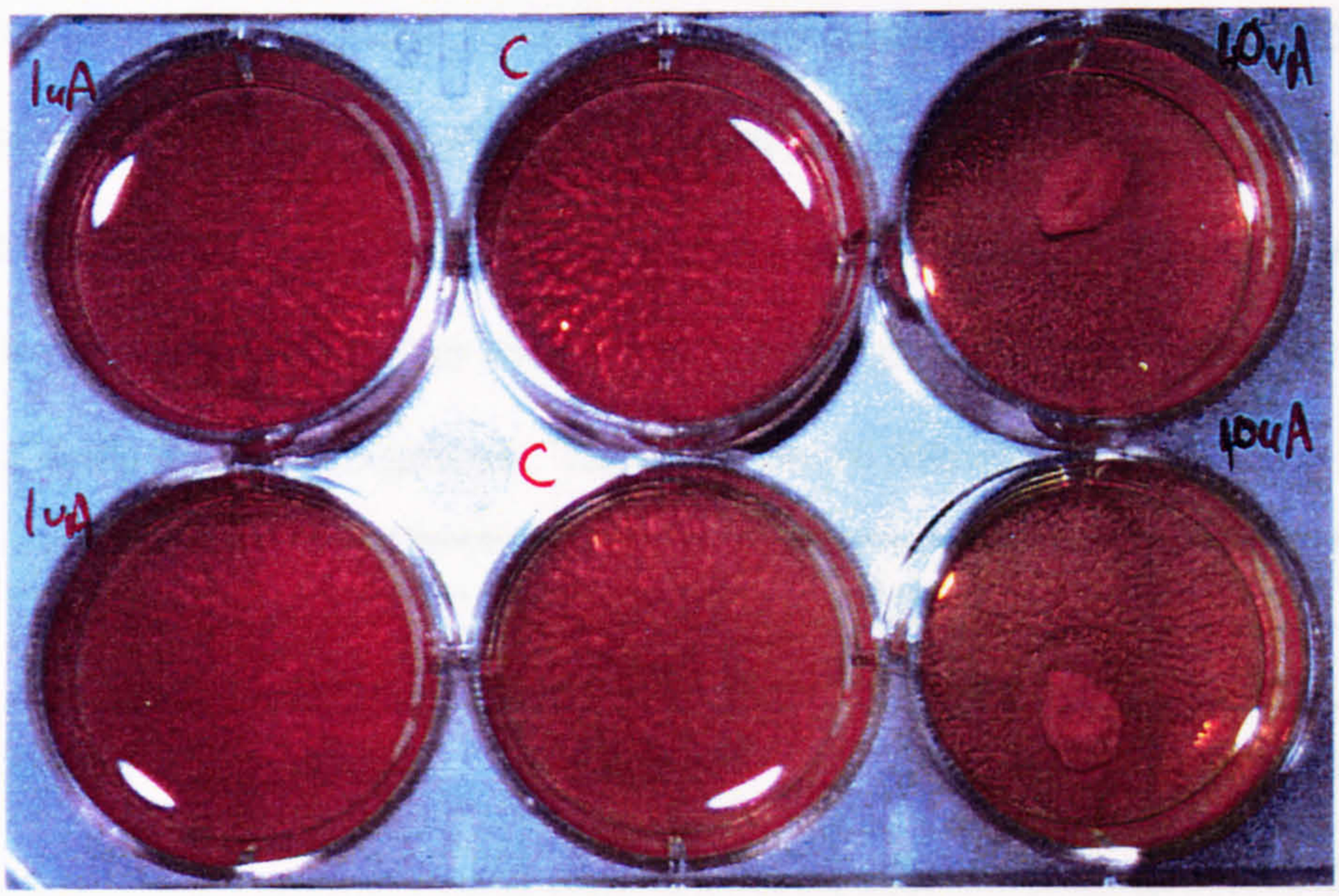


Fig.4.1. Photograph of the well plates showing visible evidence of the difference in cell proliferation of the experimental groups

4.2. Human tenocyte cell culture experiment

Prior to the experimental period some of the tenocytes were kept back and placed in a freezing mix, made by mixing 10% Dimethyl Sulfoxide with 90% fetal calf serum, in a sterile vial and placed in liquid nitrogen. This allowed a repeat experiment to be carried out when the first was contaminated with infection and the cell cultures were disposed of. In the repeat experiment the cells stimulated with an electrical current at an intensity of 40μA proliferated at a greater rate than the control group. The mean cell number per well was taken for three culture wells for the two groups. Table 4.3 below shows this.

Experimental Group	Cell Number: Mean per well/cm² Plate			
	Day 1	**Day 3**	**Day 5**	**Day 7**
Control	$3x10^3$	$8.1x10^3$ S.D± $0.17x10^3$	$5.1x10^4$ S.D± $0.3x10^4$	$3x10^5$ S.D± $0.16x10^5$
40μA	$3x10^3$	$9.1x10^3$ S.D± $0.51x10^3$	$1.2x10^5$ S.D± $0.3x10^5$	$8.4x10^5$ S.D± $0.46x10^5$

Table 4.3 Cell number of tenocytes pre and post-confluent culture. Cultures were initiated in standard six-well plates at a density of $3x10^3$. The number of cells per well was enumerated using a haemocytometer following trypsinisation of cells at three, five and seven days.

4.2.1. Comparison of the two cell culture groups

The proliferation rates of the 3T3 fibroblasts and the human tenocytes were compared to ascertain if they demonstrated a similar growth pattern. The graphs in figure 4.2 illustrate the similar behavioural response to the electrical stimulation of the different cell types. For clarity each individual plating group is shown with its mean cell density plus and minus the standard deviation.

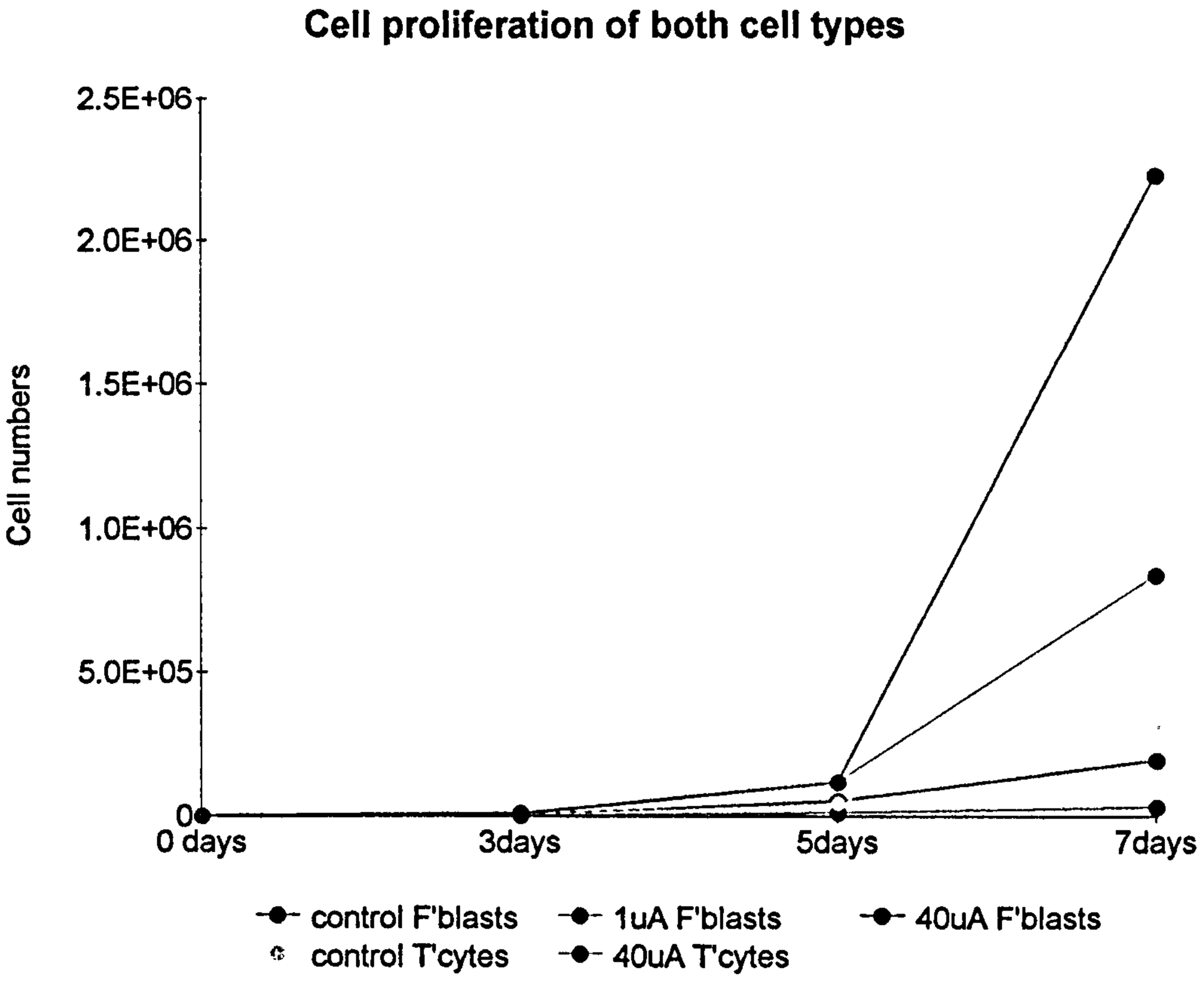
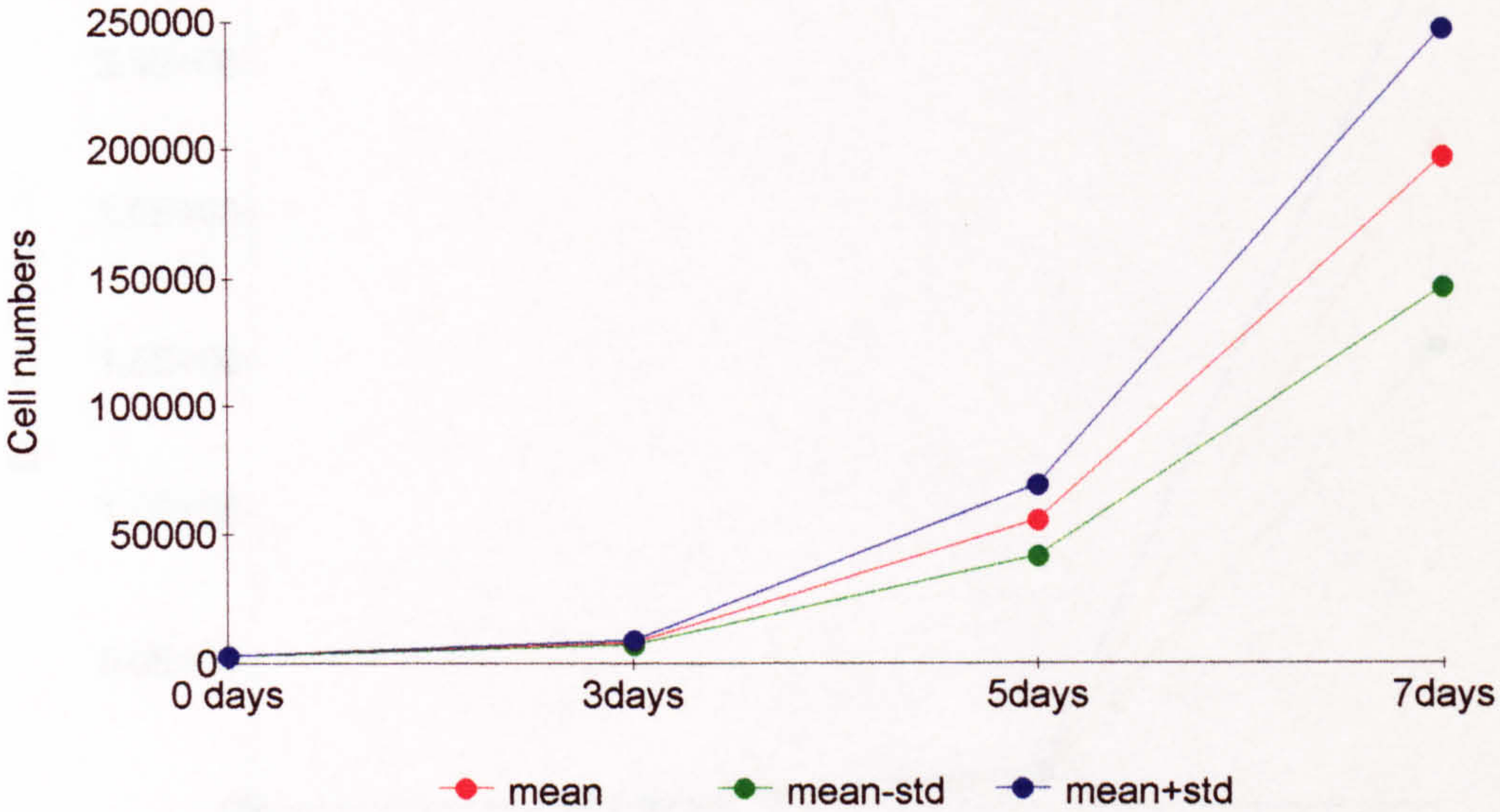


Fig. 4.2 Graphs showing the growth patterns of the two cell types



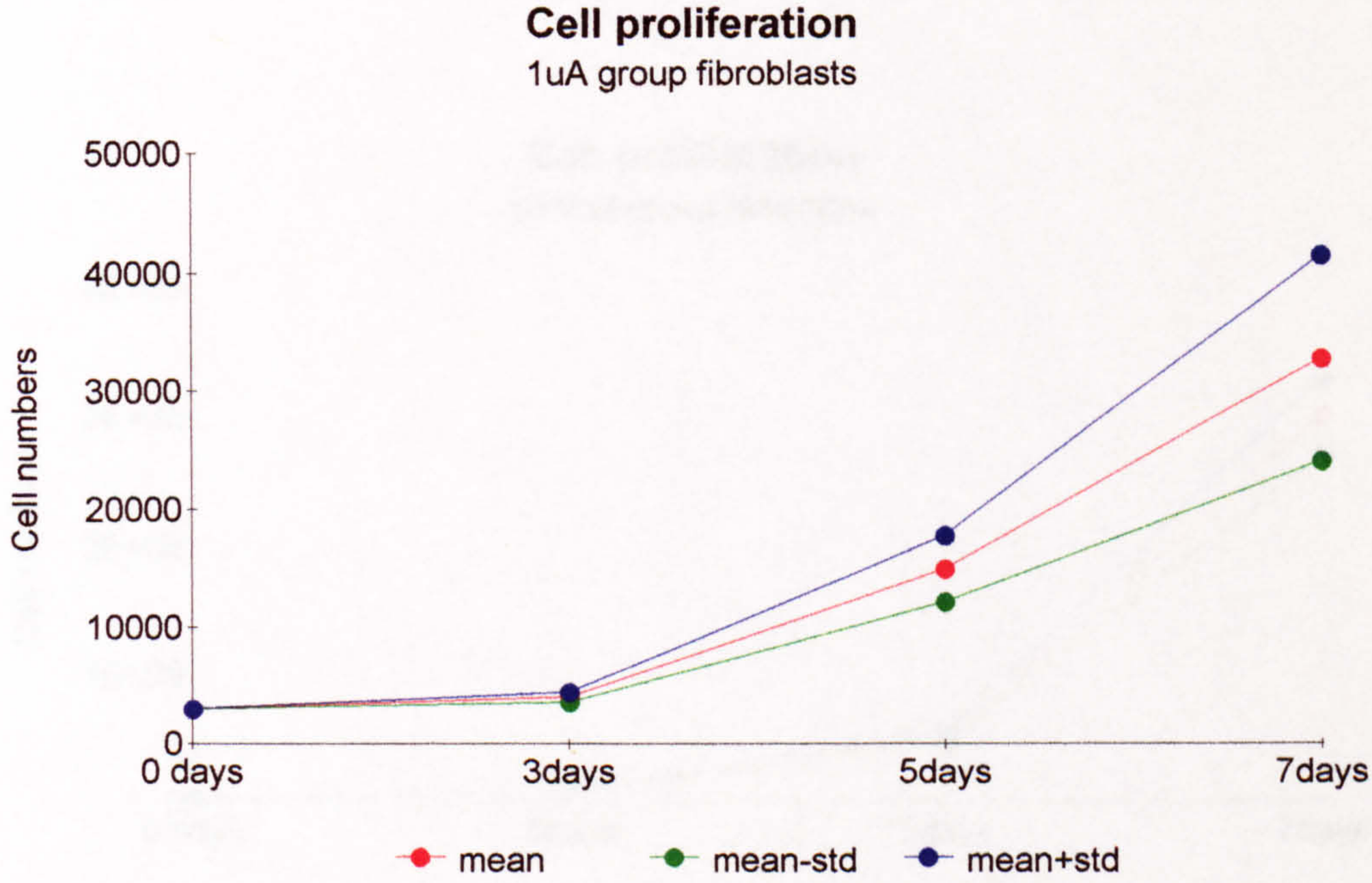
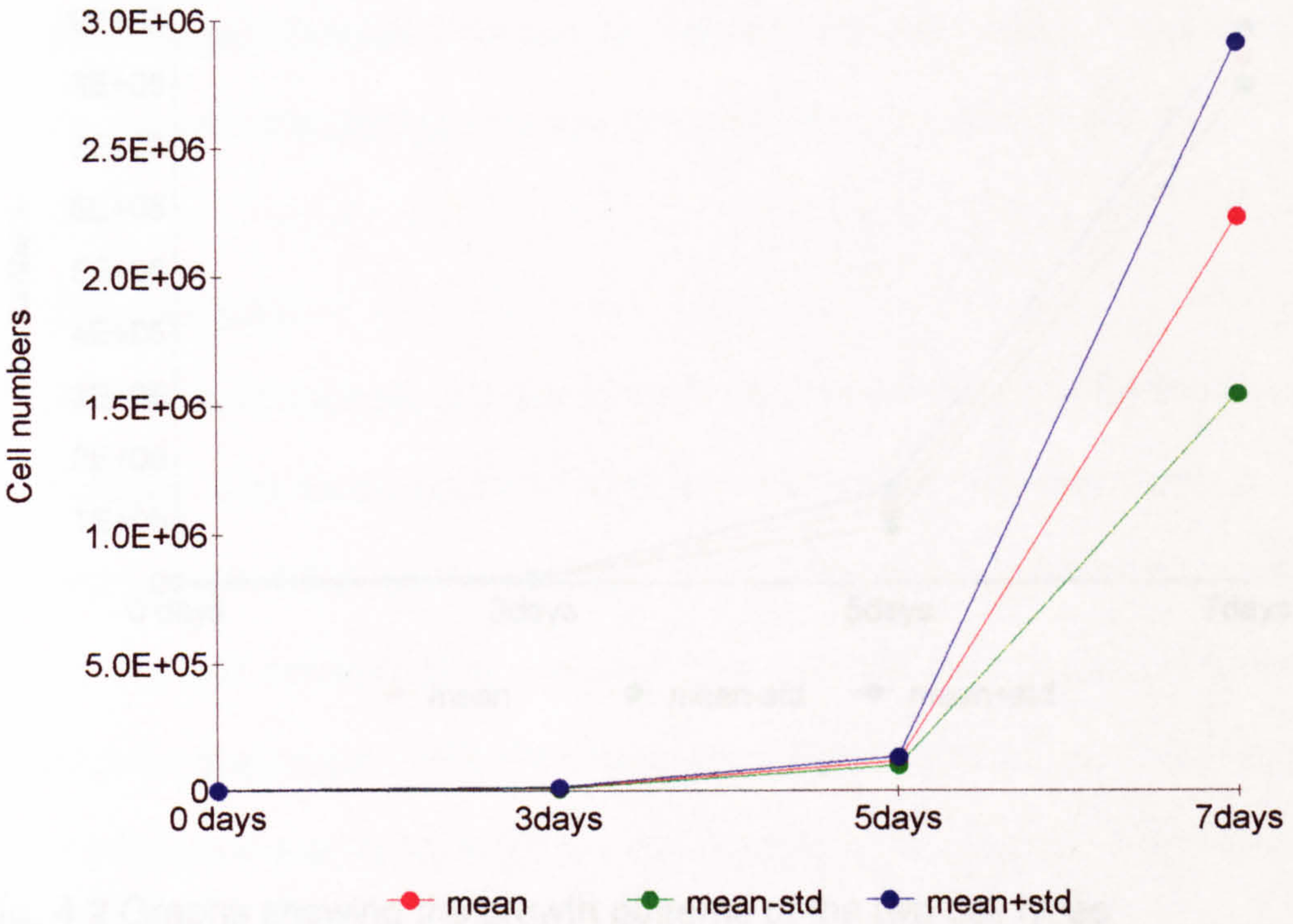


Fig. 4.2 Graphs showing the growth patterns of the two cell types



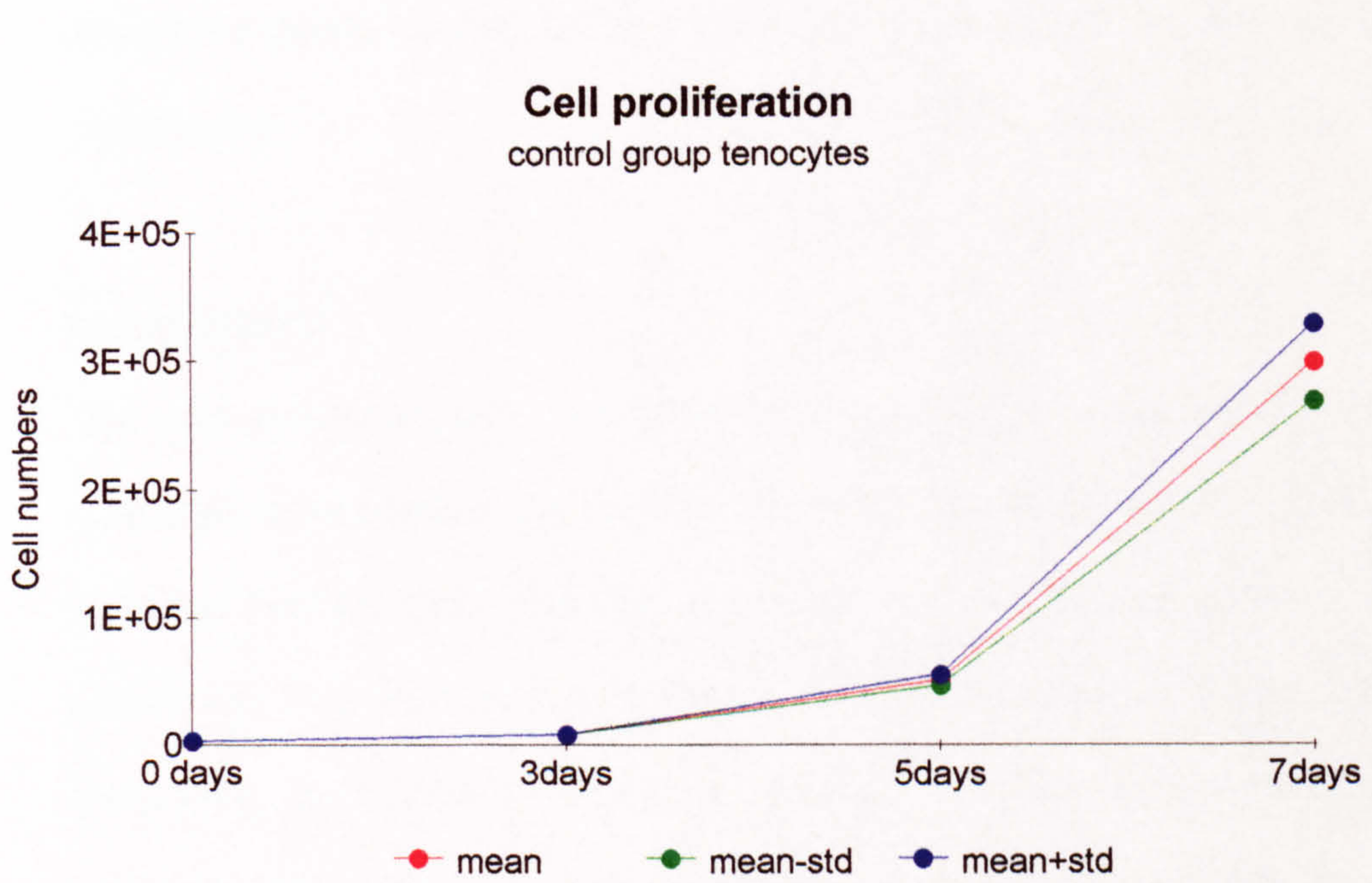


Fig. 4.2 Graphs showing the growth patterns of the two cell types

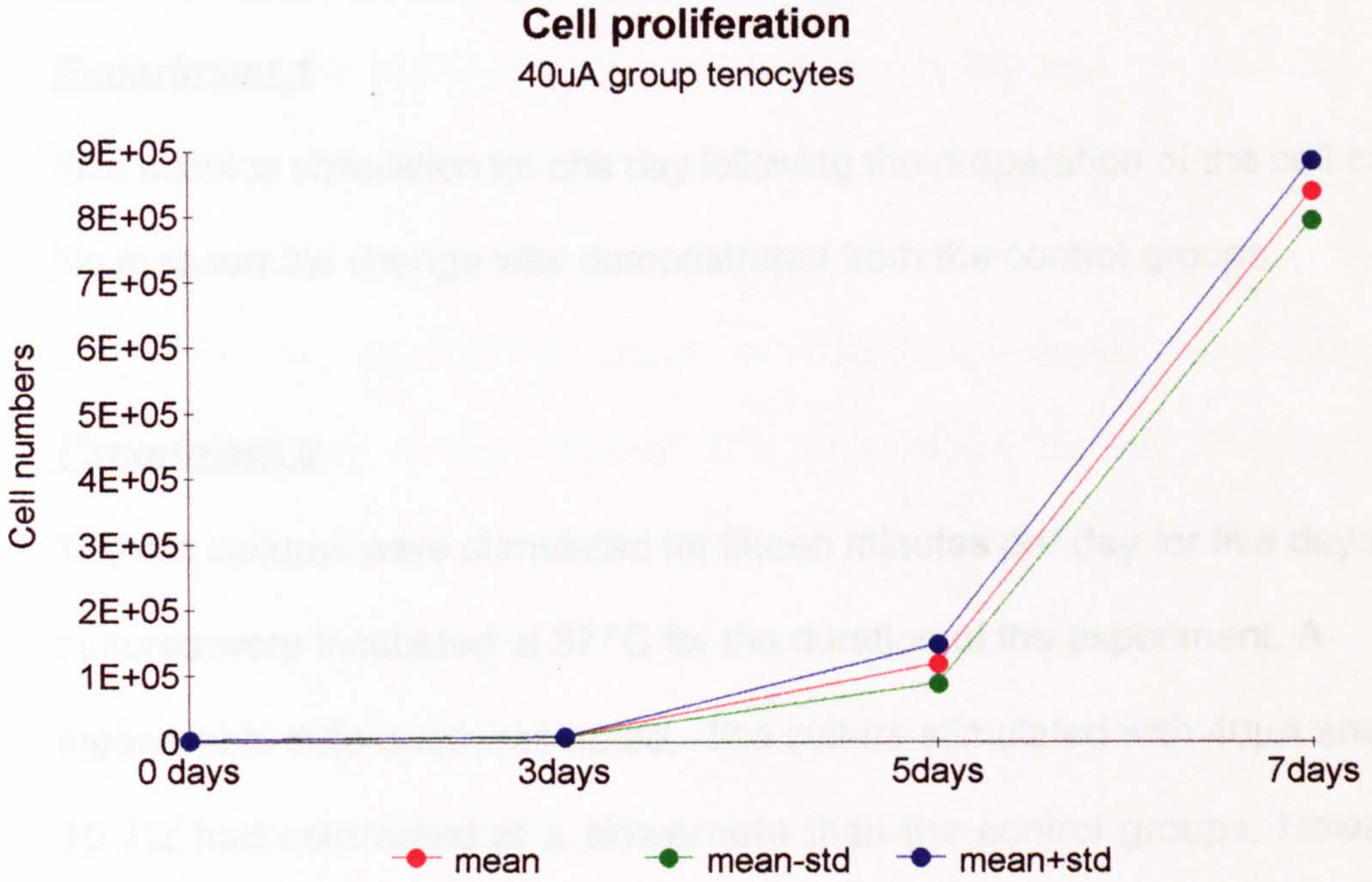


Fig. 4.2 Graphs showing the growth patterns of the two cell types

4.3. ADDENDUM: Collagen gel contraction experiment

Experiment 1

Five minutes stimulation for one day following the preparation of the cell culture.

No measurable change was demonstrated from the control groups.

Experiment 2

The cell cultures were stimulated for fifteen minutes per day for five days. The cultures were incubated at 37 °C for the duration of the experiment. A measurable difference was noted, The culture stimulated with 40μA and 10 Hz had contracted at a slower rate than the control groups. However, a problem that was not anticipated was the siting of the electrodes. They were left in place in the cultures for the five day duration of the procedure and it appeared that as the collagen cells contracted they became snared on the wire. For this reason the results were considered to be unreliable and no further analysis was undertaken.

Experiment 3

The wire electrodes were re-positioned. Instead of entering the dish from the side they now entered the medium via two holes in the lid of the plate, thus ensuring that the cells could have free movement. The parameters used in experiment Two were repeated. Plate One, stimulated with a low intensity, low frequency current demonstrated a variation from the control groups. The collagen cells in this group were contracting at a much slower rate than in the control group.

However, upon examining the cell under a light microscope it appeared that all the cells in the plates which contained electrodes had an unusual, coiled appearance.

It was considered that the choice of electrode material may have had a detrimental effect on the cultures. The application of an electric current could be releasing metal ions from the stainless steel electrodes which might effect cellular biosynthesis. The control group with no electrodes did not demonstrate this unusual pattern. It was considered that the best way to reduce the possibility of this action was to replace the stainless steel electrodes with silver ones. It was believed that silver electrodes would not release ions at the level of electrical stimulation used.

Experiment 4

The methodology was repeated as for experiment 3 using the new electrodes.

The results are demonstrated in Table 4.4. and Figure 4.3.

Gel diameter/ Hrs of culture	***Well 1***	***Well 2***	***Well 3***	***Well 4***	***Well 5***	***Well 6***
3	3.5mm	3.5mm	3.1mm	3.4mm	3.2mm	3.4mm
6	3.2mm	2.1mm	2.4mm	2.2mm	2.6mm	2.6mm
12	3.0mm	1.4mm	1.9mm	2.0mm	1.7mm	2.0mm
24	2.8mm	0.9mm	0.8mm	1.3mm	1.4mm	1.2mm
48	2.8mm	0.8mm	0.7mm	1.0mm	0.6mm	0.9mm

Table 4.4 Contraction of collagen gel in mm in each of the experimental groups.

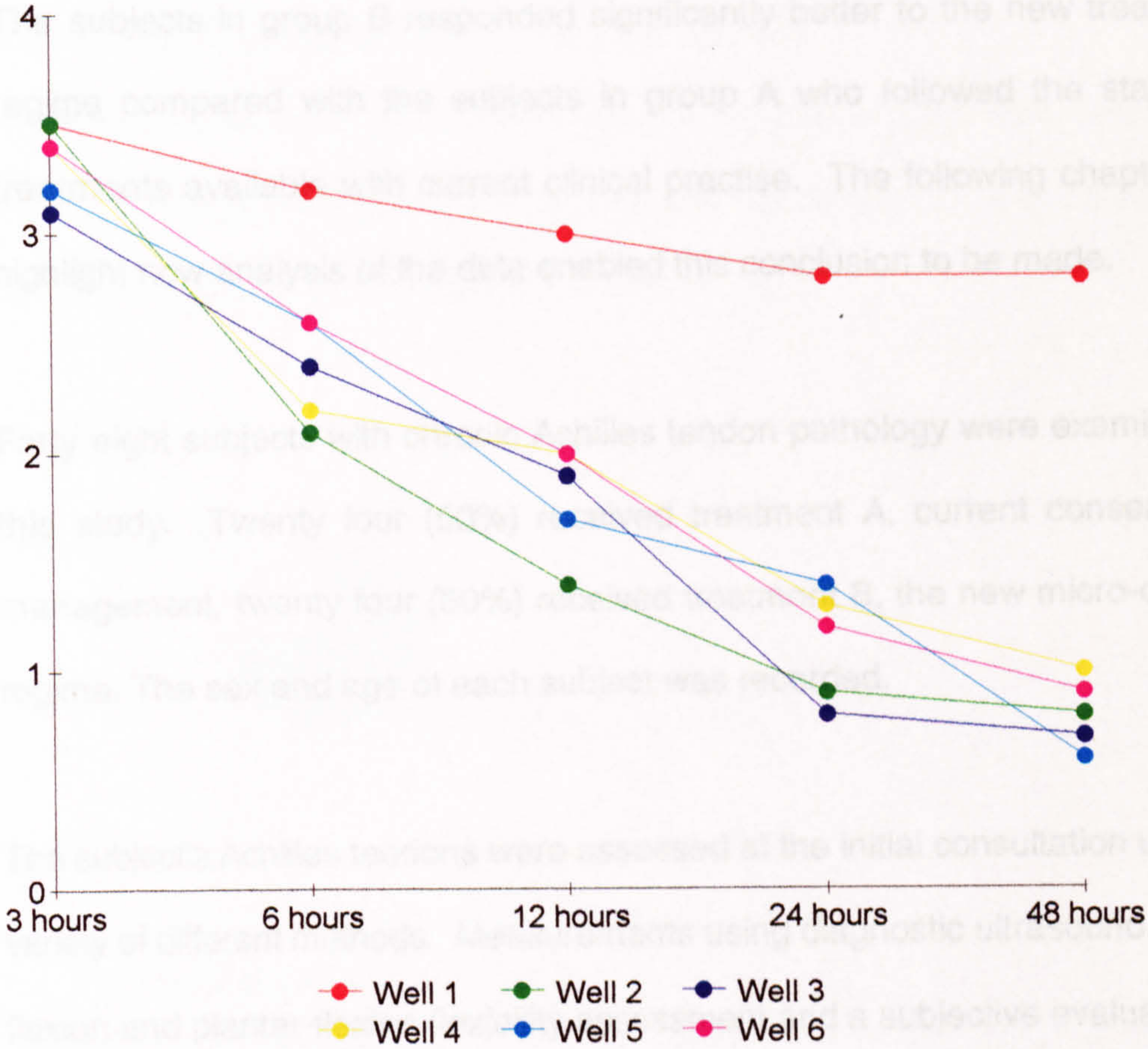


Fig. 4.3 Contraction of collagen gels following exposure to electrical stimulation

4.4. The *in-vivo* clinical study

4.4.1. Introduction

The subjects in group B responded significantly better to the new treatment regime compared with the subjects in group A who followed the standard treatments available with current clinical practise. The following chapter will highlight how analysis of the data enabled this conclusion to be made.

Forty eight subjects with chronic Achilles tendon pathology were examined in this study. Twenty four (50%) received treatment A, current conservative management, twenty four (50%) received treatment B, the new micro-current regime. The sex and age of each subject was recorded.

The subject's Achilles tendons were assessed at the initial consultation using a variety of different methods. Measurements using diagnostic ultrasound, dorsi-flexion and plantar-flexion flexibility assessment and a subjective evaluation of their level of pain and stiffness were recorded. In addition how the condition affected their daily living and if applicable participation in sport was noted. These markers monitoring the condition of the Achilles tendon were then repeated at three months, six months and at one year post inclusion in the study.

The performance of group A, the subjects following current clinical management of Achilles tendon pathology, in comparison with B, subjects undergoing the micro-current treatment regime was evaluated and compared at all four periods.

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4.4.3. Demographics: Sex and age distribution

The distribution of age, sex and the nature of an individual's pathology, providing they complied to the criteria of the study, was determined by chance. The distribution of the variable parameters are reported.

There are seventeen males in treatment group A (70.8%) and eighteen males in treatment group B (75.0%). The difference was not significant. It is clearer to show the distribution as a percentage pie chart.

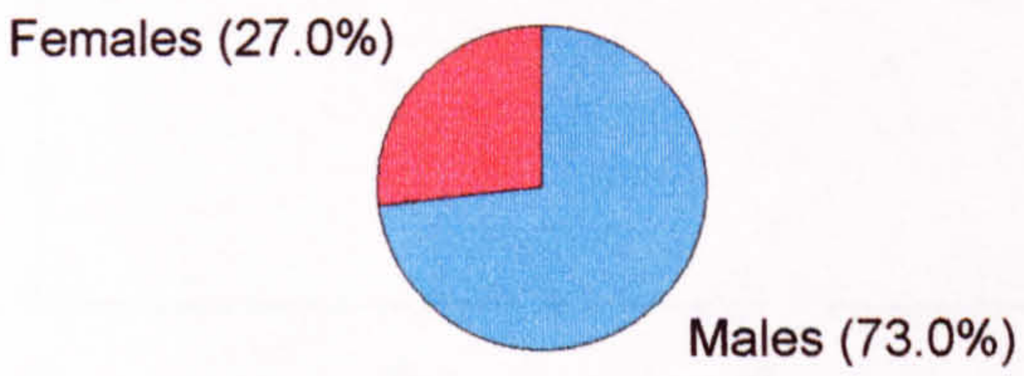


Fig 4.4 Sex distribution: Groups A & B

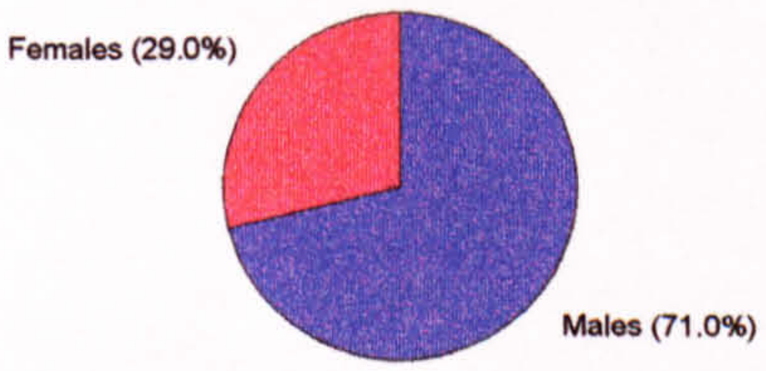


Fig 4.5 Gp A Sex distribution

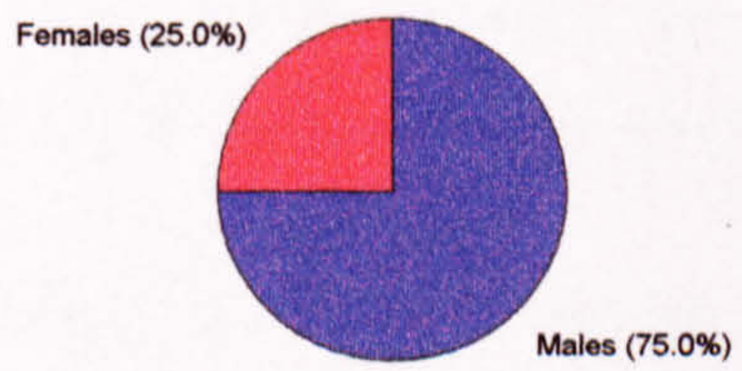


Fig 4.6 Gp B Sex distribution

The mean age of treatment group A was 36.0 years, standard deviation 7.8 years and group B was 39.3 years, standard deviation 10.4 years. There was no significant difference.

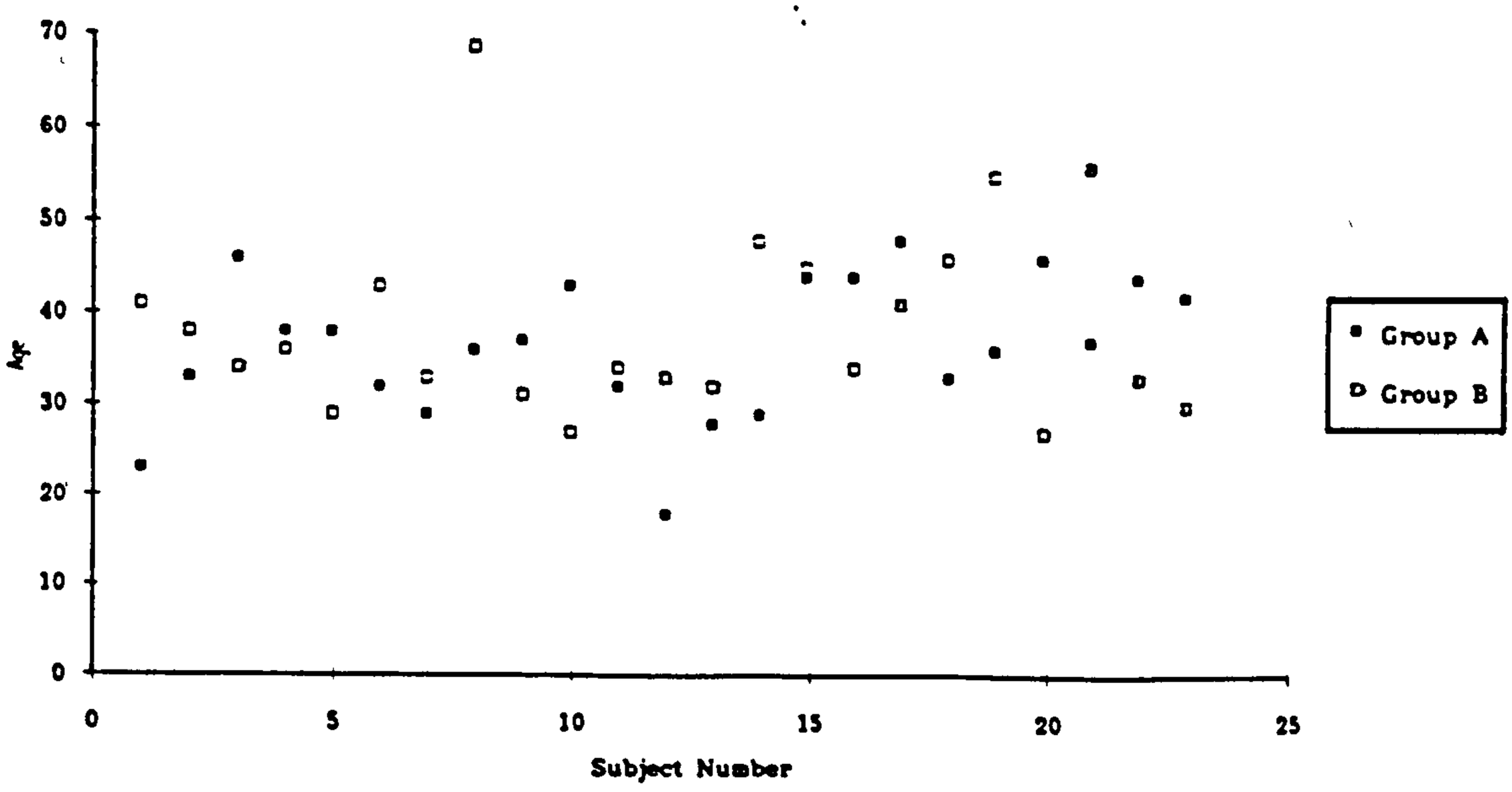


Fig.4.7 Age distribution - Groups A & B

4.4.4. Period one analysis: The Initial consultation

The method of randomisation employed ensured that there would be an equal number of subjects in group A and B. A number of subjects presented with uni-lateral pathology, (n=19), others presented with bi-lateral pathology, (n=58). In the bi-lateral cases, for statistical analysis, the outcomes for both feet were aggregated together. This was undertaken in this way for both Achilles tendons would be treated in the same manner and the condition of one will almost certainly effect the condition of the other.

This distribution of Achilles tendons affected resulted in treatment A administered to one foot only in six cases, (25%) and treatment B being administered to one foot only in thirteen cases, (54.2%).

The difference was not statistically significant at the 5% level,(X^2:p= 0.8).

The distribution of feet affected is demonstrated in Table 4.5 and Figure 4.8.

	Group A		*Group B*		
	Uni-lateral	**Bi-lateral**	**Uni-lateral**	**Bilateral**	**Total**
Left	4	18	8	11	**41**
Right	2	18	5	11	**36**
Total	**6**	**36**	**13**	**22**	**77**

Table 4.5 Group Distribution of Pathology and Left/Right Tendon.

The clinical examination and subjective assessment markers previously discussed for period one and subsequent periods were recorded as, dorsi-flexion left (DFL 1), dorsi-flexion right (DFR 1), plantar-flexion left (PFL 1), plantar-flexion right (PFR 1), pain left (PainL 1), pain right (PainR 1), stiffness left (Stiff L1), stiffness right (Stiff R1), general assessment left (GAL 1), general assessment right (GAR 1).

A comparison between the groups showed there was no statistically significant difference between the groups in each of the markers except for the general assessment score for the left side, (GAL 1). This was found to be significantly higher in treatment group A than B. (Mann-Whitney:p=0.035). Group A had a median general assessment score of 3 (range 1-7), whereas treatment group B had a median general assessment score on one (range 1-7). Group A contained n=22 left Achilles tendons affected and group B contained n=19 left Achilles tendons affected.

Therefore the group B subjects that had a left Achilles tendon affected started off with a more severe condition than the equivalent subjects in group A. In all other aspects the subjects in group A and B were comparable. This was important for it added validity to the results that followed. Essentially, apart from the difference in the left general assessment, both groups started from the same baseline.

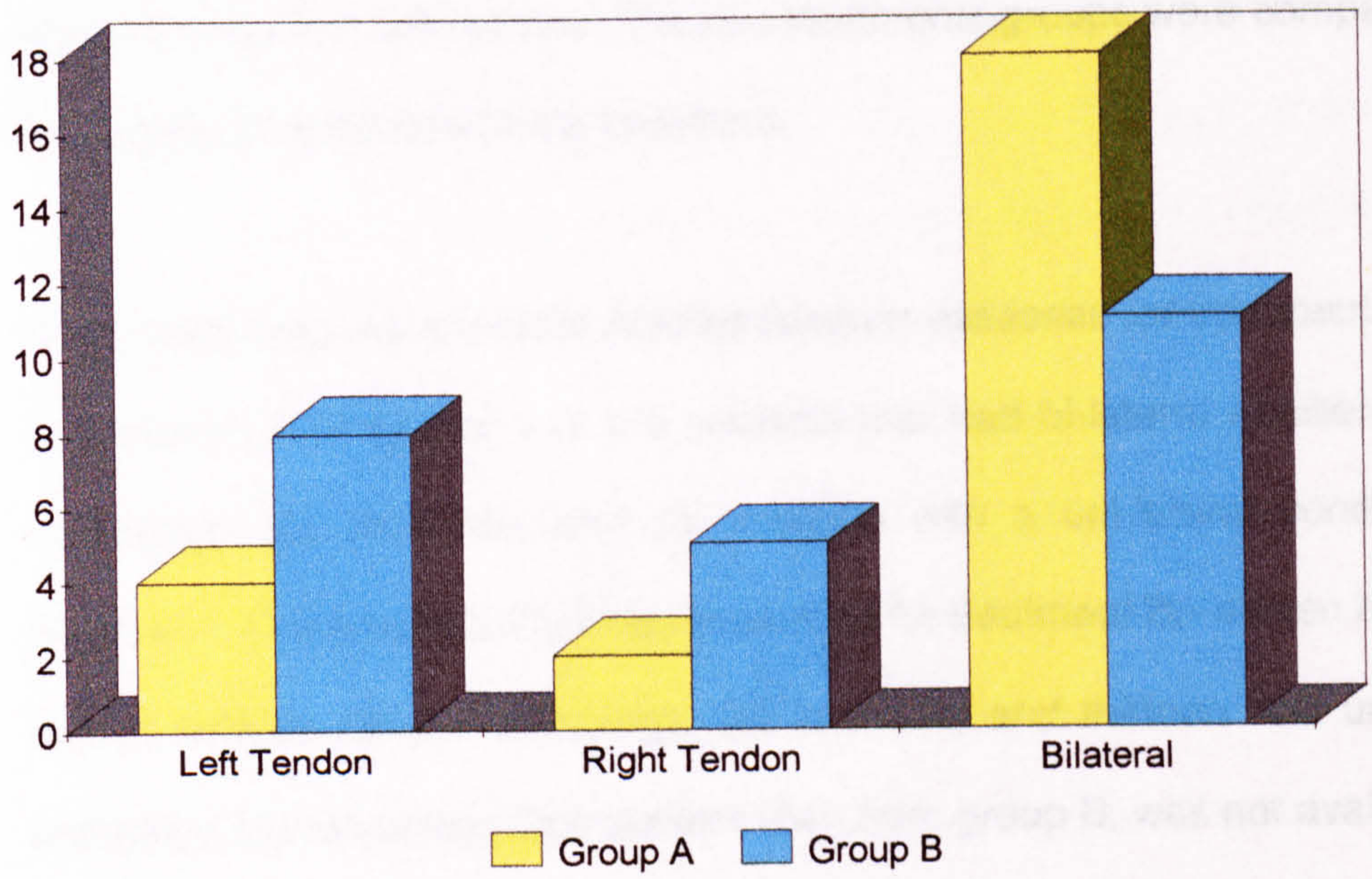


Fig 4.8 Number of subjects and the Achilles tendon affected

4.4.5. Period two analysis: The three month assessment

Statistical analysis of pain and stiffness markers were recorded at this time (summarised in Table 4.6). The numerical scores attributed to the response to the treatment for the left and the right feet in subjects with bi-lateral pathology were aggregated. These included the pain, stiffness and general assessment score change from period one. The two treatments groups were compared for the degree of response to the treatment.

There were forty two separate Achilles tendons assessed for treatment A;- this was made up of eighteen of the subjects that had bi-lateral Achilles tendon pathology, (36 tendons), and six subjects with a uni-lateral condition, (6 tendons). There were thirty three evaluated for treatment B;- eleven had a bi-lateral Achilles tendon pathology, (22 tendons) and thirteen had uni-lateral pathology, (13 tendons). One subject (24), from group B, was not available for assessment for period two. The difference in pain from period 1 to period 2 was found to be significantly more negative, i.e there was a greater improvement, in treatment group B ($p < 0.00005$). The same effect was found for stiffness ($p < 0.00005$).

	Treatment A		*Treatment B*	
	Median	**Range**	**Median**	**Range**
Pain	0-0	-82 to +50	-28.0	-56 to +26
Stiffness	0-0	-10 to +5	-5.0	-10 to 0

Table 4.6 The summary of statistics - Period two

No statistically significant correlation was found between age and changes in pain or stiffness. When comparing the fifty five male feet and the twenty two female feet, disregarding the treatment, no difference was found for pain, ($p=0.61$) or stiffness ($p=0.2$).

4.4.6. Period three analysis: The six month assessment

Period three, the six month assessment compared the pain, stiffness and general assessment scores with those corresponding scores obtained at the initial assessment at period one. Consistent with period two pain and stiffness scores for subjects with bi-lateral pathology were aggregated and analysed for changes between this mid-term assessment, the period two analysis and the initial assessment (summarised in Table 4.7). The ultrasound results are reported separately. The difference in pain, period three to one was found to be significantly more negative, i.e a greater improvement in treatment group B ($p<0.00005$). The same was found for stiffness ($p<0.00005$).

	Treatment A		*Treatment B*	
	Median	**Range**	**Median**	**Range**
Pain	0-0	-57 to +50	-53.0	-83 to +28
Stiffness	0-0	-15 to +5	-5.0	-15 to +10

Table 4.7 The summary of statistics - Period three

No statistically significant correlations were found between age and changes in pain or stiffness. There was also no difference between the male and female subjects for pain ($p= 0.78$) or stiffness ($p= 0.17$).

4.4.7. Period four analysis: One year assessment

It was important to monitor changes throughout the duration of the study in order to evaluate if there was an optimum time after treatment that the Achilles tendon showed signs of repair by producing a reduced degree of pain and stiffness. The last assessment was undertaken at one year after the initial assessment. All the tests and evaluations undertaken at the initial assessment were recorded at period four, the one year assessment.

This enabled a direct comparison of the condition of the subject's Achilles tendon to be made between the two assessment periods one year apart. The same procedure, used in the other assessment periods, for aggregating scores for the left and right Achilles tendons in subjects with bi-lateral Achilles tendon pathology was adopted for the one year assessment. There were forty two Achilles tendons evaluated for response to treatment in group A. This was comprised of eighteen subjects with bi-lateral pathology, resulting in thirty six tendons, and six with uni-lateral pathology. There were thirty five Achilles tendons evaluated for response to the new treatment, group B. This was made up of eleven subjects with bi-lateral Achilles tendon pathology, twenty two tendons, and thirteen subjects with uni-lateral pathology.

Statistically significant differences in favour of treatment B were found for four out of the five markers. Table 4.8 demonstrates this:

	Treatment A		*Treatment B*		
	Median	**Range**	**Median**	**Range**	**M-W P**
Pain	0-0	-82 to +51	-55	-99 to +25	<0.00005
Stiffness	0-0	-15 to +5	-5	-15 to +10	<0.00005
General Ass'ment	0-0	-2 to +4	3.0	-2 to +6	<0.00005
Dorsi-Flexion	0-0	-6 to +5	1.0	-4 to +7	0.0001
Plantar-Flexion	0-0	-8 to +1	0-0	-7 to +5	0.1063

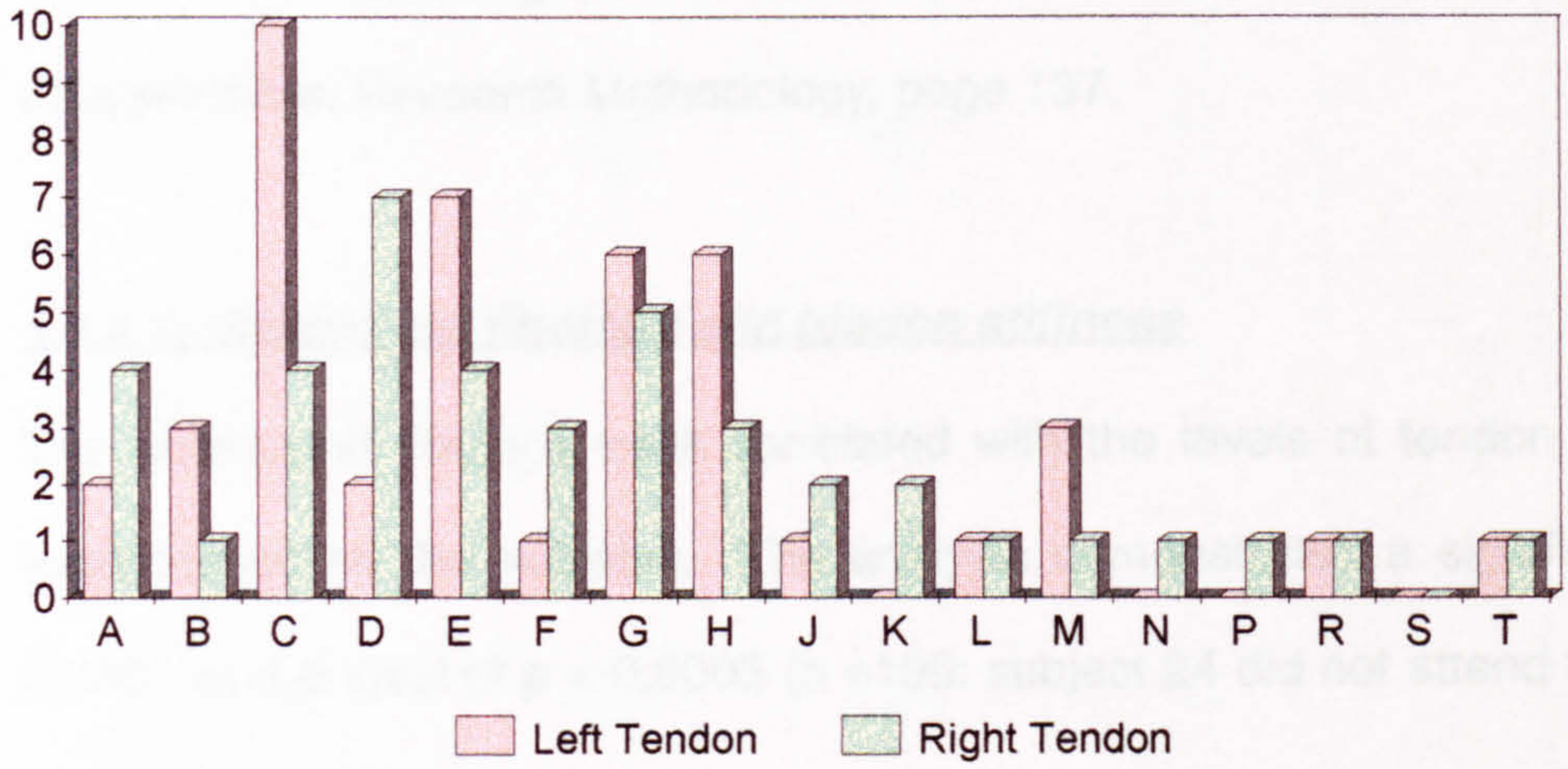
Table 4.8. The summary of statistics - Period four

No statistically significant differences were found between age and the noted changes in any of the above variables. No statistically significant differences were found between the male and female subjects for pain (p=1.0), stiffness (p=0.38), general assessment (p=0.79), dorsi-flexion (p=0.34) or plantar-flexion (p=0.22).

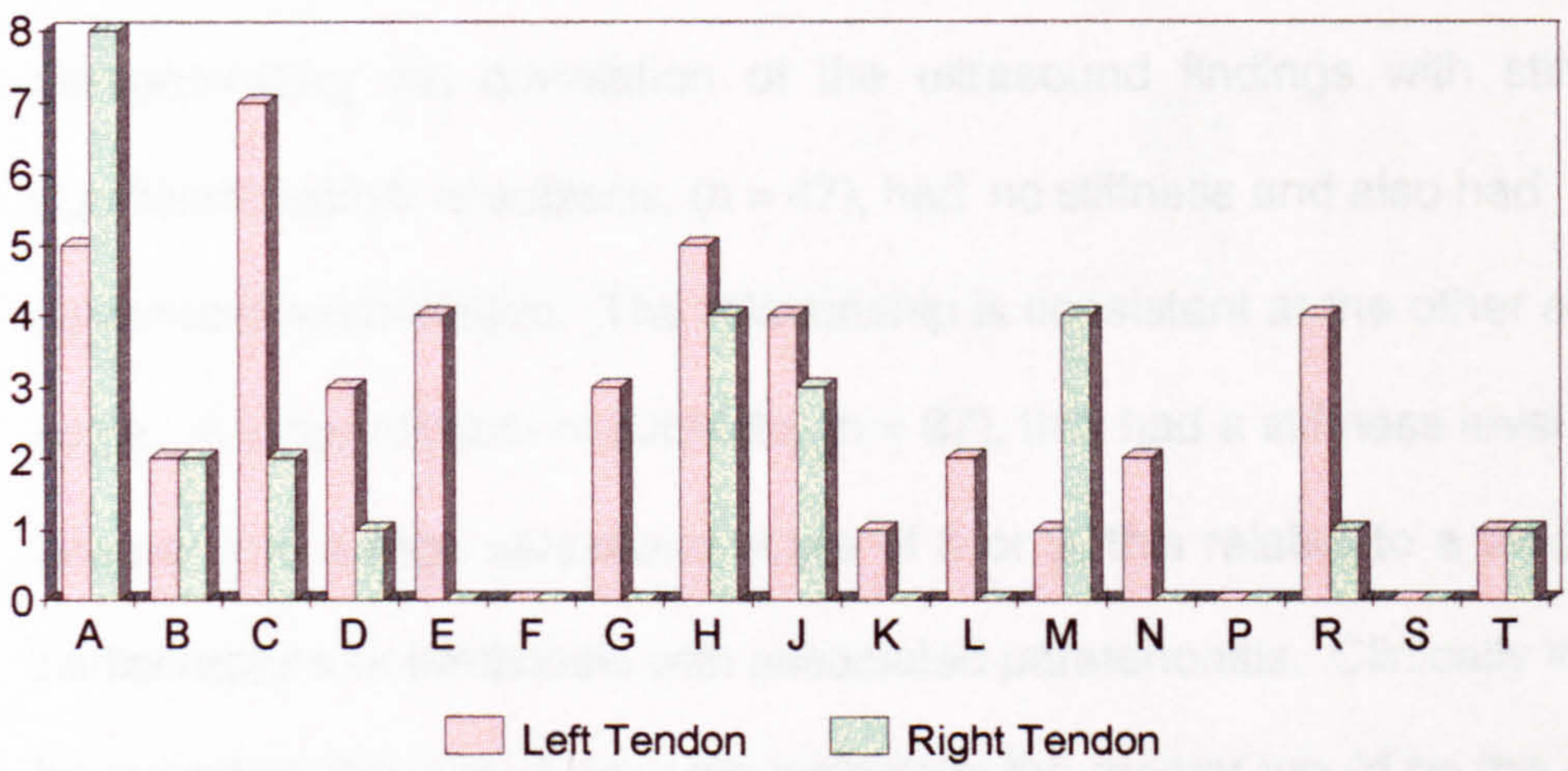
4.4.8. Pathology distribution

It is interesting to note the distribution of the pathologies in both groups. The bar charts in Figure 4.9 show the distribution as classified from the diagnostic ultrasound examination.

Group A



Group B



Key:

A	Normal	G	Enlargement 1	N	Rupture 3
B	Paratenonitis	H	Enlargement 2	P	Rupture 4
C	Tendinosis	J	Enlargement 3	R	Calcification
D	Peritendonitis	K	Enlargement 4	S	Non-surgical
E	Degenerative	L	Rupture 1	T	Cystic
F	Post-surgical	M	Rupture 2		

Fig 4.9 Achilles tendon pathology distribution

4.4.9. The accuracy of diagnostic ultrasound

Diagnostic ultrasound was used in the same manner for both groups over the duration of the study. If practicable it was undertaken for each subject at each assessment interval. This resulted in a large amount of data to analyse, (n=192, 48 subjects examined over four time intervals).

The rationale for using the Spearman rank correlation test was provided in Chapter three, Research Methodology, page 137.

4.4.9.1. Ultrasound findings and tendon stiffness

The ultrasound findings were correlated with the levels of tendon stiffness experienced by the subjects. The analysis demonstrated a significance of 0.7561 at a p level of p = 0.0005 (n =190: subject 24 did not attend the three month assessment.

Table 4.9 and Figure 4.10. shows a scatter plot and a numerical chart demonstrating the correlation of the ultrasound findings with stiffness. A significant number of subjects, (n = 47), had no stiffness and also had a normal ultrasound examination. The relationship is consistent at the other end of the scale. A large number of subjects, (n = 87), that had a stiffness level of ten or greater and a high ultrasound score of 8 or 9, this relates to a tendinosis or partial rupture or tendinosis with associated paratenonitis. Clinically this would be expected, the more severe the pathology the greater would be the reduction in the flexibility of the Achilles tendon.

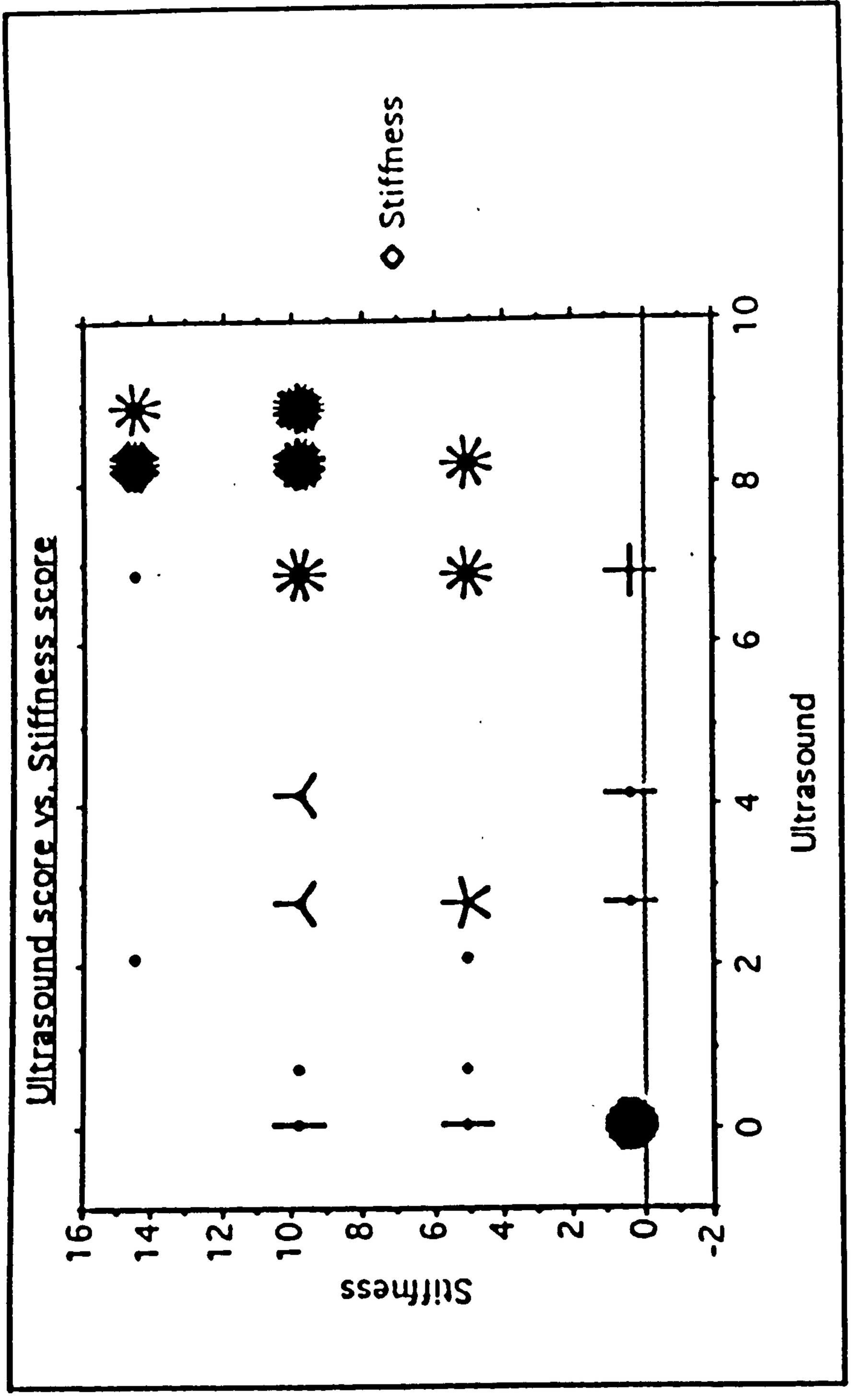


Fig. 4.10. Ultrasound findings and Achilles tendon stiffness. One marker refers to a single subject. Table 4.9. overleaf show the numerical distibution for each score.

Table 4.9 Numerical distribution of ultrasound findings and Achilles tendon stiffness relating to Fig.4.10.

STIFF by ULTRA

Page 1 of 1

Count	ULTRA .00	1.00	2.00	3.00	4.00	7.00	8.00	9.00	Row Total
STIFF									
-15.00			1			1	28	9	39 20.5
-10.00	2	1		3	3	10	27	23	69 36.3
-5.00	2	1	1	5		9	9		27 14.2
.00	47			2	2	4			55 28.9
Column Total	51 26.8	2 1.1	2 1.1	10 5.3	5 2.6	24 12.6	64 33.7	32 16.8	190 100.0

4.4.9.2. Ultrasound findings and tendon pain

Figure 4.11 and Table 4.10. show a scatter plot and numerical chart demonstrating the correlation of the ultrasound findings with the levels of Achilles tendon pain reported by the subjects. Clinical experience should lead one to believe that the ultrasound findings and Achilles tendon pain levels would show a similar distribution to the correlation of the ultrasound findings with Achilles tendon stiffness. Clinically one is commonly associated with the other. This indeed was the case. The analysis highlighted a correlation at a significance of 0.7641 at a p level of p =0.0005.

Upon examination of the scatter plot and the numerical distribution a large number of subjects, (n = 48) had no significant findings on ultrasound. These subjects had no pain. Subjects with the highest scores recorded for the ultrasound (8 and 9, relating to tendinosis or partial ruptures and tendinosis with associated paratenonitis) showed a greater proliferation at the higher levels of pain.

Deviating from the general trend was one subject, number 19, who had a high pain score of 55 and 56 but had a normal ultrasound for both Achilles tendons. This requires explanation. The subject suffered from recurrent paratenonitis. When the fluid within the paratenon resolved the tendon showed a normal appearance on ultrasound.

Adhesions within the paratenon can be demonstrated with such a condition but this was not apparent in this subject for there was normal movement of the endotenon within the paratenon when a dynamic examination was conducted.

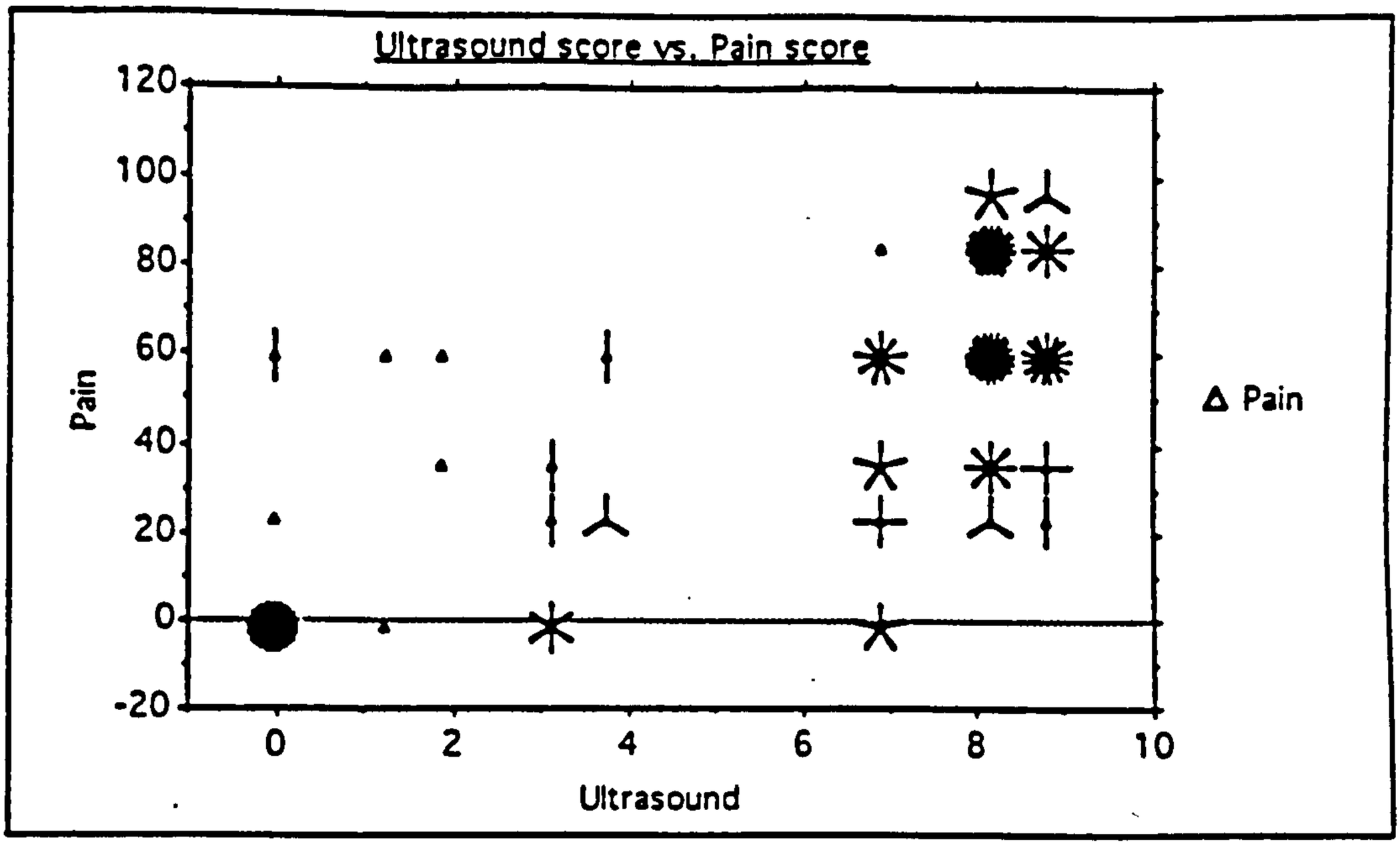


Fig. - 4.11. Ultrasound findings and Achilles tendon pain. One marker on the chart refers to one patient. Table 4.10 overleaf show the numeral distribution of Fig. 4.11

PAIN by ULTRA

Page 1 of 1

PAIN	Count	ULTRA .00	1.00	2.00	3.00	4.00	7.00	8.00	9.00	Row Total
-99.00								1		1 .5
-98.00								4	2	6 3.2
-97.00									1	1 .5
-84.00								1		1 .5
-83.00								12	2	14 7.4
-82.00							1	9	6	16 8.4
-81.00								3		3 1.6
-58.00								3	1	4 2.1
-57.00						1	4	5	9	19 10.0
-56.00		1	1			1	3	10	3	19 10.0
-55.00		1					1	4	2	8 4.2
-54.00				1			1	1		3 1.6
-33.00									1	1 .5
-32.00					1		1	2		4 2.1
-31.00					1		1	1		3 1.6
-30.00							2	2	1	5 2.6
-29.00				1			1	3	2	7 3.7
-28.00					1	1	1	3	2	8 4.2
-27.00		1			1	2	3			7 3.7
-4.00					1					1 .5
.00		48	1		5		5			59 31.1
Column Total		51 26.8	2 1.1	2 1.1	10 5.3	5 2.6	24 12.6	64 33.7	32 16.8	190 100.0

Table 4.10 The numerical distribution of ultrasound findings and Achilles tendon pain

4.4.9.3. Ultrasound findings and the general assessment

The author believed that the general assessment score, which inherently includes other markers of the subjects condition such as pain and stiffness, would provide a good comparison with the results of the ultrasound findings. Altman and Bland (1985) state that a simple graph is a good first step when measuring one test measurement against another. The paired t-test may be thought to be appropriate in order to analyse individual measurement difference and formally examine the hypothesis that zero bias exists between the two test methods.

The classifying of the ultrasound findings was problematical for it was not possible to accurately score one condition as more severe than the next for each individual subject. General agreement was sought between the general assessment scores, and the ultrasound findings. For example, if it was shown that ultrasound findings were normal when the patient had a low general assessment score then clearly it is an inexact method of assessing the condition of the Achilles tendon with chronic pathology.

A statistically significant negative correlation was found between the ultrasound findings with the general assessment score.

(n= 190, Spearman's Rank correlation: r = - 0.7693 at a p level of P<0.0005). This was consistent with the levels of significance for pain, 0.7641 and stiffness, 0.7561.

Fig. 4.12 and Table 4. 11 demonstrate the scatter plot and numerical chart of the analysis of the general assessment score and ultrasound findings. The scatter plot shows the large number of subjects, (n=49), that had a high general assessment score, good or excellent, and a normal ultrasound.

Conversely there is a cluster of subjects (n=88), that had a general assessment score of 1-3 and in agreement had a high ultrasound score of 8-9, tendinosis or partial rupture and tendinosis with paratenonitis.

However, there are a small number of subjects, (n=3), that deviate from the normal distribution. Two of these cases relate to the same subject, number 22 and one to subject number 23. Subject number 22 was the youngest participant in the study and previously had a complete rupture of her left Achilles tendon. The ultrasound score for this subject was 7 relating to degenerative changes and/or intratendinous calcification, but her general assessment score was also 7, the excellent category. This was a case where the ultrasound scan demonstrated a tendon that had been left with an anatomical variation that had the appearance of degeneration following the full rupture and subsequent repair. However, regardless of the appearances of the tendon the patient was experiencing no symptoms. Subject number 23, showed a similar pattern of deviation from the normal distribution. This subject was an ageing athlete with ultrasound evidence of long term chronic Achilles tendon pathology but was symptom free and training normally. This highlights that the sensitivity and specificity of ultrasound for musculo-skeletal examinations whilst high is not 1.0.

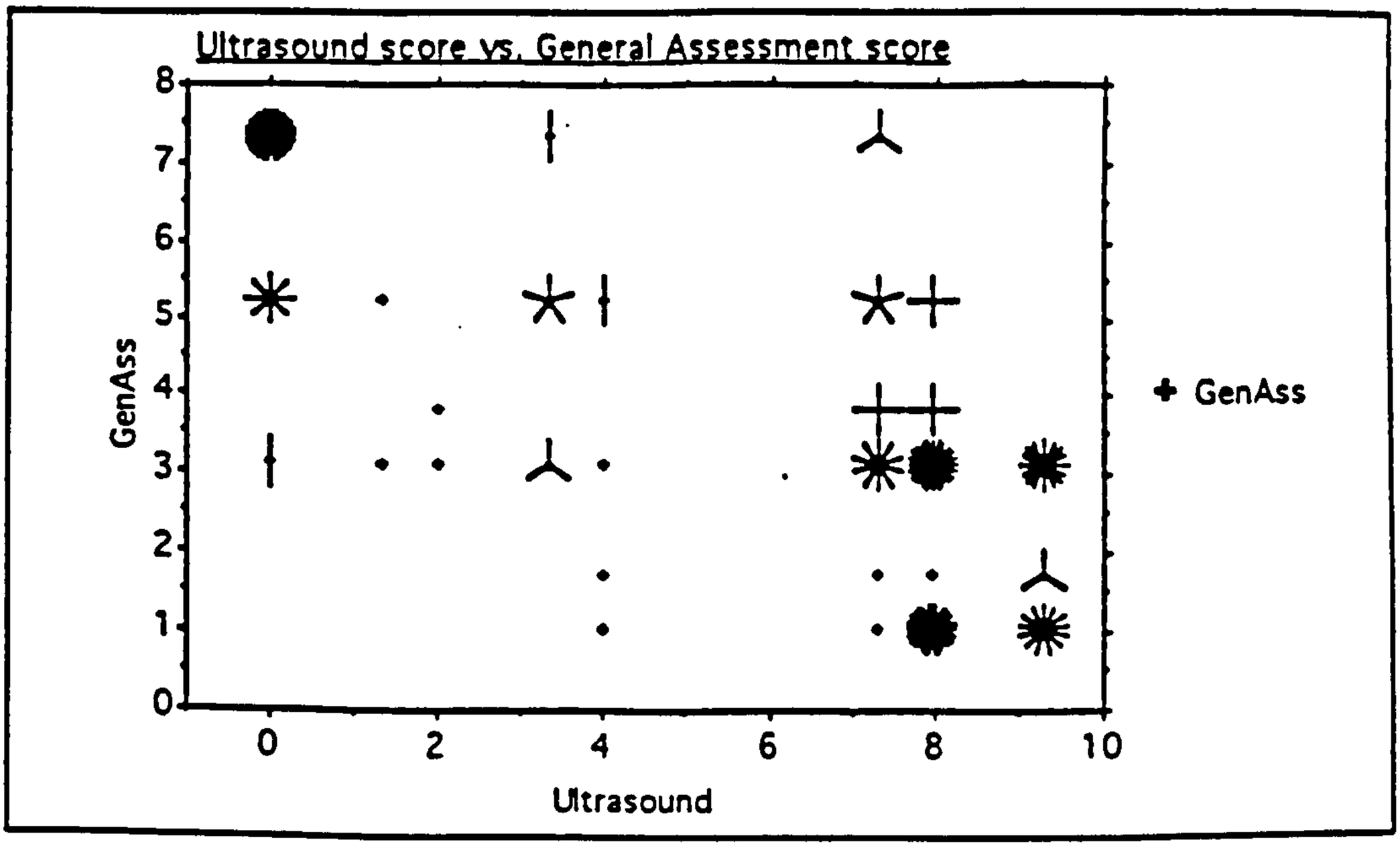


Fig. 4.12 The distribution of ultrasound findings and the general assessment score. One line on the chart refers to one patient and the table below show the number of individual cases for each score.

GA by ULTRA

Page 1 of 1

GA \ ULTRA Count	.00	1.00	2.00	3.00	4.00	7.00	8.00	9.00	Row Total
-7.00	41			2		3			46 24.2
-5.00	8	1		5	2	5	4		25 13.2
-4.00			1			4	4		9 4.7
-3.00	2	1	1	3	1	10	24	16	58 30.5
-2.00					1	1	1	3	6 3.2
-1.00					1	1	31	13	46 24.2
Column Total	51 26.8	2 1.1	2 1.1	10 5.3	5 2.6	24 12.6	64 33.7	32 16.8	190 100.0

Table 4.11 Numerical distribution of Fig.4.12 scatter plot

4.4.10. Summary of the clinical results

The progress of mean and median pain and stiffness scores for group A and group B measured over the four assessment intervals is demonstrated in Figs. 4.13.- 4.16. Table 4.12 shows this numerically. The graphs visually demonstrate that the chronic Achilles tendon pathology in the subjects of Group B, treated with the new micro-current therapy, clearly responded better than the Achilles tendon pathology in the subjects of group A treated with the current clinical management.

Ultrasound, was demonstrated to be an accurate method of assessing the progress of the pathological state of the Achilles tendon. There was agreement in the ultrasound findings with Achilles tendon pain, stiffness and the general assessment. The fact that an explanation could be given for the small number of the subjects that did deviate from the normal distribution highlights that it was an applicable method of assessment because it was used in conjunction with other methods. Clinically, ultrasound should not be used in isolation and the importance of a physical examination of the Achilles tendon and an adequate clinical history is highlighted by these cases.

Observation	Mean Pain : A	Median Pain : A	Mean Pain : B	Median Pain : B
1	47.21	56	48.02	56
2	46.42	55	27.37	28.5
3	51.67	56	16.83	10
4	47.33	55.5	13.73	0

Observation	Mean Stiffness : A	Median Stiffness : A	Mean Stiffness : B	Median Stiffness : B
1	8.96	10	10.06	10
2	8.13	10	5.76	5
3	8.75	10	5.73	5
4	9.54	10	4.23	5

Table 4.12 Mean and median pain and stiffness scores: Period 1 - 4

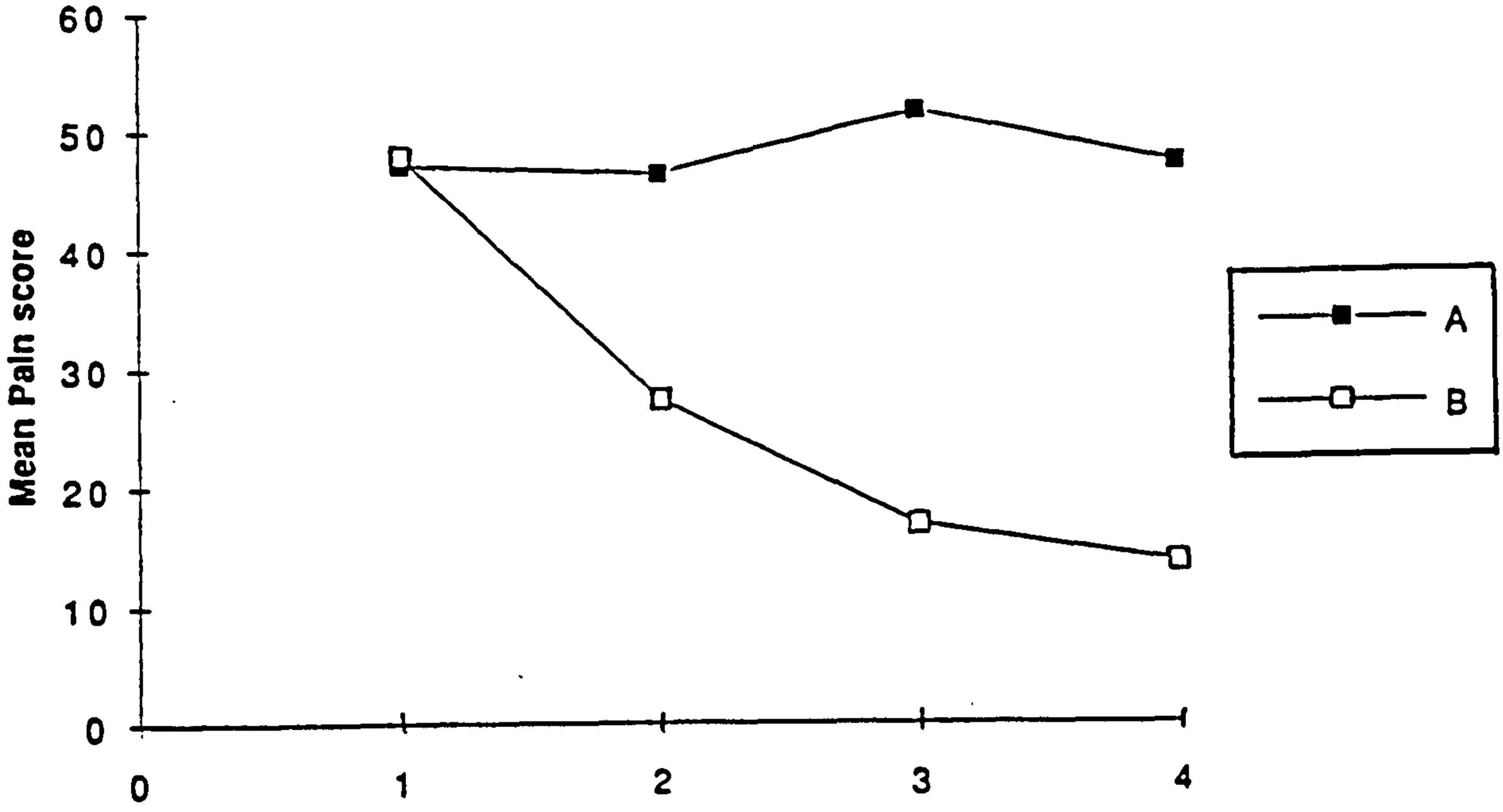


Fig. - 4.13. Mean Pain Score: Period 1 - 4

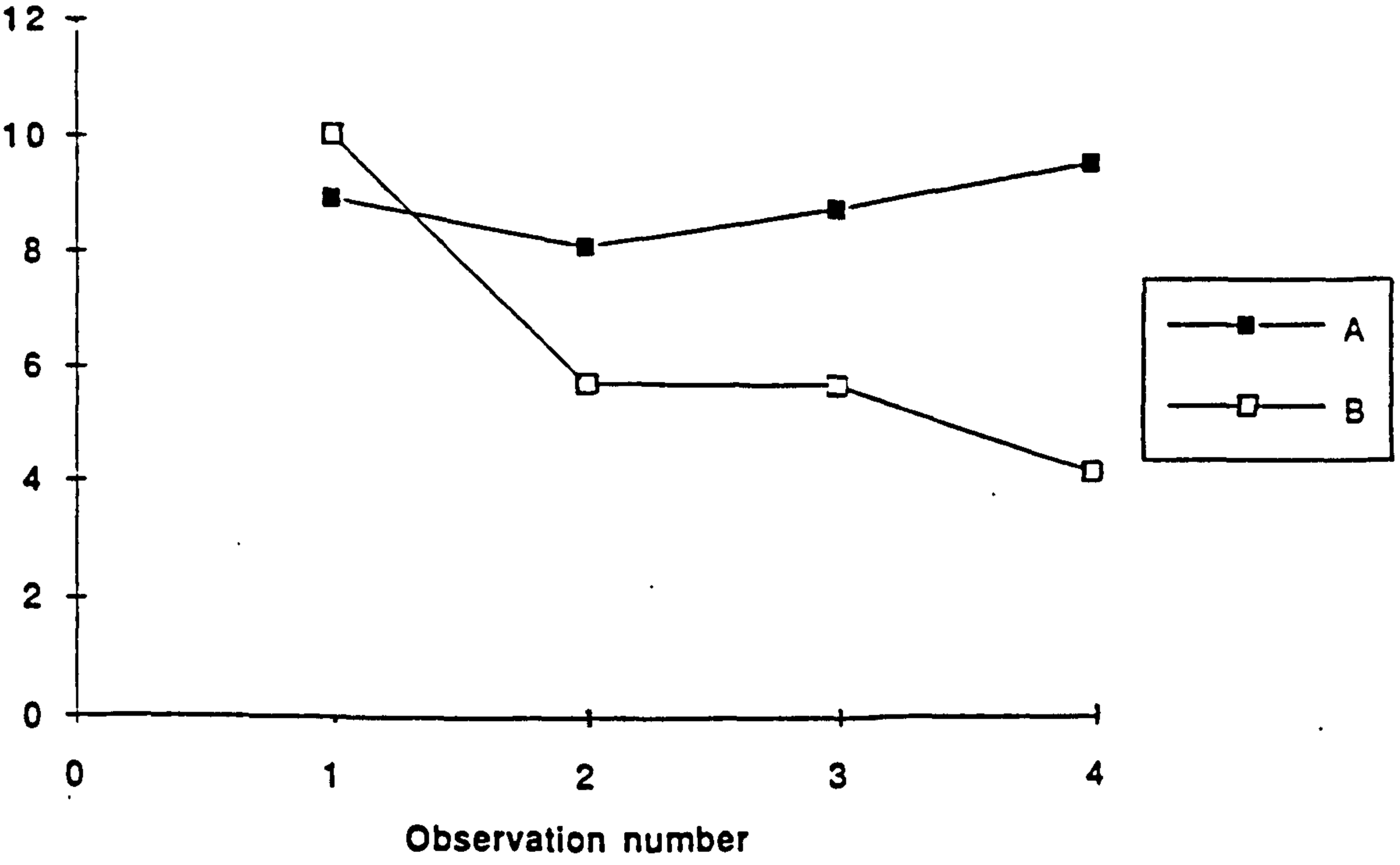


Fig. - 4.14. Mean stiffness score: Period 1 - 4

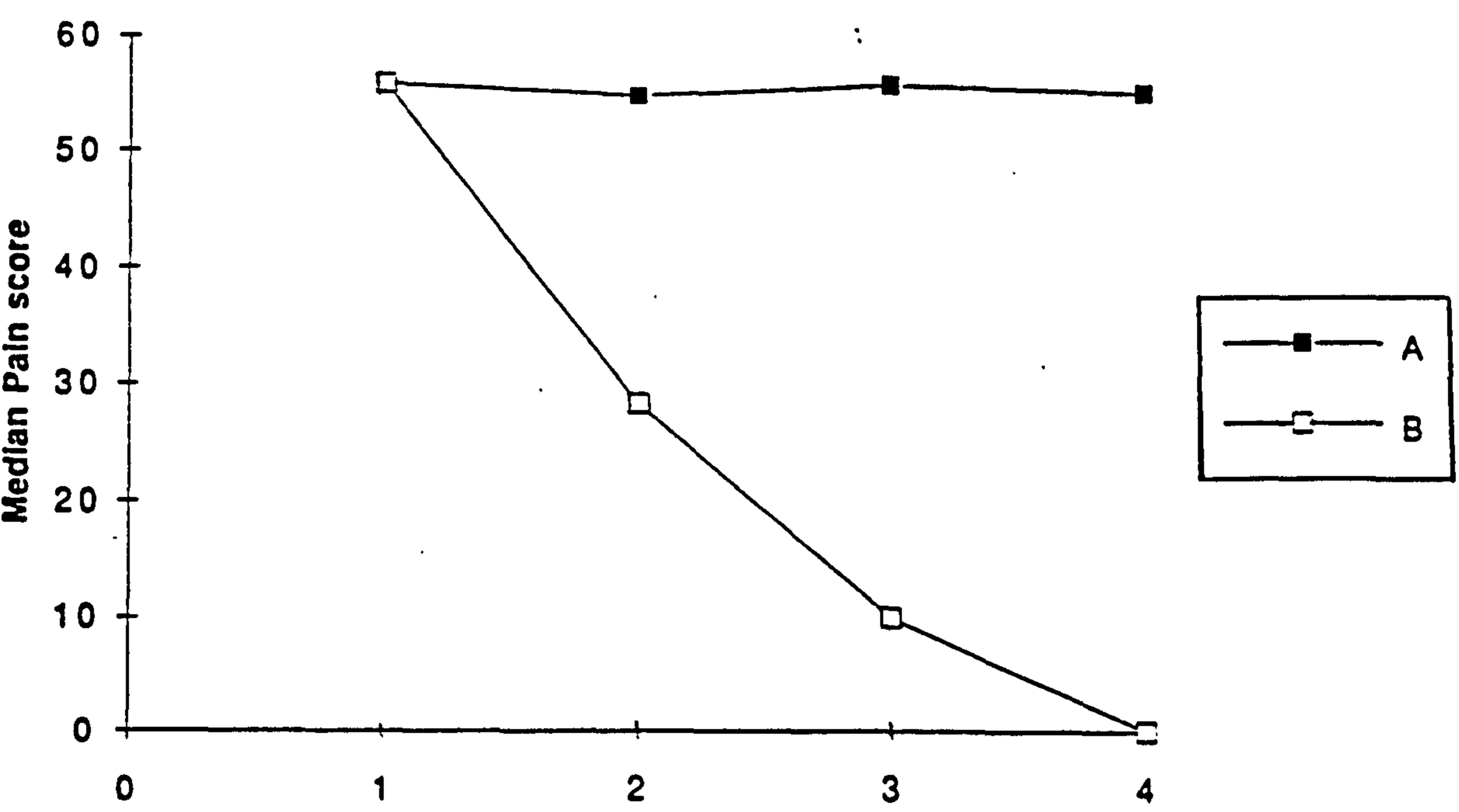


Fig. - 4.15. Median pain score: Period 1 - 4

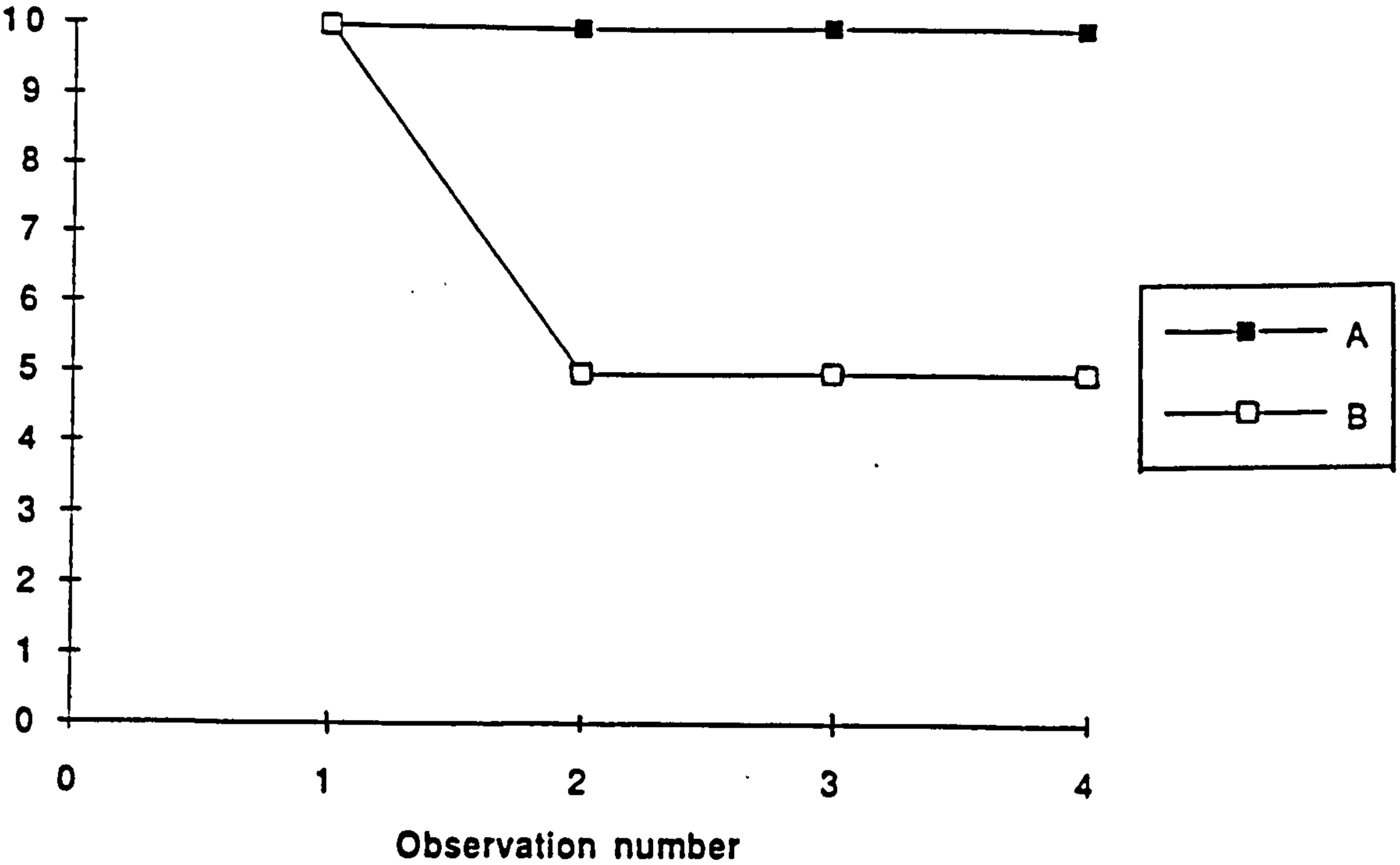


Fig. - 4.16. Median stiffness score: Period 1 - 4.

CHAPTER FIVE

Discussion

5. Introduction

The ability to repair injured or damaged tissue is a biological adaptation that is essential to the survival of complex multi-cellular organisms. With the exception of organs, such as the liver, that have the ability to regenerate themselves the formation of fibrous tissue is the usual process of repair following tissue damage. Degenerative pathology in the Achilles tendon is a fine example of how the reparative process does not always run a smooth course. This is reflected in the fact that the Achilles tendon affected by trauma or pathology is a difficult condition to clinically manage. On canvassing a group of practitioners as to the most appropriate treatment for a patient suffering from chronic tendon pathology, it is likely that the only consensus of opinion will be that this is a nemesis for both patient and clinician.

The underlying purpose of this study was to attempt to arrive at some answers as to why tendon tissue provides this unique clinical challenge and in addition marry some varied scientific evidence that micro-current stimulation can augment soft-tissue healing to the pathological processes. The study was therefore based upon the following hypothesis that:

Micro-current electrical stimulation will cause an alteration in cell (fibroblast) behaviour and induce a modification in the healing processes involved in the Achilles tendon with chronic pathology.

5.1. Review of the methodology

Initially it was planned to test the hypothesis by conducting a thorough clinical trial which would evaluate the clinical efficacy of micro-current stimulation by comparing the functional outcomes in patients suffering from chronic Achilles tendon pathology and comparing these outcomes with a comparable group of patients clinically managed with current conservative methods.

An evaluation of the efficacy of micro-current electrical stimulation in relation to the patients functional outcomes was conducted by means of a series of clinical tests and diagnostic ultrasound.

However, in order to start building a picture of the possible mechanisms involved in the augmentation in soft-tissue healing induced by micro-current electrical stimulation, and reported in the literature, a series of *in-vitro* studies was conducted.

The discussion of the experimental results will follow the order in which they were presented in the Chapter outlining the experimental methodology. The *in-vitro* studies were conducted with the aim of answering the main questions:

* *Rates of cell replication- are they modified by the application of micro-current electrical stimulation in comparison with a non-stimulated control group?*

* *Do 3T3 mouse fibroblasts and human tendon fibroblasts respond in a similar way following a period of micro-current electrical stimulation?*

5.2. In-vitro experiments with 3T3 mouse fibroblasts

The purpose of the first experiment was to establish if the application of an electric current of either 1μA and 40μA at a pulse rate of 10 pulses per second would alter the rates of cell proliferation in MC3T3 mouse fibroblasts grown in culture in comparison with non-stimulated control cells.

The results of the the present experiment re-inforced the findings from other studies and provided more evidence that the application of pulsed micro-current does have an influence upon the biological behaviour of fibroblast cells. One way this therapy apparently manifests itself is by causing an alteration in the rate of cell replication. However, the purpose of any experiment is to not only explore what happens following an intervention but also why. Establishing the mechanisms for any reported changes perhaps requires a greater exploration of biological processes than the initial experimental process itself. It is also important when drawing parallels between different studies that a careful analysis of the experimental methods employed is undertaken to ensure that like is matched with like. The author has identified this as a possible "grey area" as many of the reported studies are vague in their description concerning the exact parameters employed in relation to electrical stimulation. In addition, using commercially produced cell lines may not necessarily provide a true representation of the biological response seen *in-vivo.*

However, it is still pertinent to examine the results, particularly as this present set of experiments compared the behaviour of both mouse fibroblasts and tenocytes derived from human specimens.

5.2.1. Why the changes in the rates of cell replication?

The reason for the alteration of cell behaviour and cell replication, in the presence of, or following the application of an micro-current, is unknown. However, the fact that replication rates are affected hints at changes in the mitotic behaviour and hence the DNA of the cell nucleus. Indeed, there have been some other studies, albeit a few, that have demonstrated a change in DNA and protein synthesis following electrical stimulation. Peterson and Yamaguchi (1996) examined the regulation of DNA synthesis and proliferation in a MC3T3-E1 cells and reported the logarithmic growth cell proliferation curve. It was composed of a lag phase followed by growth phase and plateau phase of growth. Consistent with this reported response all three groups in this present study followed this similar pattern. However, the group stimulated at 40μA showed a much greater proliferation following the lag phase and then the curve showed a second peak from days five to seven.

The control group followed a typical growth pattern for fibroblast cells. The lag phase, a steep rise in proliferation and then the plateau with a 66-fold total increase.

The cell groups exposed to 1 μA demonstrated the same pattern of growth as the control group, which is an important factor when examining the results. However, the extent of cell proliferation was greatly reduced to end with only an 11-fold increase by day seven. The results of this aspect were not helpful to the understanding of the problem.

The mechanisms for the reduction in cell proliferation are not clear. The trypan blue exclusion dye showed a 92% viability rate, therefore it did not appear that the cells were being killed off by the electrical current. They were simply not replicating at the same rate as the control group. The obvious question to raise when searching for an explanation is the accuracy of the plating density. However, this is not believed to be an area of experimental error for all the well plates were plated at the same time and randomly allocated, in a set of three, to their experimental group. It is therefore unlikely that a plating error was made.

Peterson and Yamaguchi (1996), also highlighted the fact that once maximum cell density is obtained proliferation is slowed considerably resulting in a mixed population of quiescent and dividing cells. This was not the case with the group stimulated with 40μA. Examining the structural response to electrical stimuli, Yang et al (1984) reported cell shape changes and cyto-skeleton reorganisation in mouse fibroblasts that were exposed to low values of direct current. No explanation was sought or given for the modification in cell behaviour. However, other studies have highlighted that the application of a micro-current can augment the regeneration processes of various tissues and this may be due to a modification in the tissue matrix induced by a re-polarisation of cell membranes. However, studies to determine the optimal parameters have not been addressed. Relevant to this, Dunn et al (1988) also reported changes in cellular activity following a period of electrical stimulation, although this time examining dermal fibroblasts. This research group devised a collagen sponge embedded with carbon fibre electrodes which they implanted into a full thickness incised skin wound in guinea pigs.

They used currents of 20μA and 100μA and found a significantly higher concentration of fibroblasts in the experimental group when compared with the non-stimulated control group. The explanation they gave for this was the greater presence of inflammatory cells which may have been responsible for the reduced proliferation. This finding would not have been demonstrated in a isolated *in-vitro* culture.

The experimental evidence obtained to date suggests that the most probable reason for the cellular changes induced by micro-current exposure is a modification or a mimicking of the mechanisms that change the normal processes of electro-chemical signal transduction.

Lee et al (1982), discussed four reasons why the cell membrane may be involved in the process; firstly, an electric field/current is amplified within the membrane making it the most likely site of interaction. Secondly, the cell membrane is a major site of signal transduction, thirdly, changes in ion flow, especially calcium, will effect the cells behaviour and fourthly, the cell membrane is involved in controlling the electrical aspects of the cell, maintaining the potential gradient though the active regulation of ion influx into and out of the cell. It may be possible to postulate that electrical currents of differing strengths have the effect of either opening or closing the door of the fluid mosaic membrane. The phospholipid bilayer arrangement is reported to be a strong electrical insulator for maintaining electro-chemical gradients. Therefore a possible explanation for the induced changes in rates of cell replication is that the application of a micro-current may cause a redistribution of cell-surface receptors which could in turn alter ligand receptor constants to then change cell sensitivity to chemical messengers.

This would have the knock on effect of altering internal concentrations of cytosolic ions which then could implicate the activity of the cell nucleus. This may provide an explanation for the reduction following 1μA of stimulation. This level of stimulation may not kill the cell but compromise cytosolic harmony which may discourage cell replication. Whether this effect is permanent for the cells' life or a temporary phenomenon was evaluated by re-plating each cell group to their original density of $3x10^3$ and leaving it to grow with no intervention. This showed that a normal growth pattern was re-established.

5.3. In-vitro experiment - Human tenocytes

The second aspect of the *in-vitro* study was to evaluate if the application of an electrical current of 40μA would promote cell proliferation in isolated fibroblast cell cultures in comparison with non-stimulated cells acting as a control.

The objective of this aspect of the study was to evaluate if cells derived from human tendons would exhibit a similar biological response following a period of micro-current electrical stimulation as the 3T3 mouse fibroblasts. Unfortunately there were in-sufficient cells to conduct the experiment using 1 micro-amp of electrical stimulation. Two important facts drawn from this second experiment warrant further discussion. Firstly, the results from the tenocyte experimental group were entirely consistent with the results from the previous experiment. A greater rate of cell replication was witnessed following the period of electrical stimulation. However, the high rate of cell death (50%), in the human tenocytes groups, was not consistent with that of the mouse fibroblasts (92%).

Of the total cell count for the control group ($3x10^5$), $1.3x10^5$ were not viable at day seven. In the experimental group the total cell count was $8.4x10^5$ of which $4.6x10^5$ were non-viable. It was considered that there may have been a connection between the nature of the specimens harvested and the high rate of cell death in the isolated tenocytes. It is presumed that the cells, that comprise the tendon tissue, would have been exposed to an altered chemical environment after the patient's death, than in life. This change may not have been sufficient to kill the cells, however, there is the possibility that it could have interfered with their ability to reproduce to their full capacity. It has to be a matter for speculation as to why this was only noticed in the isolated cells. We may have been witnessing a normal biological situation.

The author believes that it is not unreasonable to hypothesise, an unproven theory, that all cells are believed to be genetically programmed to reproduce a given number of times after which time they die. Cultured cell lines do not tend to behave in this way and may be mutated in some way for they appear to reproduce ad-infinitum. The other relevant point to highlight is that the mouse fibroblasts, may be behaving as mutant cells, a result of multiple passaging.

Whether the application of micro-current electrical stimulation had the effect of "kick-starting" the fibroblast into life is still open to debate. It is believed that the synthesis of collagen begins with the lining up of a number of amino acids according to the code stored in the deoxyribonucleic acid (DNA). Messenger RNA provides the correct sequence, and transfer ribonucleic acids to their places in the αchain which occurs on the ribosomes.

If the chain sequence is not complete the ration of amino acids will not allow the next stage where hydroxyproline and hydroxylysine are made on the ribosome by hydroxylation of proline and lysine. These two enzymes are unique for they are not present anywhere else in the body and they are active in the supply of oxygen and co-factors such as vitamin C, αketlglutarate and iron. The alteration of replication rates in the fibroblasts implies an alteration of a DNA sub-unit nucleotide.

Scientists are well aware of how easy it is to alter genetic material which can produce both somatic and genetic effects. Only a study examining DNA sequencing of the fibroblast nucleotide following the micro-current application would provide the answer to this.

Collagen synthesis is stimulated by lactic acid and vitamin C. Lactic acid is formed by granulocytes and macrophages. Differences in acidosis in the growth medium following intervention were not measured and perhaps should have been clarified. However, in a similar study conducted by Bourguignon and Bourguignon (1987), evaluating the effect of electrical stimulation upon diploid fibroblasts, no change in pH in the growth medium was found during or following the period of electrical stimulation.

Arriving at an explanation for the effects on cell behaviour, following a period of micro-current electrical stimulation, is helped by the study of Illingworth and Barker (1980). They reported that there was an electric current density of between 10-50μA/cm^2 emerging during the healing of the stumps of children's fingers that were accidently amputated measured with the fingertips immersed in saline solution.

Lee et al (1982), commented that a commonly held view in paediatric and hand surgery circles is that fingertip amputations are best treated by changes of moist dressings.

Advocates of this method believe that it produces better functional and aesthetic results than does immediate closure with a graft. Whether the explanation is related to the electric-current induced regeneration is not known. However, a skin graft would have the potential of blocking or changing the current flow.

This type of study has led to work that has experimented with applying an external current of a similar intensity in order to encourage the regeneration process. Smith (1967) and Becker (1985), have both had partial success with limb regeneration by implanting a device designed to deliver a current through an amputated limb.

5.4. Cell replication and chronic tendon pathology

When discussing cell replication rates it is pertinent to examine what happens when a tendon is affected by chronic pathology. When an area of tissue is damaged the fibroblasts cells infiltrate the area and produce an immature form of the protein collagen, known as pro-collagen. This protein forms the cell matrix as it matures and therefore re-builds the damaged area. However, this process of cell repair can cause problems if the matrix does not reconstitute itself adequately or forms new tissue inappropriately, for example between the tendon and its sheath. The understanding of cells adhesion helps to clarify cell matrix formation and behaviour.

Cell adhesion is crucial for the assembly of individual cells into three-dimensional tissue matrix. Cells do not simply stick together as many basic text books imply, particularly with reference to tendon sheath adhesions. The cell-adhesion system should be viewed as a mechanism that translates genetic information into the three-dimensional patterns of cells in tissue. Gumbiner (1996), reports that an important adhesion mechanism is the prevalent morphogenetic transition mediated by the process of cell condensation or compaction. Cell compaction is mediated by cadherins, a glycoprotein, in a process that is mechanically analogous to integrin-mediated spreading of fibroblasts. The functional units of cell adhesion are multi-protein complexes. The cell adhesion receptors are transmembrane glycoproteins that are thought to mediate binding interactions at the extracellular surface and they determine cell to cell recognition. At the extra cellular surface the receptors recognise and interact with either other cell adhesion receptors on neighbouring cells or with other proteins on the extracellular matrix of other cells (ECM). These include collagens and fibronectins which may explain why adhesions can form between the paratenon and the endotenon.

Andujar et al (1992) suggested that the presence of plasma fibronectin promotes a faster rate of cell adhesion and spreading on collagen fibrils. In acute paratenonitis there is an influx of plasma containing inflammatory mediators with may promote cell adhesion. Cell migration seems to be an important factor by which cell contraction in controlled. If the stimulation does initiate any modified structural behaviour then this may go some way to explain the modified cell behaviour.

Additional factors affecting fibrillogenesis, such as the removal of telopeptides by proteinase digestion and the addition of glycosaminoglycans are debated by authors such as Rubin et al (1963) and Wood (1960).

5.5 *In-vivo* study: clinical tests

The reliability and viability of the clinical tests that were used to evaluate the functional outcomes in the patients participating in the study is central to the integrity of the *in-vivo* study. The tests were based upon ones used in previous studies, for example Carden et al (1987), that evaluated functional outcomes in patients following a full Achilles tendon ruptures that followed different treatment regimes.

The tests found to be utilised commonly in other studies can be divided into two distinct groups:

- strength testing
- clinical examination in conjunction with subjective assessment

Strength tests were performed on a variety of equipment.

The Cybex dynamometer, used to measure strength and power, was used by several authors including Steele et al (1993) and Inglis et al (1986). The high cost of this equipment prohibited its use for this study. A significant study undertaken in the United Kingdom by Carden et al (1987) examined the early and late management of the Achilles tendon following acute rupture employed a dedicated device which was produced by the bio-mechanical department at Salford University. This device measured isometric plantar flexion and was kindly loaned for the purpose of this study.

The device was reported by Carden et al.(1987) to give reproducible comparisons between lower limbs. In that study it was used to assess the functional capacity of a ruptured Achilles tendon following treatment. Therefore, this appeared to be an appropriate method to use for this study for functional disability of varying degrees as seen in Achilles tendons with both acute ruptures and chronic pathology. The device did not provide absolute measures of strength, therefore comparison could not be made between one subject and another. Carden et al.'s study also used a subjective assessment in the form of a verbal enquiry to the patient: "are you happy with the result of your treatment?" In addition to the yes/no answer the reason for a negative response was noted.

In practice, in the study reported here, the strength testing device was found to be a very unreliable method of assessing the condition of the tendon. It was used at initial assessment but it soon became apparent that it was not reflective consistently of the condition of an individuals' Achilles tendon pathology. There were a number of reasons for this:

* Many patients presented with bi-lateral Achilles tendon pathology so comparisons could not be obtained. The measuring scale used is arbitrary so absolute levels were of no value.

* If pain and stiffness were brought on by exercise then static isometric plantar-flexion measurement did not accurately reflect the intensity of this.

* Many athletes, even with quite severe pathology continued to train with their injury and had quite high levels of pain and stiffness which were not demonstrated by the test. One patient walked with a limp such was the extent of his problem but he performed the test to a satisfactory level before expressing any significant discomfort.

* Similarly to the point above, particularly amongst the athletes in the study, subjects that were accustomed to training with a level of pain performed the test with the same psychological approach .

Despite instructions advising that the test should be performed pain free, it was impossible to be convinced that this was always the case.

For these reasons it was felt that the test was neither valid nor objective. Hence, as other tests, such as diagnostic ultrasound, pain and stiffness assessment, were able to provide a more accurate assessment of the pathology or condition, it was decided not to continue with it.

5.6. In-vivo study: Diagnostic ultrasound

5.6.1 Introduction

The use of diagnostic ultrasound for musculo-skeletal imaging has been reviewed earlier in the thesis, (see Chapter Two). Ultrasound was demonstrated to be an accurate method of assessing the progress of the pathological state of the Achilles tendon. It was able to add significant detail to the whole clinical picture concerning the specific type of pathology and the proportion of the tendon affected. Differentiating between different types of pathology, which can present with the same symptoms of pain and a loss of flexibility, was important. For example, the presence of intra-tendinous micro-calcification can only be confirmed by imaging, this would be vital information for the practitioner treating the disorder for an inappropriate treatment such as massage may well be a further irritant to an inflamed or degenerating tendon.

Several authors, O'Reilly & Massouh (1993); Maffulli et al.(1987); Fornage (1986a,b) and Mathieson et al (1988) have documented the use of diagnostic ultrasound to investigate pathology occurring in the Achilles tendon and all produced similar conclusions. It is therefore perplexing that many of the studies evaluating various forms of surgical intervention for chronic Achilles tendon pathology do not mention the use of imaging to assist in the evaluation of the efficacy of the given treatment.

A paper was produced from this study, *Diagnostic Ultrasound: The Appearance of the Achilles Tendon Following Surgery*, Chapman-Jones and was published in 1996 (Appendix Three).

It described the sonographic appearances of the Achilles tendon following surgical intervention for chronic pathology. The conclusion was drawn that surgical intervention did not always leave the patient without symptoms and it was felt that diagnostic ultrasound could have made a contribution to the post-surgical assessment of the tendon. Certainly, and perhaps controversially, the paper showed that, it was at least, for some clinicians, the first time their surgical techniques on the Achilles tendon had been scrutinised using diagnostic ultrasound with the less successful cases highlighted with clinical imaging evidence of the recurrence of symptoms.

Improvements in ultrasound equipment and subsequently image quality have enabled both the confirmation of a diagnosis of chronic Achilles tendon pathology, and the ability to identify the alteration in normal tendon anatomy and its anatomo-pathology stage. It is, for example, now possible to differentiate easily between the bundles of collagen fibres of a tendon contained within the tendon sheath. Fluid transmits ultrasound with little reflection and attenuation so ultrasound imaging is particularly suitable for assessing inflammatory processes such as paratenonitis. In this study this was one of its specific uses and the efficacy of ultrasound imaging in detecting paratenonitis will be discussed later in the text.

Williams (1986), advocated the use of soft-tissue radiography as an aid to clinical diagnosis, but it is argued that in this study that its relative insensitivity in the differentiation of subtle pathology makes its value limited only to gross pathology, dense calcification, anterior tendon calcaneal impingement and substantial degrees of peritenonitis.

5.6.2 Scanning technique and the validity of diagnostic ultrasound

Consistent with all ultrasound examinations, the skill of the operator is essential to produce quality diagnostic images, (Fornage, 1986 a&b).

A standard technique for scanning the Achilles tendon was employed in this study. Both left and right sides were scanned routinely to exclude or include bi-lateral pathology. The tendon is relatively small and the examination technique must be meticulous to avoid artifacts. The major pitfall consists of false hypo-echogenicity resulting from an oblique ultrasound beam. Fornage (1986a,b and 1987) has written several separate articles on this subject. It is imperative to ensure that the surface of the probe is placed parallel to the tendon. This is particularly important for this imaging modality. In the right hands ultrasound has proved to be a reliable method of assessing musculo-skeletal pathology in the Achilles tendon. The study has demonstrated a correlation with the general assessment evaluation of 0.769, pain of 0.764 and stiffness of 0.713. This statistical analysis was undertaken using the Spearman rank correlation test, at a 0.05 level of significance.

However, it must be acknowledged that there are potential operator errors. If the study was to be repeated and resources were plentiful, then the use of magnetic resonance imaging, (MRI), would be an advantageous adjunct to imaging of the tendon.

MRI differs vastly in cost and availability compared with ultrasound and these factors prohibited its use in this clinical study.

5.6.2 In-vivo study: Subjective assessment

Perhaps the most pertinent evidence in the evaluation of the efficacy of the clinical management regimes employed for both groups, in this study, is provided by the subjects themselves. A majority of the subjects, involved in the study are athletes in some shape or form. They entered the study because they were having little success with their current treatment regimes or because they could not race or train at the same level as prior to their injury. For all these patients their prime objective was to return to the sport of their choice.

The debate as to whether subjects may lie or exaggerate their progress to "please the doctor", cited as a potential problem when subjective assessment is used as a method of evaluation in clinical medical trials, was not thought to be a sufficiently significant factor in this. Anecdotal evidence from the initial assessment in this study shows that many subjects were fed-up with their condition and as a consequence it was not felt that they would claim an improvement when there was in fact no improvement.

The visual analogue scale used in this study in order to subjectively assess a level of a pain is a standard subjective assessment tool. The fact that one person considers, for example, a pain level of six to be more or less intense than another person also selecting his pain level as six does not matter because the study tool measures an individual's improvements.

The numerical scale employed to assess pain and stiffness was devised for this study primarily because there did not appear, from the literature, to be a suitable model that had been previously used. It was considered important to assess the intensity of pain but also how often pain occurred and how it affected the subject's life.

It is recognised that there is always going to be a degree of difference between subjects. However, a quite remarkable level of consistency was found when considering and comparing all the markers for clinical assessment that were used in the study. This was borne out by the Mann-Whitney U tests reported in the results chapter.

The four point scale for general assessment of, "Excellent", "Good", "Fair" and "Poor", suited the requirements of this study as it was possible to categorise particular levels of participation and take into consideration the other clinical markers. This was important for some athletes were still training although not to the same intensity as they were prior to their injury or the onset of their problems.

If this study were to be repeated subjective assessment would be used again in the same manner and with confidence. The assessment was straight-forward to convert to a numerical scale in order to conduct the statistical analysis; the subjects found it easy to understand, and it could be reproduced within a questionnaire if the subject was unable to attend a follow-up appointment personally. An example of such a questionnaire is contained in Appendix Four.

5.7. *The comparison between group A and group B*

5.7.1. Introduction

The aim of the study was to investigate the healing processes involved in the Achilles tendon with chronic pathology and to determine whether the application of micro-current influences these processes. The statement from Clement et al (1984) that Achilles tendon pathology is a nemesis to the athlete and physician can be challenged by the results of this study. The response of the chronic Achilles tendon pathology in those subjects exposed to the micro-current treatment provides valuable information concerning the processes involved. In addition it suggests that relevant physiological, biochemical and histo-pathological evidence from previous studies using micro-current may be correlated to this study's specific application of micro-current.

When comparing the response of subjects in group A to current clinical management and group B to the new micro-current treatment it is relevant to examine if there was a physiological or clinical explanation for the poor response to the current conservative therapy in comparison to the good response to the micro-current treatment regime. Alternatively, was it that some treatments in group A were applied inappropriately?

Undoubtedly the key to the successful treatment of any clinical or pathological condition must be the clinical basis for the treatment and understanding by the practitioner of the given condition.

Dr. J.G.P. Williams, described in his obituary in the British Journal of Sports Medicine, No.29 Vol 4 (1996), as a "pioneer of British sports medicine and soft-tissue injury", began a lecture at the National Sports Medicine Institute, London (February 1995) by asking the audience;

> *what was the major problem affecting the Achilles tendon? - It was the people who treat it. It is a major interest of mine and I do not claim to know how to treat all its problems, whereas many 'experts' do.*

Whilst it may not be diplomatic to approach the issue in such a confrontational manner as that of Williams, the apparent *ad-hoc* application and the inconsistency of current conservative treatment regimes, which perhaps prompted William's comment, is not surprising given the vague basis for some of the treatments in current practice coupled with the biochemical and physiological environment in which the tendon exists.

Many authors have, as was shown earlier in the literature review, commented upon the unsatisfactory reproducibility of treatments widely used by physiotherapists such as ultrasound, laser or interferential regimes.

5.8. Micro-Current: The treatment parameters used

A most important point to highlight initially in discussing the new micro-current treatment regime is that its only similarity to other forms of electrotherapy is that it utilises electrical current. There the similarity ends.

A significant factor, for the pathologies treated in this study, in determining the resultant outcome is the timing of the treatment and the post-treatment rehabilitation.

An explanation of the theory of application will assist in putting the this statement into some sort of context and to correlate this with other relevant studies in order to put the findings of this current study into a scientific context.

The works of Becker (1985) and Nordenstrom (1967) have been highlighted earlier in this work as providing the impetus for much of the subsequent work done in the field.

Many of the studies reported have examined the effect of micro-current application to animal tendons, mainly rabbits, rats and dogs, by analysing the resultant strength and healing times of tendons in experimental groups compared with control groups. These studies are helpful in order to establish a relevance for this current treatment application under consideration and to demonstrate whether a trend or pattern emerges from a series of parallel but unconnected studies. Unfortunately, many of these studies fail to give an explanation for their results or the basis for their selection of treatment parameters. Nessler and Mass (1985) examined the biological activity of rabbit tendons *in-vitro*. They experimented with applying a small electrical stimulation of 7 μA to the tendons.

Histologically, both the control tendons and the electrically stimulated tendons showed signs of healing and at seven days, the tenocytes in both groups began to lose their normal elongated shape and became plump. However, the stimulated tendons exhibited large scattered areas of florid cellular proliferation and collagen synthesis while the control tendons displayed far fewer new collagen fibrils. The maximum proline uptake reached its peak at two weeks in the control group and at one week in the experimental group. At six weeks in the experimental group the uptake was still greater than the peaks attained by the control group. The conclusion reached was that the tendons exposed to electrical stimulation showed enhanced and accelerated early synthetic activity with the possibility that the enhancement may persist for as long as six weeks. The histological findings indicated that the healing response in the tendon was enhanced by the electrical stimulation. These findings included increased cellularity, change in cell shape, epitenon proliferation and bridging of the gap, the appearance of delicate new collagen fibrils and the capping of the tendons. These characteristics are consistent with those described during tendon repair *in-vivo*, by Gelberman et al.(1983) and Lundborg and Rank (, 1978).

Bourguignon & Bourguignon (1987) conducted a controlled study that was carried out to determine the specific conditions required for electrical stimulation of soft tissue in order to effect the reparative processes within it. This study used human dermal fibroblasts and whilst they are one of the primary cells involved in human tissue regeneration, they are specialist to the type of tissue being regenerated. It was therefore unknown if it was reasonable to correlate the findings from Bourguignon & Bourguignons' work with a clinical application on tendon fibroblasts, tenocytes.

Three parameters were examined in the study; voltage, pulse rate and the location of the cells relative to the electrodes. The study revealed that the electrical stimulation induced fibroblasts to:

- significantly increase their rate of protein synthesis indicating a greater synthesis of collagen
- increase the DNA synthesised suggesting that the fibroblasts were stimulated to proliferate.

These two factors could indicate why the application of micro-current electrical stimulation was able to influence the rate of soft-tissue healing.

Bourguignon and Bourguignon state that the mechanism by which any type of electrical stimulation induces enhanced cellular activity is unknown at the present time. They suggested the idea that an increase in the temperature could result in a stimulation of metabolic activity. They did not, however detect any change in temperature(>0.1 °C) in the medium used.

If this was an acceptable explanation for the enhancement of the healing processes then any temperature inducing treatment, such a laser treatment, should produce a similar effect, but because the current used was so low, 50μA, any consequent heating effect would be minimal. Consideration was given to the pH of the medium and whether it may be altered by either the release of ions into the medium or by a change in the chemical composition of the medium. No significant change was detected and the pH remained within not more than >0.1pH/unit.

A third possibility to consider was whether the electrodes were releasing ions that could affect cellular biosynthesis. This was eliminated by exposing the growth medium for both the control and the treatment groups to the current but with no fibroblasts present within it. The original experiment was then repeated with the treatment group receiving the stimulation and the same protein and DNA enhancement was found.

The low levels of current used in micro-current applications may suggest that an electro-physiological effect rather than an electrochemical reaction may be induced. This was suggested in paper by Binder (1981) and was supported by the work of Bourguignon and Bourguignon. Using a fluorescent potentiometric dye Bourguignon and Bourguignon demonstrated that cell membranes exhibited an immediate depolarisation following electrical stimulation. It was shown that plasma membrane on the side of the cell facing the negative electrode depolarised, whereas the membrane on the opposite side of the cell hyper-polarised to the same degree. Bourguignon and Bourguignon hypothesised that this changing of electrical depolarisation and hyper-polarisation could trigger membrane related physiological events such as gating ion channels or activating membrane-enzyme activity.

This systematic exclusion of possible contributing factors to the induced cell changes helped to clarify the work of the current study to ensure that the same influences could be excluded. No conclusion was drawn or explanation offered for the different voltages used or the amount of stimulation required to produce an active response.

However, when considering the selection of treatment parameters for this study the work of Stanish (1984) who reported "a new technique that promotes healing of soft-tissue injuries through electricity that could revolutionise sports medicine", was of particular relevance. The Canadian orthopaedist implanted a tiny electric stimulator into surgically repaired knees and claimed to cut plaster cast and rehabilitation times by two-thirds. Stanish repaired 125 ruptured tendons and ligaments over a three year period using his novel stimulation technique. He reported that all of his first seventy patients showed improved stability at the thirty month follow up.

Stanish's technique was to implant a tiny titanium battery next to the newly repaired ligament or tendon. The pencil thin battery delivered a constant 10-20 μA current through an eight inch wire coiled around the tendon. The patients were unaware of the stimulation. The first seventy patients underwent anterior cruciate ligament repair and had moderately unstable knees. After the period of stimulation, it was reported that three stress tests revealed that 84% had completely stable knees or had only mild instability. It was unhelpful that Stanish provided no physiological explanation for the results, but he did conclude that his treatment's main benefits were the fact that it reduced healing time significantly and appeared to return ligaments and tendons to their original form.

The final point to examine in relation to the new treatment regime used in this study is what dictated the duration and intensities of the parameters used? Drawing any valid conclusion from previous studies was difficult. The only common thread that ran through the previous work was that the studies employed low levels of current and produced results that were fairly consistent with one another.

The choice of current and waveform was based on the assumption that if a flattened, modified, waveform was used, such as a square waveform, it would produce a more evenly distributed peak intensity. This would be less irritating to the peripheral nerve ending and therefore remain subsensory in nature which in turn may be more acceptable to the body's own electrophysiological healing system.

Hence parameters such as wave form and duration were chosen on the assumption that the body, as Becker (1985) proposed, works on very small levels of electrical stimulation and the replication of this would have the most beneficial results.

Owoeye, Spielholz and Nelson (1987), summarized the results of studies on tendon repair in experimental animals: -

> *"It is interesting to note that in this study the group with ten times higher current (400µA) certainly didn't have stronger tendons. In fact they were not as strong as the 40 µA group."*

Based upon this statement and the evidence from other studies a choice of 40µA was selected and believed to be as valid as any alternative within a similar range.

The voltage used in the device used to deliver the electrical stimulation is variable and automatically adjusted moment-to-moment based upon a computer controlled internal circuit that monitors the percentage change of resistance through the tissue being treated via a negative feedback mechanism. This type of impedance-sensitive voltage adaptability is an essential feature of a constant current generator, (Picker, 1987).

The current generators are designed to only use as much voltage as necessary, up to a designated maximum peak, to achieve the selected average value of the current . As an area of resistance increases, or one patient has a thicker skin, tissue or oedema, the voltage increase commensurately to maintain the desired current flow (based upon Ohm's law).

5.8.1. Micro-current: Rationale for the treatment regime

The healing processes involved in chronic Achilles tendon pathology are complex and not yet properly understood, particularly in the context of what actually triggers a healing response and what stops it. The discussion will analyse how the micro-current application may augment the healing process.

The collagen fibre disorganisation, reparation and degeneration coupled with the breakdown of the matrix structure, could be considered to be the cornerstones for the cyclic tendon breakdown found in chronic pathology. In chronic conditions it would be reasonable to believe that there is an unknown stimuli that has interfered with the normal processes which has caused an initial acute condition not to resolve. The cascade effect characterises the process in which each successive factor is activated by its predecessor.

Important mediators in the healing processes are described by van der Meulen (1982). Whether chronic pathology found in the Achilles tendon is inflammatory or degenerative in nature warrants further discussion particularly, in the context of the clinical management of the condition.

Distinguishing between the two processes in order to explain the mechanism of therapeutic treatment, particularly involving micro-current, is relevant in order to address the aim of this study.

Leadbetter (1990) described the common overuse injury as a failure of the cell matrix to adapt to a sudden or accumulative overload. The rate and mechanism of onset categorises injuries as acute or chronic.

Elementary biological studies conclude that inflammation is a localized tissue response to cell or tissue destruction or damage caused by mechanical overload, for example trauma; whether macro or micro, or by some other means, for example an invading pathogen or microbe. Inflammatory response is primarily confined to vascularised tissue since part of the essential purpose of this response is to increase the biological activity within the area to ultimately establish an environment suitable for the repair processes to occur and the equilibrium to return to that particular area.

Referring to the current study, the distribution of the various pathologies demonstrates that often the conditions affecting the tendon are not found in isolation. Therefore does one process induce another?

In group A fifty per cent, and in group B seventy five per cent, of the subjects, had more than one clinical condition on initial assessment.

Paratenonitis, inflammation of the paratenon, in isolation, was less prevalent than one would expect if inflammation was the tendon's initial response to trauma.

When the paratenon is inflamed there is restriction to the normal movement of the endotenon within the paratenon and this results in reduced flexibility. This appears to cause disruption of the endotenon.

Conversely, if the primary problem was that the endotenon was suffering from degenerative change, the paratenon may only become involved latterly when cumulative overload induced an inflammatory response.

It would perhaps be pertinent at this juncture to speculate as to what would cause an isolated inflammation of the paratenon and leave the endotenon unscathed. It is a acute condition with the chief aetiological factor being either acute muscular fatigue or blunt trauma at the musculo-tendinous junction; the sequel is a circulatory disturbance and oedema of the muscle and/or the paratenon. Crepitus is due to movement of the tendon inside the fibrin precipitated from the fibrinogen-rich fluid. Howard (1938) and Rais (1954 and 1961) have contributed to the understanding of the condition and although the work is not recent the findings have not been challenged.

Ultrasound and short-wave diathermy, ice packs, massage and passive stretching are commonly employed for the treatment of this condition. If treatment fails the fibrin in the tendon sheath becomes organised and adhesions bind to the endotenon.

Kvist & Kvist (1980), commented that conservative methods of treatment have little success when the Achilles tendon pathology condition does become chronic. This is often at the time when the subject seeks medical advice. In the chronic conditions there is often no significant crepitus. Clinical examination will reveal the presence of tender nodules around the tendon and diffuse thickening of the paratenon.

If paratenonitis can be identified early then one could conclude that an appropriate treatment would be one that accelerates the inflammatory phase.

Whilst this is an essential phase in wound healing the reparative process may only occur once it is over. Histo-chemical studies on patients with chronic paratenonitis have demonstrated that there is evidence of an increase in collagen breakdown and anaerobic metabolic enzyme activity. This can result in degeneration of the tendon tissue, (Kvist, Lehto & Jozsa , 1988). If the tendon has reached this stage then collagen production will need to be encouraged to compensate for the collagen lost. This links with the previously stated effects on fibroblasts attributed to micro-current applications.

Consistent with the above, at a Sports Medical Congress, Per Renstrom, editor of Clinical Practice of Sports Injury, Prevention and Care (1994), reminded delegates that injury to the Achilles tendon is usually a degeneration of the tendon rather than an inflammation.

This degenerative process can result in the partial ruptures, calcification and tendon enlargement which, in this study, has been shown to be associated with fibrillar degeneration.

Tendinosis denotes degenerative change. The tendon failure occurs when loads of greater than physiological magnitude are applied to a normal tendon or when a defective tendon is overcome by normal loading. A popular theory summarised by Galloway et al.(1992) is that overuse injury is caused by the inability of the tendon to resist a repetitively applied load which results in micro-tearing. This appears to most commonly present in the mid-portion of the tendon which corresponds with the relatively avascular area.

Histologically, there are differing opinions on the reason for collagen degeneration. Galloway et al (1992), reports that collagen breakdown products arising from sites of tendon injury can initiate a potent inflammatory response of proteolytic enzymes by inflammatory cells. The crucial question which would influence the design of a new treatment is whether there is a spiralling decline of degeneration as these enzymes prevent normal collagen synthesis. This in turn will result in further degeneration and a further loss of tensile strength. If the pathology affecting the tendon has reached this stage then a treatment should be based upon promoting collagen production and halting the degenerative processes.

It was stated at the beginning of this section that the conditions affecting the tendon are diverse in nature however, there are many common elements that draw the conditions together.

A tendon with an inflammation of the paratenon will not heal adequately whilst still in an active state. As discussed, the environment is unsuitable for healing mediators. If the Achilles tendon remains inflamed then the formation of paratenon based adhesions will affect the endotenon. Therefore, practitioners will then have to treat two conditions instead of one.

A pertinent question to pose therfore is how then can a clinician tell how advanced is a paratenon inflammation? Information gained from this study suggests that, from ultrasound scanning of many normal and abnormal cases, fluid is the first response to a traumatic attack.

It was possible with some subjects to tell how long it was since a person had exercised, and hence exposed the tendon to the aggravating stimuli, by the amount of fluid demonstrated within the paratenon on the diagnostic ultrasound examination. For some subjects the inflammatory stage, which should be biologically an acute response, had been present for months, sometimes years. These subjects were initially given a stretching regime in association with, if appropriate, some light exercise. Once the inflammation had stabilised the treatment regime was commenced.

An isolated paratenonitis was seen in four subjects in group A and four subjects in group B. More commonly, a combination of a tendinosis and paratenonitis was demonstrated, nine in group A and four in group B subjects. Tendinosis was demonstrated in fourteen subjects in group A and nine subjects in group B.

The most common condition demonstrated was the degeneration or inflammation of the tendon substance itself, the endotenon. These appear to be caused by failure of the cell matrix to adapt to a cyclic overload. Cumulative trauma disorder is the term that has been adopted. Leadbetter (1992) refers to a accumulative cell-matrix adaptive response, which is felt to be a more accurate description.

Degenerative tendonopathy is thought to be a result of a hypoxic degenerative process involving the tenocyte and the matrix components. Leadbetter (1992) reports that specimens examined in the adult athlete with overuse tendon injuries displayed varying degrees of the following:

1. tenocyte hyperplasia
2. blast-like changes in morphology from normal tenocyte appearance
3. prominent small vessel in-growth with accompanying mesenchymal cells.
4. paravascular collections of histiocytic or macrophage-like cells
5. endothelial hyperplasia with micro-vascular thrombosis
6. collagen fibre disorganisation with mixed reparation and degenerative change
7. micro-tears and collagen fibre separations

Leadbetter reported that inflammatory cell populations were prominent in the paratendinous structures as well as intra tendinous calcification at the site of previous intra tendinous steroid injection. Reparative cells were evident in patients with tendinosis and tendinitis pathology despite the co-existent findings of cell matrix degeneration. From these findings it seems apparent that the tendon makes an attempt to undertake a repair process but regeneration fails to reverse or catch up with the degenerative process.

A prominent source of degeneration is cell atrophy, which can be described as a decrease in the size and/or function of the cell in response to the presence or lack of an environmental signal. The reduction in the capacity of the cell matrix results in a decrease in protein synthesis, replication, contractibility and other activities such as energy production.

Several authors, Gallin et al (1988), Gamble (1988) report that a cause of such cell atrophy in the tendon is immobilisation. Taking this into account, the first aspect of the new micro-current treatment regime was that all the subjects were encouraged to maintain or start a prescribed level of exercise during the treatment plan. Additional causes reported by Leadbetter (1988), are, decreased nutrition, diminished endocrine hormonal influence, persistent inflammation, ageing and de-nervation. Degeneration represents a breakdown in the cell matrix homeostasis. The mechanism which converts the acute inflammation to a chronic inflammatory process is not known although explanations in some papers have been given.

The continued overload or irritation may stimulate the local release of cytokines which may result in autocrine and paracrine activity.

Kvist et al (1987) reported that an increased degree of enzyme activity is mainly found in the fibroblasts and inflammatory cells. The result is a lowered pH and a decreased oxygenation of the inflamed areas. A change in the size and shape of the mitochondria in the nuclei of the tenocyte are reported in the electronic microscopic appearance of the micro-traumatic tendon degeneration.

Many factors have been cited for the disruption of the processes. Age, for example, may be considered to have a epigenic and genetic role in injury response. Leadbetter (1992), summarises that ageing is characterised by a failure to maintain homeostasis under physiological stress.

It would perhaps be pertinent in this study to consider whether this would affect people in their mid-thirties, the mean age of both groups involved in the study.

Certainly many of the subjects had been actively involved in sport for many years so it may be that the life of a cell, its capacity to reproduce, is curtailed if the functional unit. of which it is a part, is stressed continually for a long period of time. Menard and Stanish (1989) note that the tendon collagen fibres possesses all of the cross-linkages shortly after its synthesis. During the maturation phase, reducible cross-linkages gradually stabilise, Eyre et al (1984). This results in a less compliant collagen fibre subject to sheer stress injury.

Therefore, as collagen synthesis has been thought to decrease with age the total content and subsequent strength of the cell matrix may be compromised by these two factors.

Documentation of age related factors perhaps provides one of the strongest clues as to the reason for a minor micro-traumatic incident giving rise to a cumulative decline in biologic factors resulting in a chronic condition.

Ippolito et al (1980) reported morphologic, immunologic and biochemical ageing processes.

The main thrust of the findings is that there is a decrease in proteoglycans and a decrease in water content. With ageing, collagen fibres increase in diameter, vary more in thickness and there may be an overall increase in insoluble collagen. Therefore, this may be why an Achilles tendon with chronic pathology is enlarged when there is a degenerative, rather than an inflammatory, process occurring.

Ippolito proposes that with age, adaptation requires longer intervals of rest and recovery. The probability that all tendon healing progresses in a typical pattern irrespective of the mechanism of injury is, in the light of the discussion, probably remote.

5.8.2 Group B: Why the improved outcome?

As was highlighted, the randomisation disadvantaged Group B, the new treatment group. There were no statistically significant differences between the two groups at the initial assessment except for the general assessment on the left Achilles tendon. It was significantly higher in the group A subjects than group B subjects. (Mann-Whitney U test p= 0.035). Group A had a median general assessment score of 3 (range 1-7), whereas group B had a median general assessment of 1 (range 1-7). This means that the subjects in group B started in a worse condition than those in group A.

In addition to the aim of the study there were two specific objectives:

1. The healing time in cases of chronic pathology of the Achilles tendon is reduced where a treatment regime is followed?

This will be covered by an evaluation of the response to treatment of the group A and Group B subjects.

2. Where a micro-current treatment regime has been followed, was the resultant functional outcome of the healed Achilles tendon sufficiently altered to allow a resumption of activity pre-symptoms?

Evaluation of the response rates for the group B subjects will enable an extrapolated physiological explanation for the positive response of the pathology to the new treatment. Much of the relevant discussion on the physiological basis for healing has been conducted.

It is now appropriate to directly link this with the treatment basis for the application of micro-current and how a physiological or bio-chemical explanation could help to rationalise the results and draw a conclusion for the treatment and how micro-current application may fit into this.

It is only possible to hypothesise how the treatment has had a positive effect upon chronic tendon pathology for detailed bio-chemical studies were not conducted for this study. Such further work may have provided a more definitive discussion but was beyond the remit of this study. However, there is greater than coincidental evidence to substantiate the rationale that tendon degeneration is the key area where micro-current can play a significant clinical role.

Further discussion was based upon the above text and upon previous data and current information and observations drawn from this study. With reference to the micro-current application, it was pertinent to postulate how such a simple treatment could be so effective, how does it differ from other forms of electro-therapy and what was the physiological basis for its action?

To rationalise an explanation it is appropriate to relate its effect to the biological basis of healing and the histo-pathological causes of a chronic condition.

* what triggers a healing cycle ?
* what causes an interference with this process and causes the acute condition to become chronic?

Such had been the longevity of some of the chronic conditions seen in this study it appeared that the low metabolic rate of tissue regeneration and maturity was a significant factor in the aetiology of chronic Achilles tendon pathology. This could subsequently have a significant bearing on the clinical management.

If micro-current does, as suggested by the *in-vitro* studies, have a stimulating effect on fibroblast activity and as a consequence collagen production, then the trigger to the healing cycle and the cyclic decline to a chronic condition perhaps holds the key to the success.

It would be reasonable to assume that a normally functioning biologic unit, such as the human body, will always attempt to repair damaged tissue in order to establish normal function. Some internal and external influences may interfere with this process.

The internal factors have been discussed with reference to cell inflammation and/or degeneration and do not warrant further analysis. The cell degeneration-reparation cycle does not, in chronic pathology, follow a normal pattern of events.

External factors are equally as difficult to quantify. For example, an injured athlete, it appeared, will continue to train which may result in a slowed or halted healing response or further tissue damage. It is important to note that although all the subjects in Group B underwent a micro-current application the treatment was more involved than simply placing the electrodes on the patient and applying the current regardless of their clinical condition.

The way the injury/condition affects the patient from a psychological perspective was an important factor. Many Achilles tendon injuries occur in people who are physically active, often well motivated about their sport, at times bordering on the obsessive. To suggest for them a treatment regime which entailed a cessation of training or activity would not, it is thought, be endured for long. It is fortunate that evidence has shown that complete rest induces a hypoxic environment within the cell matrix which results in further tissue degeneration, (Leadbeater 1992). For this study controlled levels of exercise were used to augment the micro-current treatment.

Testaments from athletes involved in this study who have previously either been told or forced to rest will substantiate the belief that individuals attain a mentally low state. This manifests itself in depression and being disheartened about their condition. Even the non-athletes were fed up with a condition that at times was preventing normal participation in daily activities.

An incidental, but nevertheless interesting finding from the study involves intra-tendinous calcification. A number of subjects seen in this study, from both groups presented with intratendinous calcification. This was demonstrated on the diagnostic ultrasound scan.

It was noted that following the application of micro-current, within six months, the calcification had markedly reduced or had disappeared in all subjects that had initially presented with this pathological feature. This finding was previously unheard of and when it was initially noticed in the first subject it was thought to be a coincidental occurrence. However, the same or similar results were demonstrated in three subsequent subjects, and it was deemed to be a significant finding in terms of possible future applications. A plausible explanation for the findings is difficult. However, it is relevant to outline how the calcium was laid down in the tendon matrix in order to conclude why it may be resolved.

Weiss & Jayson (1982) report that dystrophic calcium pyrophosphate salts precipitate in degenerative tendon tissue as a result of mitochondrial injury. The resulting calcification deposited within the collagen matrix has been described as the tombstone of tendon injury.

Calcium is an essential requirement for cell metabolism. The concentration of free calcium ions in cytoplasm is maintained at about 100nmol/litre. The concentration of calcium in interstitial fluid is 1,200,000nmol/litre. This difference results in an inwardly directed concentration gradient and electrical gradient.

Calcium enters the cells through two kinds of channels, voltage gated calcium channels and ligand gated calcium channels.

There are four types of voltage gated channels which are activated by depolarisation-repolarisation, whereas the ligand channels are activated by neuro-transmitters and hormones.

Of relevance to this study some channels are thought to be activated by stretch. Calcium is physically pumped out of cells in exchange for hydrogen. It is transported out of the cells by the sodium gradient that exchanges three sodium ions for one calcium ion.

Increases in intracellular calcium can be a result of increased cytoplasmic concentrations by releasing calcium from intra-cellular fluid. Calcium binding proteins have been identified. With relevance to this study Troponin is involved in the contraction of skeletal muscle.

The cause of abnormal deposits of calcium salts in organic structures is not fully understood. Certainly it has been noted that following injury the resultant haematoma has revealed the presence of calcium salts. The disruption of cell concentration gradients may be a reason for this. At osseous-tendinous junctions osteoblastic activity has been recognised as a factor that may result in intratendinous calcification, in the Achilles tendon this appears at the insertion at the os-calcis.

In degenerative bone disease such as arthritis the presence of osteophytes, bony outgrowths or spurs usually at the margins of the joint surfaces are apparent.

Osteophytes and accessory ossicles are seen in the calcaneum and the talus even when there is no apparent degenerative disease. For example, an os-trigonum sits behind the talus and is then caught between the tibia and the os calcis, much as a nut in a nut cracker, causing impingement in plantar flexion. The plantar fascia is not an uncommon site for bony growths into the tendon. This implies inappropriate osteoblastic activity. Osteophyte formation may occur as load bearing stresses change in a diseased or elderly joint. In the Achilles tendon calcification is commonly seen tracking upwards from the insertion at the os-calcis.

Osteoblasts may be playing a part in the degenerative process, however, throughout the process of metaplasia in the tendon the deposition of calcium may be totally independent of this process.

The resolution of this condition following the application of micro-current may be connected with the voltage-gated channels. The external application of small levels of current delivered at a low voltage may have the result of altering the polarisation of the channels which could have the result of releasing the free calcium ions into the extracellular fluid.

Investigating why calcium is deposited within the tissue matrix of a tendon with chronic pathology is an interesting aspect in helping to understand the processes involved with chronic pathology and would be valid for a future study.

5.8.3. Group B: An examination of cases and non-responders

A discussion has been conducted concerning the possible explanation of the effects that are attributed to the micro-current treatment. An examination of some selected cases and non-responders for the group B subjects will help to put the theories into a clinical context. Some of the subjects did not achieve results that were consistent with a normal distribution within the group.

Subject number 8 presented with pain during daily activities at an intensity score of 6. Ultrasound demonstrated a grade three partial rupture. The patient had been previously treated with two steroid injections. Whether there was a correlation between the gross tendon degeneration and the steroid injection is difficult to decide.

The subject, at the time of presentation, found his work as a labourer difficult.

Following the application of the micro-current treatment the subject's condition did respond favourably and was, after three months, giving less pain with daily activities. His ultrasound did however show a ring of fluid within the paratenon suggestive of an inflammatory response. The rupture was resolving. The condition stabilised at this point and at the one year assessment there was little change from the improvement at three months. The ultrasound appearance was significantly improved in comparison with the original scan. It is felt that two points are pertinent.

The inflammation demonstrated at the three month assessment did not return and may be attributed to the subject undertaking a greater level of activity as the tendon was less painful then was previously experienced.

It does appear that the main problem with this patient was severe degeneration of the collagen matrix. Partial regeneration of the matrix was seen, and this could be attributed to the micro-current application. It was evidently insufficient to promote a complete recovery. In order to comply with the standardised nature of the study all the subjects were only exposed to one course of treatment. However, it is believed that another application of the treatment may have produced a further regeneration which would have resulted in a better improvement. This highlights why careful monitoring of a subject's condition is essential, for no two subject's pathologies appear to be consistent with one another.

The second subject, number 9, was an international class athlete. Previously he had undergone bi-lateral steroid injection to the tendon substance followed by decompression surgery. Neither tendon was pain free on presentation, the left being worse than the right. The diagnostic ultrasound scan demonstrated on the right side that following surgery the tendon had a nodular appearance but was otherwise unremarkable. The left tendon demonstrated areas of fibrillar degeneration and hyper-echogenicity of Kager's triangle. This could have represented a tendonitis although the antero-posterior diameter of the left tendon was not enlarged.

At three months post- treatment the subject reported the tendon as:

Pain: Subsided over the last eight weeks

Stiffness: Tendon still stiff but manageable

Flexibility: Flexibility and movement - excellent

The tendon got worse for ten days following treatment, then began to improve significantly allowing a resumption of training to the following level per week:

- **running:** 5 times/ week *moderate*, 2 times/week *high* level of effort.

- **weights:** 1 time/week *moderate* level, 4 times/week of general conditioning.

The subject was an international athlete and was advised by the author to scale down the quantity and intensity of training. He was doing too much too soon. He was beginning to feel he was on the way back for the first time in six months.

At six months post-treatment the subject raced in a road relay and over cross- country and reported no problems during the race but the following morning found the tendon extremely stiff. The subject was again advised to reduce the training load and the author feels this advice was not taken.

The tendon flared up again and a letter of advice was sent.

He had a cold at this time and as a consequence was forced to rest.

The ultrasound appearance three weeks later showed an improvement from the original assessment. The antero-posterior diameter was reduced to be within normal limits. The subject reported a reduction to only mild pain levels with moderate exercise and resumed training again with renewed gusto and broke down once again.

The subject decided to have surgery in February 1995. He was readmitted with an infection post-surgery and was given no post-surgical advice by the surgeon. At three months post-surgery he was still in considerable pain and unable to properly bear his weight.

Six months post-surgery the subject had sought the advice of an alternative practitioner. He was using heel wedges in his shoes and has reported an improvement. This would be expected in the short-term due to the effect of shortening the Achilles tendon.

It was felt that the subject's enthusiasm for a speedy return to training and competition may have been his down-fall. This though, may be being unfair on the individual concerned who had previously undergone a myriad of treatments that had all been unsuccessful in resolving the condition long-term.

There may be some pathological conditions present, such as this degenerative process, and one really has no definitive answer as to why it occurs. This subject may be one such individual who has experienced all that modern medicine can do and still has shown no significant improvement.

Subject number 10 had a previous left Achilles tendon complete rupture whilst playing squash. He was treated surgically with an end-to-end suture and was in a plaster cast for three months. He presented with persistent left Achilles tendon pain since surgery.

The right tendon has no symptoms.

The diagnostic ultrasound scan demonstrated the following:

The left tendon showed a grossly enlarged tendon, with an Andorra-posterior diameter of 1.6 cm and a transverse diameter of 2.2cm. This was almost certainly a result of the surgery. The tendon had lost its normal fibrillar appearance and there was a hyper-ectogenic area measuring 0.3 cm antero-posteriorly x 0.8cms transversely, lying 1cm superior to the insertion at the os-calcis.

The dense area noted was unlikely to be calcification within the tendon for there was no posterior shadowing from it. It was probably an area of fibrous tissue or haematoma. On the transverse scans the tendon was demonstrated as round instead of the normal oval appearance.

His assessment score was as follows:

Pain: Lt - 82 (75+7)

Stiffness: Lt - 15

General Assessment: Lt - Poor

The subject reported a gradual improvement in his symptoms following the treatment and found the set of prescribed calf raising exercises were helping to improve the flexibility of the tendon. Pain (55) and stiffness (10) were reduced at the three month assessment.

The diagnostic ultrasound report at three months showed the tendon to be still enlarged at its insertion with a maximum Andorra-posterior diameter of 1.5cm. The hyper-echogenic area previously noted was still present. It was unchanged in size. A soft-tissue lateral ankle radiograph was taken in order to help evaluate the density of the area. However, despite its size it was not of sufficient density to be demonstrated radiographically.

At six months post-treatment the subject had started doing some steady runs. The tendon was stiff, (10), whilst jogging and remained so for the rest of the day. The level of pain, (56), was not as intense and daily activities did not aggravate the problem any longer.

The subject was unavailable for another ultrasound scan as he has moved away from the area.

Why did the subject not go on to recover? It was felt that the disruption to the normal anatomy either through trauma, surgery or both are possibly the most difficult to rectify. This subject had stabilised and then shown no significant change from the last assessment. If there is, as has been suggested, a correlation between age and degeneration then perhaps when the tendon is exposed to severe disruption the regenerative processes are not sufficient to counteract the degenerative processes or the hypoxic state that exists in the degenerative process prohibits a resurgence of normal metabolic phase.

Perhaps one exposure to micro-current was insufficient to be of any significant value. Continuous application of the current may have been more appropriate for this subject; as Stanish (1984), used in his study. The restrictions of the study methodology prevented this application from being feasible.

Subject number 24 was always going to be a gamble and the fact that by chance he was allocated to group B helped to demonstrate that the study was not biased towards the group B subjects. The patient was an international high jumper. At the time of the initial consultation he was unable to compete, but nevertheless was selected to compete in the 1994 Commonwealth games. His only priority was to resolve the condition of his Achilles tendon in order that he might jump again. He had tried all available treatments without success.

He was prepared to take the gamble that the randomisation procedure may mean he was not selected for the new treatment. In the event he was drawn to be a member of the new treatment group.

For the research study, he would be an interesting inclusion to evaluate whether exposing the tendon to a high level of competition relatively soon after treatment would have a positive or negative effect.

He presented with bi-lateral Achilles tendon pain and stiffness. The left was worse than the right. The diagnostic ultrasound report demonstrated:

Left: Enlarged 3-4cm superior to the insertion at the os calcis. The Andorra-posterior diameter measures 0.9 cm, the transverse diameter 1.6 cm.

The general appearance of the tendon is of fibrillar disintegration. These areas are small and probably represent chronic tendonitis.

Right: The Andorra-posterior diameter measures 0.6 cm, the transverse diameter 1.6 cm. The right tendon is of a more normal appearance, although there is an area, three centimetres superior to the insertion, which could represent some disruption of the fibrillar structure.

The subjects assessment score was as follows:

Pain:	Lt - 83 (75+8)	Rt - 56 (50+6)
Stiffness:	Lt - 15	Rt - 10
General Assessment:		
	Lt - Poor	Rt - Fair

The subject competed in the Commonwealth Games with a reasonable degree of success. He described the tendons as better, and summarised his condition as:

Pain: Reduced at one point to almost disappear, but now beginning to increase again as a twinge. Lt - 4 Rt - 0

Stiffness: He stretches the tendon five times a day ,but the stiffness has not completely gone. Lt - 10 Rt - 10

General Flexibility: Stiff in the mornings or after being seated for long periods of time.

The subject was now resting from training and it was decided to test the tendon again upon the resumption of training.

The ultrasound report was as follows:

Left: The tendon is less hypertrophied with an Andorra-posterior diameter of 0.7cm and a transverse diameter of 1.6cm. The fibrillar structure of the tendon now looks normal.

This is consistent with the subject's report on his symptoms reporting that whilst the tendon is still stiff from time to time there is a total cessation of pain.

Right: A normal looking tendon. The paratenon has a ragged appearance on the longitudinal scan.

At the final assessment the subject was complaining about anterior knee pain around the patella tendon which is probably unconnected with the Achilles tendon condition but has prevented any further training.

The subject was pleased with the progress of the Achilles tendon but due to the knee problem has decided to cease International competition. He believed he was too old!.

The one year assessment scores were:

Pain:	Lt - 28 (25+30) ↑83	Rt - 0 ↑56
Stiffness:	Lt - 10 ↑15	Rt - 0 ↑10
General Assessment:		
	Lt - Fair/Good	Rt - Excellent
D-F:	Lt - 21°	Rt - 24°
P-F:	Lt - 51°	Rt - 54°

The ultrasound report was as follows:

Left: The appearances are unchanged from the previous examination.

Right: The endotenon has a normal appearance. The paratenon remains ragged looking.

This subject obviously had a long history of problems which had not responded to previous treatments. The micro-current regime had not completely resolved the problem but the patient was able to compete successfully. It was difficult to categorically correlate the new treatment to his recovery but the fact was that prior to the new micro-current treatment he had, despite many other previous attempts at treating the condition, given up the chance of competing in his last International competition.

It does appear that, consistent with the other subjects, long-term athletic activity, coupled with the subjects age had contributed to the degenerative process and the micro-current had a short-term regeneration effect.

Following the patient completing his year in the study he was exposed to further micro-current treatment which was having a positive effect and he is currently training for the 1996 Olympic games. This provides stronger evidence that older, more active subjects with degenerative disease require further application of the micro-current treatment.

Subject 19 was a good county standard 400m athlete who presented with bi-lateral Achilles tendon pain since 1984. His condition had prevented him from training or competing. Rest helped to alleviate his symptoms. Any more than light exercise following a long period of rest resulted in the Achilles tendon returning to its original poor condition within three weeks. The subject was previously prescribed physiotherapy treatment, none proved to be successful in the long-term. Additionally the subject was evaluated for bio-mechanical function and was prescribed orthotics by a podiatrist. These did give relief short-term but compensatory problems appeared on the contra-lateral side manifesting as knee and hip pain.

The ultrasound report was as follows:

Right: The tendon shows areas of fibrillar disruption, which may represent cystic lesions, particularly in the anterior portion of the tendon. The tendon is not significantly enlarged.

Left: Similar appearances are noted in the right tendon.

Dorsi-flexion/plantar-flexion angles were as follows:

D-F	Lt - 21°	Rt - 20°
P-F:	Lt - 52°	Rt - 54°

The overall assessment score for this patient was as follows:

Pain:	Lt - 83 (75+8)	Rt - 83 (75+8)
Stiffness:	Lt - 10	Rt - 15
General Assessment:		
	Lt - Poor	Rt - Poor

At one month post-treatment the patient reported a significant improvement in his symptoms in both tendons. His enthusiasm for a return to athletics got the better of him in the shape of some 300 metre intervals on the track. Unsurprisingly, he reported a severe re-occurrence of symptoms. An ultrasound scan was performed which demonstrated a complete ring of fluid within the paratenon indicative of acute paratenonitis. The left was worse than the right.

Elevation, ice and gentle eccentric stretching exercises were prescribed.

The subject was re-assessed at six months post-treatment.

The subject reported that the tendon had settled down and was not as painful as at the original assessment. He undertook some gentle jogging which he was able to do with discomfort rather than pain.

The ultrasound report demonstrated the following:

Right: The tendon is much improved from the last scan. It is normal in size throughout its length and the fibrillar pattern has a more homogenous echogenicity than was previously noted. There are however small areas of fibrillar disruption on the transverse scans.

Left: The tendon structure looks normal, with no areas of irregular echogenicity.

At the final assessment the subject was still not totally symptom free although he was better than when he first attended for assessment. His ultrasound scan demonstrated a more normal appearance. He still had discomfort which was aggravated by more intense athletic activity.

The subject continues to experiment with the inclusion and exclusion of the orthotics. Maybe this was not helping the problem?

Why was the treatment not successful for this subject? It is believed that the premature athletic activity was almost certainly responsible for the acute attack of paratenonitis. Due to the constraints of the protocol of the study it was not possible to give the patient another exposure to the treatment once the acute attack had stabilised. The breakdown of the immature collagen would have returned the tendon to essentially its original state.

The periods of rest the subject underwent before the treatment, on the evidence presented previously, imply that the inactivity would have left the tendon in a hypoxic state, promoting an anaerobic metabolic processes, and thus not providing an ideal environment for normal collagen production.

In a study involving a large number of subjects it was probably inevitable that an unpredictable event would occur. Subject 34 had previously undergone surgical decompression of both Achilles tendons which was effective for three years.

After the birth of her first child she found on returning to running that both Achilles tendons again became painful. Her symptoms settled intermittently, but following the birth of her second child in 1993 the same pains developed, this time preventing her from running.

The clinical examination of both tendons showed tenderness and lumpiness.

She was referred for physiotherapy in the form of the interferential therapy.

This did not bring any relief.

The ultrasound report demonstrated:

Left: There is an area of dense tissue adjacent to the insertion at the os-calcis. It does not represent calcification as there is an absence of posterior shadowing.

The tendon is enlarged at the insertion and continues to be so to the avascular area, to an antero-posterior diameter of 0.7cm.

The appearance of the tendon is of an irregular pattern, with areas of fibrillar disruption. The echogenicity of the tissue is not consistent throughout the Achilles tendon. It has the appearance of chronic tendonitis with degenerative change.

Right: The appearance of the right tendon is worse than the left. The tendon is enlarged with an antero-posterior diameter of 0.8 cm and a transverse diameter of 1.6 cm. The transverse section demonstrates a large area of fibrillar breakdown which covers a third of the tendons cross-section. It is irregular in shape.

The subjects assessment score was;

Pain:	Lt - 81 (75+6)	Rt - 83 (75+8)
Stiffness:	Lt - 10	Rt - 10
General Assessment:		
	Lt - Poor	Rt - Poor

Due to the subject's personal circumstances she was unable to attend her next appointment until five months after her treatment. The subject had reported that the tendon had been more painful following the treatment then it improved. By three months the subject was running again. Like many athletes her eagerness to return to full training caused a different set of problems. During a ten mile race she suffered an inversion injury to her left ankle. She completed the race, albeit with a painful and swollen ankle.

She was advised that it would be better to deal with the damaged ankle ligaments and then re-assess the Achilles tendon. Because the ankle was significantly swollen it was difficult to assess objectively whether the Achilles tendon had been affected by the injury.

The subject attended for an ultrasound scan five months post-treatment.

The right tendon was improving and exhibiting a lot less symptoms than was previously experienced.

The ultrasound scan report was as follows;

Right: The tendon is slightly smaller than demonstrated on the original scan.

The large area of fibrillar breakdown is still present, although the area has reduced in size.

Left: The left ankle is still swollen. Whether there is a direct correlation between the injury to the ankle and the state of the Achilles tendon is difficult to quantify.

The Achilles tendon looked poor. It was enlarged from the insertion at the os-calcis with an antero-posterior diameter of 1.1 cm and a transverse diameter of 2.0 cm. There was an area of either fluid or fibrillar degradation on the anterior aspect of the tendon, demonstrated on the transverse scan.

The subject realised that she had returned to running too early and she should have stopped when she received the injury instead of running a further five miles. The subject's personal problems were curtailing her activities but as a physical education teacher she still continued to undertake some daily physical activity.

The subject was next seen almost one year following the treatment. Assessing the success of the treatment for the left tendon was considered to be rather academic considering the events of the past year. The effects of the injury to the complete ankle joint were still evident in the form of oedema and restricted function.

The subject reported that even though she had not been running much she has had to play netball and other sports associated with her job. The right tendon was symptom free, apart from a little stiffness.

The final assessment provided some interesting results particularly on the ultrasound scan. The left tendon was grossly enlarged with an antero-posterior diameter of 1.2cm and a maximum transverse diameter of 1.8 cm. The tendon tissue itself appeared very oedematous, indicative of an inflammatory response and the presence of immature collagen tissue. There was a significant amount of fluid surrounding the endotenon, contained within a swollen paratenon, which showed as round instead of oval.

Because of the large amount of fluid present it was difficult to give an accurate reflection on the state of the tendon tissue itself.

The right tendon had improved considerably since the previous ultrasound examination and the area of fibrillar disruption had resolved.

Clinically the tendon was not, according to the subject, giving her any problems.

The final assessment was summarised as:

Pain: Lt - 83 ↔ Rt - 0

Stiffness: Lt - 15 ↕10 Rt - 5 ↕10

General Assessment:

Lt - Poor ↔ Rt - Good

The obvious reason for the left side problems was essentially outside the remit of the study. The final assessment still contained the results of the left side although it did not reflect the success or otherwise of the treatment.

The data was included because it was felt that selectively removing subjects from either group may have jeopardised the validity of the overall results. Similar to the previous subject, if the methodology had accommodated a second course of treatment following the injury there may have been a more successful outcome.

The final subject that did not respond to the same degree as the other group B subjects was number 37. Similar to the previous subject she had a long history of bi-lateral Achilles tendon problems and had undergone surgery in the form of a left tendon decompression. A lack of mobility followed this surgery. At the initial assessment the subject complained that both Achilles tendons continued to swell and give pain and significant degrees of stiffness. The subject tried orthotics for a while but they made the condition worse.

Ultrasound therapy was given but there was not a positive response in either Achilles tendon so the subject ceased attending.

The subject was a good standard veteran athlete competing over 200/400m events. Her ambition was to regain sufficient fitness to attend the world veteran championships held in Buffalo, Canada. The condition of her tendons did not allow her to either train or contemplate competing.

The ultrasound report showed a bulbous enlarged area 3-4cm above the insertion at the os-calcis on the left side. The tendon was not greatly enlarged at this point but the appearance of the endotenon and the surrounding paratenon looked irregular and ragged. There was a degree of fluid at the posterior part of the paratenon, indicating a peritendonitis. The appearances on the right were strangely a mirror image of left.

The assessment score was as follows:

Pain:	Lt - 57 (50+8)	Rt - 57 (50+7)
Stiffness:	Lt - 15	Rt - 10
General Assessment:		
	Lt - Fair	Rt - Fair

At the three months assessment the patient has started training in an attempt to be prepared for the world veterans championships. She had been encouraged to take things gently. The ultrasound scan revealed that the tendon was getting worse as the exercise level increased. On the left side the transverse scan demonstrated a large hypo-ectogenic area on the lateral posterior aspect of the tendon. This had the appearance of fibrillar degeneration rather than fluid.

On the longitudinal scan the appearances were similar to the original assessment.

On the right the appearances were unchanged from the original assessment.

The subject had not been treated at this point but there had been a time delay between the first assessment and treatment, hence the need for a re-assessment.

At three months post-treatment the subject reported that she had progressed well with her training since the commencement of her treatment.

She was intending to participate in the games as planned and was planning to undertake some specific sprint training which would test the Achilles tendon to its full.

To summarise, the subject still had some stiffness post-exercise but the pain had ceased.

At five months post-treatment the subject was pain free except when undertaking specific sprint training. She wears distance track spikes which have a slight heel in comparison to a sprint spike. This reduced the degree of stretch on the Achilles tendon when the foot is in full dorsi-flexion.

The subject competed successfully in the World veterans championships 200/400m making the final in both events. The Achilles tendon's were reported to have "stood up" well to the demands of the competition. The patient still had stiffness but did not have a lot of pain. At the one year assessment the subject was given a diagnostic ultrasound examination. The report was as follows:

Left: The general appearance of the tendon on movement shows a marked anatomical abnormality, particularly when the tendon is stressed against a resistance.

The tendon does not move freely within the paratenon, but bunches when the foot is plantar-flexed or dorsi-flexed. This is demonstrated to be a mechanical problem that is unlikely to be solved by any conservative treatment.

On the positive side the hypo-echogenic area demonstrated on the previous scan has resolved. There is still some evidence of where the area was.

Right: Degenerative changes are present, otherwise the appearances are unremarkable.

The final assessment revealed:

Pain:	Lt - 30 (25+5) ↑57	Rt - 28 (25+3)
Stiffness:	Lt - 15	Rt - 10
General Assessment:		
	Lt - Fair	Rt - Fair

Although the subject managed to train and compete successfully there was no cessation of symptoms. The level of pain was reduced and continues to be so. The ultrasound report was self-explanatory as to why the subjects progress was not as successful as one may have hoped for. Consistent with the other subjects in both groups it does appear evident, although there are insufficient numbers to draw a statistically significant conclusion, that the subjects that have undergone previous surgical intervention do appear to do less well than subjects who have not.

The brief outcome of two other cases will conclude the discussion for the group B subjects. Complete subject clinical reports are contained within Appendix one.

Subject number 3 presented with bi-lateral pain and stiffness. The right Achilles tendon was worse than the left. He was a keen runner and the condition had prevented his participation for a number of months.

He had significant levels of pain, 56 on the left and 83 on the right, and stiffness, 10 on the left and 15 on the right. The ultrasound scan showed a right grade two partial rupture and a degenerative appearance on the left with calcification noted immediately above the insertion into the os calcis.

This was felt to be a chronically degenerating tendon. The patient was 39 years old and had run as a hobby for ten years.

He had undergone various forms of conservative therapy none of which had altered the condition. It was noted that the subject felt it was getting worse.

Following treatment the subject reported a steady progress and by six months post treatment had resumed training to a moderate level every other day. He was experiencing no pain or stiffness.

This state remained and the subject was pain free at one year post-treatment. The subject was seen at two years post-treatment and he was still running pain free.

This subject's progress was particularly satisfying as he had previously undergone other methods of conservative treatment to which the Achilles tendon had not responded. This was one of the cases in which calcification within the tendon demonstrated at initial assessment was absent at final assessment on the ultrasound scan.

Finally, subject number 26 warrants discussion because he had previous surgery in the form of a decompression and a tenosynovectomy which had left him with symptoms of severe pain and stiffness. Despite the surgical intervention he responded well to the micro-current treatment. Following his surgery he had undergone various forms of physiotherapy and was eventually signed off because it was felt there was nothing more that could done. The subject was a good standard 400 metre runner.

The left tendon contained micro-calcification and the right side showed the presence of degenerative nodules. This subject reported that, like others, the tendons had become extremely painful during the first week of the micro-current treatment. This was not anticipated in advance of the study. This effect was worrying when it was first noted, but it only lasted for a few days before subsiding. It was speculated that it may indicate that activity was being stimulated.

The subject reported a steady reduction in pain levels following completion of the treatment. At this point, four weeks after the treatment, the subject started a programme of progressive stretching exercises. These had been tried previously and in isolation had no effect. The patient was sceptical they were of any use but agreed to "give them a go".

To summarise the results. At the six months assessment the subject had progressed to being able to complete sets of ten repetitions of dynamic heel raisers at a fast speed with no pain. The subject was pleased to say the least. He returned to jogging at this point and apart from stiff calf muscles progressed to being able to complete a four mile run pain free.

At one year post-treatment the subject was training more intensely and was only reporting minor occasional symptoms with hard exercise.

It was felt that this was an example of what a long-term task it is to deal with this type of degenerative pathology. Constant monitoring and progression of overload is required. It is believed the micro-current played a vital role in the overall management of the condition. Without it, it is felt that the other aspects of the treatment would have been ineffective. A second course of the micro-current application may also have been applicable with this subject to accelerate the healing processes.

5.8.4 Group A: Current conservative treatment regimes

In order to investigate the healing processes involved in the Achilles tendon with chronic pathology it was important to evaluate the response of the subjects in group A receiving the standard treatments. The clinical management of Group A subjects was not under the control of the author but left to the individual clinician responsible for their patient. The clinical management of the Group B subjects was dictated by the author.

Following the randomisation procedure the subjects allocated to group A were referred back to their clinician or general practitioner.

An important factor in this study is the fact that many of the subjects had very long-term chronic conditions which had not responded to the individuals prescribed clinical management or had symptoms that reoccurred following previous pathology. Two consistent factors in patient management were noted:

1. The inconsistency of a common treatment plan from different practitioners for the same patient - commonly physiotherapists. This point was noted when patients sought advice and subsequent treatment from different sources.

This study reports that subject's felt that their treatment plan "seemed to jump from one thing to another"

2. The apparent discrepancy in application of a treatment modality was mirrored by the similar discrepancy in the clinical diagnosis. Interestingly, few patients had undergone any sort of diagnostic imaging test previous to the application of a treatment.

(whilst a diagnosis should be made with a clinical history and examination appropriate imaging may assist this process)

However, one could argue that if the practitioner only has one set of treatment tools at his or her disposal then a correct or incorrect diagnosis could be deemed as irrelevant if the treatment was going to be applied irrespective of a given diagnosis. It appears that often ignorance of the differing nature of the different pathologies affecting the Achilles tendon and the regeneration processes involved has resulted in the inappropriate treatment of some subjects.

Having studied many "sad" Achilles tendons it is felt that if some of those who are "qualified" to treat these patients were made more aware of the vastly differing nature of different pathologies that present, with the same or similar symptoms to the subject, some techniques acceptable in current practice would cease. This point is felt to be particularly applicable to some complementary practitioners such as massage therapists.

Conservative treatments such as ultrasound, laser and various forms of electrotherapy are widely used in an attempt to assist in the healing process.

The physiological basis for these treatments is underpinned by a variety of features.

The therapeutic use of ultrasound is perhaps the most widely used. Sixty five percent of the subjects in group A had undergone this treatment at some point during their clinical management.

It is worth examining the relevance of electrotherapy, including ultrasound, in respect to the biological processes involved in tendon degeneration/ inflammation and the healing processes.

Ultrasound is widely used as a therapeutic modality for the reduction of muscular spasm and pain. Unlike other forms of electrotherapy, ultrasound is unique in that the longitudinal waveform associated with sound is not electromagnetic in nature, (Ferguson, 1985). Sound waves require a medium for transmission, they represent the compression and refraction of the given medium. It is also possible to pass molecules of chemicals through the skin by a process known as phonophoresis.

Khan (1991) claims three physiological effects for ultrasound:

* Chemical: vibrations stimulate tissue which in turn is reported to enhance chemical reaction and processes and thus ensure the circulation of necessary elements and radials for recombination
* Biological: the permeability of membranes is increased which in turn will enhance the transfer of fluids in and out of cells. This is the basis of phonophoresis where molecules are pushed through the skin by the sound wave front.
* Mechanical: weakly bonded molecular structures may be broken or modified by a mechanical vibration. - Tendon Extensibility: the sclerolytic action of ultrasound, in the words of Khan, apparently increases the extensibility of tendons. No explanation is given for this and there is no clinically based evidence to support this claim.

The response rate of the group A subjects makes it apparent that for subjects in this study a single blanket approach to all conditions was an inappropriate method of approaching the clinical management of their condition. It had been previously described that the conditions affecting the Achilles tendon are diverse.

It is suggested that a set of criteria could be applied to a given pathology which would by their histo-chemical/-pathological and aetiological nature deem some treatments at best inappropriate and worse detrimental to the progress of the condition.

The first example of this is the use of friction massage to the tendon. Williams (1986) commented, "that because its effect is a counter-irritant the patient may suggest he is feeling better in order to avoid repetition of the treatment".

This method of treatment became apparent early on in the study when a subject was found, on diagnostic ultrasound, to have a significant amount of fluid within the paratenon which was not present on the previous scans. Searching for a possible explanation for the findings led to the conclusion that since the subject was undertaking no significant level of physical exercise at the time then something else must be acting as a irritant which triggered an inflammatory response. The friction massage was stopped and the patient return for a follow -up scan two weeks later.

A simple 'first aid' treatment of ice for twenty four hours, rest and elevation was suggested to reduce the inflammation which was causing the patient some degree of distress in terms of pain and stiffness. A follow-up ultrasound scan was performed and the inflammation and fluid was significantly reduced, along with the patients level of discomfort. A similar procedure was undertaken with other subjects undergoing friction massage. The results were consistent. This had highlighted an interesting point, that was discussed within the Introduction, that a double blind method would be inappropriate if one treatment was detrimental to the progress of the condition.

It was pertinent to examine the theory behind the treatment and highlight why it was an example of how a poor understanding of the aetiology of the pathological processes involved and the difficulty in treating the range of pathologies, had resulted in the use of an inappropriate form of treatment.

A brief revision of anatomy will assist in explaining why it is an unsuitable treatment modality unless the practitioner can be sure both about his/her diagnosis and have means to adequately follow-up the results of the treatment using some appropriate imaging modality.

The Achilles tendon can be distinctly divided into two separate parts, which are so different in both anatomy and physiology that the clinical condition affecting the two, it is believed, should be clinically managed and considered differently.

It is important to distinguish between a condition affecting the tendon substance itself, the endotenon, and the surrounding sheath the paratenon. The paratenon consists of a series of thin membranes that lie adjacent to the epitenon and are rich in mucopolysaccarides. This layer enhances tendon gliding by minimising friction between the tendon and surrounding areas. The membranes are vascular and are susceptible to inflammation which can cause subsequent thickening and adhesion formation which can reduce tendon flexibility and in turn may promote further injury.

A test at clinical examination of the Achilles tendon used to confirm paratenonitis is described by Williams (1986) and was named the painful arc sign.

This test differentiates between paratenonitis and lesions involving the tendon substance itself. In paratenonitis the area of tenderness and thickening remains fixed in relation to the malleoli when the foot is moved through dorsi-flexion and plantar-flexion. When the lesion is in the tendon itself any point of tenderness or swelling moves up and down as the foot goes through its range of movement.

The explanation for the purpose of the friction massage was that it broke down scar tissue and adhesions within the tendon and in addition the massage would also assist in improving the circulation.

If a friction massage was applied to a paratenonitis then it is believed that it would act as a further irritant to the paratenon. If the treatment was designed to reduce or breakdown the paratenon adhesions then this would just reinforce the inflammation cycle which in turn would result in further adhesions and have a further degenerative effect on the endotenon.

It is felt that the only place for friction massage to be used as a treatment modality is with a carefully planned management when an individual's condition has been identified as paratenon based adhesions which have resulted in a functional disability in the form of reduced movement of the Achilles tendon when the foot is dorsi-flexed and plantar-flexed. Friction massage may be used to break down the adhesions if an appropriate method of treatment could be used to enhance collagen production, the postulated effect of micro-current.

As previously stated there is no sound clinical or experimental evidence to resolve the issue as to whether micro or acute trauma induces an inflammatory response or the more insidious process of chronic tendon degeneration. These two contrasting processes, would by their nature, imply that a suitable treatment to treat one may not have the same desired effect on the other.

As was previously stressed it is believed that ideally, diagnostic imaging would be employed to aid in obtaining or confirming an accurate, preliminary diagnosis or follow-up check. Acute paratenonitis provides a good example of this treatment-diagnosis cycle.

The following approach is suggested as appropriate: - if the condition can be confirmed in its acute stage then it can be managed accordingly, consistent with any inflammatory process. This will be relatively straight forward with anti-inflammatory medication, ice, elevation and rest. An inflammatory process will normally respond quickly unless the Achilles tendon is re-exposed to the traumatic stimuli which caused it. It is reported though that there is often failure in treating this condition. Why should this be so? It may be suggested that it is because the inflammation of the paratenon has affected the endotenon itself. If this proves to be the case then there would be no value in continuing with this as the only form of treatment.

Once a tendinosis has been caused then it is suggested that a new set of rules apply. The pathology will have multiple features which need to be considered in the order of their effect on the whole Achilles tendon and not its individual parts.

A degenerative or inflammatory process should, by its physiological consequence on the Achilles tendon, dictate the nature of the clinical management and subsequent treatment modality used.

Drawing the discussion back to the clinical relevance of ultrasound therapy leads one to conclude that it is not too surprising that its successes in treating chronic Achilles tendon pathology are few if viewed from a long-term prognosis.

Subjects involved in this study have reported short-term relief from ultrasound treatment both in terms of pain levels and flexibility. If ultrasound treatment does have the ability to breakdown small adhesions arising from the paratenon then one would expect that the reduction in the 'snagging' that occurs when the foot is dorsi-flexed and plantar-flexed would lead to the reported improvement. Certainly the reduction of the inflammatory process may help to lessen the pressure on the paratenon itself and may assist in reducing the degenerating enzyme activity. Because anaerobic glycolysis is so prominent in energy metabolism of chronic paratenonitis, the accumulation of lactate in inflamed tissue, which is increased during times of strain, may probably be temporarily slowed. The release of vaso-active amines is thought to lead to the pain associated with stress on the damaged area.

The crucial and relevant question is; does the treatment encourage or promote a normal healing response? The clinical evidence from the subjects in this study would seem to confirm that it does not.

It is unreasonable to quantify a time span before recurrence because as has been highlighted no two conditions can be satisfactorily compared to each other when one take into account age, lifestyle, time and duration of injury etc.

If ultrasound were to have a positive effect on pain reduction then it may be suggested that during the elapsed time the condition would be returning to its original form or worse. The speed of the return would presumably be dependent upon many unquantifiable factors as stated above, such as the level of physical activity undertaken.

The reported effects of both ultrasound and other forms of electro and heat therapy, for example interferential and laser therapy, are vasodilation and stimulation. In addition it is claimed there is an analgesic effect to nerve endings and a metabolic stimulant. Vasodilation and stimulation may be attributed to a local heating effect which is well documented within the previously reviewed literature.

With reference to vascularity, the tendon lacks a true synovial sheath and is bound by the confines of the superficial posterior compartment. It receives a part of its vascular contributions from the muscular and bony attachment sites. The majority of its blood supply is derived from the epitenon, the thick, vascular connective tissue layer that is contiguous with the epimysium. There is an avascular area 2cm to 6cm proximal to the tendon's osseous insertion. This area is reported to be susceptible to ischaemic insult and is a clinically observed site of tendon degeneration and rupture, (Largergren and Lindholm, 1958).

The metabolic rate of the Achilles tendon is low, which is perhaps consistent with the fact that the tendon has such a limited blood supply. To apply a vaso-stimulating treatment would seem, to be of little value to a relatively avascular structure. If the system was being preventing from returning to a normalised state because of inflammatory processes then the application of a localised heat treatment could induce further inflammation. If cell membrane permeability was increased then there may be reduction in oedema.

Exploring the conservative treatment from a surgical perspective, Denstead and Roaas (1979) reported on the surgical treatment for partial rupture of the Achilles tendon. They concluded that the most common defect of the tendon was either due to paratenonitis with tendinosis or pure tendinosis. They examined fifty eight patients who had all undergone conservative treatment prior to their surgery. It is interesting to note that, similar to this study, the subjects underwent a myriad of conservative treatments which were not successful in treating the conditions.

5.8.4. Group A: Why some subjects condition Improved

The most successful treatment among the group A subjects, in which four subjects reported a significant reduction in their symptoms, was prescribed progressive stretching exercises. These type of exercises are documented in the literature review, but it is worth further exploration to examine why it had benefitted the subjects.

Curwin and Stanish (1984) and Stanish et al.(1986), postulated that trauma to the Achilles tendon occurs under eccentric loading and that eccentric exercises should be included in rehabilitation.

Their theory was based upon the fact that eccentric contraction place a greater load on the tendon than isometric or concentric contractions. Certainly this theory would be consistent with the work of Peacock (1967) which chronicles the stages of tendon healing.

Immature collagen contains a higher saline content and is weaker than normal collagen. In the final stage, the remodelling phase, which is stated to go on throughout life, longitudinal tension helps to increase the saline extractable from collagen and aids this remodelling. In a chronic tendon pathology it is difficult to clinically assess at what particular stage an injury is at. If there is a presence of immature collagen then eccentric stretching would logically assist this process.

On a similar physical basis it could be suggested that there might be a correlation between the reduction in adhesions and an eccentric stretching regime.

Two subjects in group A only underwent this treatment and responded well to it. The two subjects differ in almost every way but both experienced a cessation of symptoms.

The first subject was an 18 year old female, the youngest subject included in the study. She presented with bi-lateral Achilles tendon pain with a history of a left acute rupture which occurred when she was running in a 200 metre track race. She was surgically treated within twenty four hours with an end-to-end suture. The subject's Achilles tendon was then placed in a plaster cast for six weeks set in a gravity equinus position.

This was followed by six weeks in a plaster cast in a neutral position of dorsi/plantar flexion. At the initial assessment the subject reported that the right tendon felt worse than the left in terms of pain, stiffness and functional disability. The subject had a significant difference in the size of her calf muscles. The circumference measurement on the right side was 36.2cm and on the left side was 33.9cm. Additionally, the left side was weaker than the right and the muscle atrophy on the left side was almost certainly due to the length of time she spent in the plaster cast. The subject reported that she was given little post-operative physiotherapy care. It was realised that her problems may have stemmed from this lack of post-operative care, the left leg being weaker than the right which in turn has caused a compensatory injury on the right. The subject was prescribed specific exercises designed to build-up and strengthen the left side. Pain free, progressive, eccentric stretching exercises were performed on both sides.

Over the year period of assessment a steady but progressive improvement was reported and at the final clinical examination she was pain free and had resumed a normal amount of training.

The other subject was a 47 year old, recreational runner, male patient with bi-lateral Achilles tendon pain for one year. The right was worse than the left. The subject had previously been treated with physiotherapy which had included ultrasound, laser and interferential. This had no long-term positive effect.

The subject was a long-haul airline pilot so was relatively inactive for long periods of time.

It was considered that this may be an influencing factor in the condition assuming there was a predisposition to the formation of adhesions either from a previously inflammed paratenon or by the inappropriate use of ultrasound therapy.

The subject was prescribed a set of progressive stretching exercises not only for his calf and Achilles tendon but also for the hamstring muscles, an area where the subject was particularly tight. The subject followed the regime, performing the exercises regularly throughout the day, including during his pilot duties.

At the final assessment the right tendon was asymptomatic and the left tendon still had a little pain and stiffness but it was not preventing him from running twice a week at a moderate level. It is believed that with this subject the stretching exercises assisted in the formation of a more normally functioning fibrillar collagen matrix.

There has been some discussion in the popular athletic press about orthoses used to treat bodily disfunction by means of externally worn devices. They are designed to correct an "abnormal" gait into a "normal" one.

This study had several subjects in both groups that had experimented with these and only one found permanent relief.

Whilst they may have a role to play in the management of a problem it is believed that often the condition can be made worse by changing an athletes running gait on an Achilles tendon that is for a physiological reason predisposed to a faulty tissue regeneration cycle.

To conclude the discussion of the group A subjects it is felt that two points are pertinent; firstly, all of the subjects in both groups had previously undergone some sort of treatment prior to their inclusion in the study. This was evidently unsuccessful otherwise they would not be still seeking medical attention for the condition. It was not therefore, unsurprising that they did not respond to further courses of treatment. Secondly, the subjects in group B were equally in the same position with regard to their pathological state so one must question the relevance of either the treatments used or their application.

5.9 ADDENDUM : Discussion collagen contraction study

The discussion on the experiment examining collagen contraction following micro-current stimulation is separate from the main chapter because the experiment was terminated before a conclusion was reached. This was due to the fact that laboratory space was no longer available for the continuation of the study. However, the author believes that as it was a time consuming area of study from which some valuable lessons were learnt it warrants further analysis. In addition, it was felt to be of value for this type of experiment may inch science forward in order that an eventual conclusion may be drawn concerning the use mechanism of micro-current upon cell behaviour and interactions The purpose of the study was to analyse the influence of low amperage electrical stimulation on the behaviour of fibroblast contraction contained within a collagen gel.

Relevant to this experiment was a study by Andujar et al (1992). They examined cell migration influences upon collagen gel contraction. They suggested that collagen gel contraction is a striking feature where the presence of serum factors is critical. These factors were not isolated for this study. They reported that during collagen contraction fibroblasts pass through a number of distinct phases. The lag phase takes approximately three hours, except in serum free conditions where it did not occur at all. During this phase cell adhesion and spreading leads to cellular interconnections. It is shortly after this phase that rapid contraction occurs and intra cellular connections increase. Andujar et al believed that cell-collagen and cell-cell interactions are related to the onset of contraction.

Consistent with other studies, Guidry and Grinnell (1985), Schafer & Cooper (1995) Anderson et al (1990) and Asaga et al (1991), contraction was suggested not to be dependent upon fibro-nectin. However, thought appears to be divided as to whether fibro-nectin does influence the binding of fibroblasts to collagen molecules, (Schor, 1980; Dedhar et al 1987). If contraction is an essential process in wound healing where cell-cell connections are associated with cytoplasmic microfilament re-arrangement then this could be deemed to be a disadvantage for a healing tendon. Adhesion formation from the paratenon to the endotenon is not a desired feature of the healing process.

The mechanisms by which factors control the contraction processes are poorly understood and therefore the potential role of electrical stimulation is unclear. Collagen contraction is seen an essential process in wound repair. However, the role of cellular organisation within a damaged tendon is less clear.

Clearly, the reorganisation of collagen fibrils is a vital stage of the repair process.

It is generally accepted that the native collagen molecule of Type 1 collagen consists of three polypeptide chains which are coiled in a helical structure. It is this helical structure which gives the collagen molecule its unique physical properties including high viscosity and negative optical rotation. Type 1 collagen exhibits a high level of contractile strength, a one millimetre diameter fibre having the tensile strength of ten kilograms. A better understanding of the collagen contraction process may generate useful information regarding the mechanisms of the healing processes at a cellular level.

Whether electrical stimulation has a role to play is unclear. It is evident that on the one hand inhibition of contraction may be advantageous to prevent adhesion formation, whist on the other hand promotion of contraction may be a useful process for a healing endotenon developing an extracellular matrix.

The influence of electrical stimulation on the contraction of collagen gel. Non-contractile cells are able to exert tensional forces on collagen substrate. These forces have been implicated in the contraction seen during wound repair. The effect of fibroblast contraction of collagen gels has been studied extensively as a model for wound contraction,(Eastwood et al; 1994). Their work based upon the studies of Tranquillo and Murray, (1992), Ehrlich and Rajaratnan (1990), Garana et al (1992). The mechanism by which the tension is generated is still to be ascertained. Eastwood et al (1994) believe that tractional forces are the basis for the re-organisation and alignment of collagen substrate, as cells move during development or repair.

A review of the relevant literature on collagen is contained in the main body of the thesis but it is relevant to restate the work of Boedtker and Doty (1956) who showed that collagen has the ability to reconstitute itself and assemble in fibril *in-vitro*. This is particularly pertinent to the present work, for if the production of collagen from fibroblasts is enhanced by electrical stimulation, then the subsequent behaviour of this collagen would be a useful to explore. *In-vivo,* most cells are in contact with the extracellular matrix which then forms a three dimensional structure. Cell matrix interactions are thought to control cell adhesion, migration growth and differentiation.

It is believed that specific cell genotype is controlled and regulated by biochemical and mechanical properties of the extracellular matrix, (Gospodarowicz et al, 1978; Hay, 1992; Watt, 1986; Opas, 1989; Ingber, 1990, Ingber and Folkman, 1989 and Nakagawa et al 1989).

Type 1 collagen, has commonly been used as a culture substratum, where cells have been cultured on or within collagen gels. These three-dimensional collagen gels are designed to simulate the structure of normal connective tissue and have been used a an *in-vitro* model to study the biological response of cells such as fibroblasts. Andujar et al (1992) describe gel contraction as a striking feature observed when cells are seeded in or onto collagen gels. The mechanisms of gel contraction however, are not yet clear. It is reported by Steinberg et al, 1980; Buttle and Ehrlich , 1983; Guidry and Grinnell, 1985; and Gillery et al, 1986, that the efficiency of gel contraction is dependent upon the cell type and the integrity of the cyto-skeleton, not the cell proliferation or collagen degradation. If this is the case then it may be of relevance when relating it to a tendon with chronic pathology where there is thought to be collagen degradation.

However, *in-vivo* this also may result in a cyto-skeleton that is compromised. Andujar et al (1992) suggest that the presence of plasma fibronectin promoted a faster rate of cell adhesion and spreading on collagen fibrils but did not effect contraction. Other serum factors led to less extensive gel contraction due to the impairment of cell migration. They concluded that cell migration seems to be an important factor by which the effectiveness of gel contraction in controlled. If the stimulation does initiate any modified structural behaviour then this may go some way to explain the improved functional outcome.

The factors affecting fibrillogenesis, such as the removal of telopeptides by proteinase digestion and the addition of glycosaminoglycans are debated by authors such as Rubin et al (1963) and Wood (1960).

Also relevant to the growth of collagen fibrils are the observations by Eastwood et al (1994) that cell-free collagen generates a small force of contraction during a phase corresponding with maturation and growth. Certainly some authors, for example Kvist and Jarvinen (1982) have reported disorganised collagen fibrils in chronic Achilles tendon pathology from surgical findings.

The molecular basis of the mechanical effect is unclear but it is suggested that it may reflect an increasing entanglement and intermeshing of collagen fibrils during the accretion phase. Eastwood et al (1994) proposed that this may be a significant factor for fibroblasts synthesising their own collagen in granulation tissue.

In unpublished data, Eastwood suggests that there is a cellular response to changes in tension within the extra cellular matrix. He indicated that the contractile forces generated are greater when the collagen matrix relaxes, similarly when the collagen gel matured the cells responded with a reduced force output.

The normal behaviour of cell-free collagen gels follows a distinct and reproducible pattern. Eastwood et al (1994), demonstrated, using a culture force monitor to measure contractile forces, that non-contractile cell types generate a force of contraction. A steady state of contraction of collagen fibrils is noticed after a three hour period.

In the second phase a near linear increase in force and occurs between three and twenty four hours. After this period there is a steady state of force.

The theories explored and exploded by various authors have attempted to investigate and ultimately explain the processes which occur when there is structural damage to a collagen based matrix.

The mechanisms involved in wound healing are still to be clarified. However, it is generally agreed that returning the matrix to its original form is the aim of the healing processes.

Contrary to the above statements, it could be argued that one process involved in healing and implicated in the process of collagen contraction is the formation of adhesions which form between the paratenon and the endotenon. This is a debilitating condition which reduces the free movement of the tendon substance within its sheath and as a consequence results in an exacerbation of symptoms.

If the contraction of collagen is a vital process in wound contraction, for example in dermal damage, then it could be advantageous to slow the process. This was discussed in a paper by Fujita, Hukuda and Doida (1992), unfortunately the findings cannot be correlated with this study for they used flexor tendons for their experimental model which differ from the Achilles tendon since they possess a synovial sheath. They reported that the application of micro-current suppressed adhesion-causing synovial proliferation.

CHAPTER SIX

Conclusions and Recommendations

6. Introduction

This thesis has addressed the experimental hypothesis that the application of micro-current electrical stimulation will cause an alteration in cell behaviour and induce a modification in the healing processes involved in the Achilles tendon with chronic pathology .

At the commencement of this study the author was in possession of some interesting and perhaps convolutedly connected facts. In summary, these were that the Achilles tendon pathology presents a particular clinical challenge that no one has yet conclusively solved and that micro-current stimulation has the potential to augment soft-tissue healing. On the positive side, there was some scientific evidence that tendon tissue was receptive to this application. On the not so positive side no study had yet drawn a conclusion as to the biological mechanism for micro-current stimulation, although many different hypotheses were put forward. Worse still, the diversity of different studies that applied micro-current electrical stimulation to various tissue types only contributed to further muddy the waters.

It was agreed with this portfolio of facts that the author of the current study attempted to clarify some hither to unclear facts. If some of the strands of study could be brought together then the potential of this novel therapy could be properly evaluated and a coherent plan devised for future study.

With reference to the *in-vivo* study, whilst several objectives were addressed it was clear that in conducting the study two main ones were paramount. Did patients that underwent the micro-current therapy return to a normal functional outcome more quickly than those patients undergoing current conservative methods? And are present conservative treatment regimes applicable to the pathologies occurring in the Achilles tendon?

With reference to the *in-vitro* study the main objective to be addressed was did the application of micro-current electrical stimulation induce changes in cell behaviour. An experimental objective that arose from this was concerning the biological behaviour of different cell types. Did the mouse fibroblasts behave in a similar way to human tenocytes?

6.1. Micro-current applications

Further narrowing the gap between experimental evidence and clinical findings should be the objective of future studies. In general, the studies evaluated in this thesis indicate that under certain circumstances biological repair and healing processes may be augmented by the application of micro-current. The clinical aspect, undertaken in this study, evaluating the effect of micro-current on the Achilles tendon with chronic pathology, has highlighted that it may have a useful clinical application. However, in order to best maximise its potential it is important to undertake further *in-vitro* studies and selected *in-vivo* studies to establish if there are optimum treatment parameters with regard to fibroblast activity and subsequent collagen production. The findings of this study showing a reduction of cell activity using 1μA could be an important finding and further investigation of this deviation from other studies is relevant.

Perhaps the most relevant question is what are the clinical conditions that indicate the use of micro-current therapy? As yet, there is no evidence to suggest that it can be considered as a blanket treatment for all conditions where tissue regeneration is required. However, there are so many strands to the experimental evidence from skin to tendon healing that its full potential may not be fully explored.

The most productive way forward is to evaluate the behaviour of the tissue matrix with and without pathology following micro-current therapy from both an *in-vivo* and *in-vitro* perspective. Biopsy or operative samples, from patients with chronic tendon pathology may be cultured *in-vitro* which will provide useful information concerning tissue changes *in-vivo.* With reference to wound healing some studies have investigated wound healing by topical treatment with growth factors and it would be intriguing to investigate if the effects of micro-current are effected by the environment within the cells are situated. It should be borne in mind that the *in-vitro* effects were demonstrated on fibroblasts that are grown in ideal culture conditions. If it were possible to replicate these conditions *in-vivo,* which is often not the case when tissue is affected by pathology, the results could be significant.

The structure of the connective tissue matrix appears to depend upon the interactions of a variety of macro molecular components. The simplest example perhaps is the interaction provided by the collagen fibril.

As the collagen molecule does not act as a single unit but as fibrils which consist of axillary arranged structures, it is pertinent to evaluate how their structural function is altered by trauma and how the reorganisation process is undertaken.

The strength of a tendon is derived from it ultrastructure and it appears that when this is compromised by repeated episodes of micro-trauma the deterioration cycle commences.

Consistent with the above the author proposes that the most appropriate method of assessing the influence of electrical stimulation upon the cyto-skeleton matrix is to examine tissue *in-vivo* following treatment with functional assessment and reliable imaging methods. Many biological processes that occur in mammalian life are not yet understood, however this does not prevent their usage in medicine and it is often by the wider adoption of a process or therapy that helps clarify our understanding of it mechanism of action. The experimental effects of micro-current upon living tissue are diverse and have been replicated by different studies across the globe but as yet the way that it influences cell growth patterns under different conditions is still to be clarified.

Despite the previously unsuccessful clinical management of some of the pathologies prior to their inclusion in the study, subjects in group B, receiving the micro-current treatment, did produce a significant improvement in their functional ability. It is important to highlight that this improvement was demonstrated in subjects which had previously undergone conservative management to which their Achilles tendon pathology had not responded.

Essentially, the study was disadvantaged because it primarily involved subjects who had little or no success elsewhere. This makes the total number of positive outcomes in the group B subjects even more remarkable and may go some way to explain why the group A subjects did so poorly. They were being offered more of the same treatment which had already proved to be unsuccessful.

The efficacy of the micro-current treatment was evaluated at a functional level and confirmation may be obtained from the statement by Stanish et al (1985), who undertook a number of significant clinical studies using micro-current, that a distinct gap exists between laboratory experiments and a conclusion that the clinical success is entirely due to electrical stimulation. It is possible to hypothesis that the micro-current therapy enhanced fibroblast activity and collagen production and promoted the reversal in the pathological state of the Achilles tendon tissue as reported by Bourguignon & Bourguignon (1987) and Nessler & Mass (1985).

6.2. Achilles tendon pathology

After examining the nature of the chronic pathology occurring in the Achilles tendon it was felt that there is sufficient literary evidence (previously cited), both histological and anecdotal, to suggest that a degenerative process does appear to be a dominant factor in the Achilles tendon's propensity to develop chronic conditions from cyclic overload. As this is essentially micro-trauma in nature the subject is often unaware of its presence until it has reached a significant point which then gives rise to symptoms.

When there is a degenerative cycle the healing process of the Achilles tendon appears to be little aided by the conservative methods presently used. A good level of success is reported with surgery. The removal of degenerative tissue and the anaerobic environment this created may be a reason for this.

When a patient presents with an acute inflammatory condition, it is essential to recognise it and ensure that it is differentiated from a degenerative process and treated appropriately. Paratenonitis is a condition that should be easily distinguishable from a tendinosis and should resolve quickly.

Evaluation of tissue samples using biopsy techniques would provide valuable information concerning a tendon's pathological state. It would then be useful to correlate biological changes with clinical and imaging findings.

6.3. Clinical management

Another issue was thought to have a significant bearing on the results of this study. This was the apparently haphazard way in which some subjects are clinically managed by some practitioners. The Lancet (1988) published a relevant article entitled,

"Sports Medicine - Is There A Lack of Control?"

It was suggested that sports medicine should be brought under the umbrella of a recognised body with an accredited higher training programme. In Australia sports medicine is defined as a total care of the exercising individual. This may be part of the problem in the management of the group A subjects.

It appeared that the subjects were given a treatment in isolation regardless of the individual nature or causation of the pathology.

In recent years there has been a proliferation of sports injury, massage and therapy courses aimed at the "non-medical" person which has resulted, it is believed, in people being involved with sports injuries and conditions for which they are, at times, inexperienced or unqualified to treat. For a notably difficult pathology or condition to treat it is felt that it is unfair to blame these practitioners for the failure of treatments.

The fact was that for many of the subjects involved in this study, some of them very good athletes, there was not an adequate system in place for them to seek suitable treatment within a reasonable time span without resorting to the "Yellow Pages".

6.4. A role for diagnostic Imaging

In relation to imaging, the vital questions which need to be answered are; do the clinical findings correlate with the deviation from the normal appearances and do both those examinations accurately reflect the biological tissue changes?

This study has demonstrated that ultrasound findings can be correlated with clinical symptoms such as pain and stiffness. It has confirmed the findings of other studies, for example Maffulli et al.(1987) that diagnostic ultrasound can give a precise picture of the alteration of paratenonous soft-tissue and of the internal structures of the Achilles tendon. With regard to correlating these appearances with specific pathology a wider study would need to include a histological examination of tissue to answer this point.

Magnetic resonance imaging, because it excludes operator dependency, may be more widely accepted by clinicians. However, this modality also requires the same scrutiny as ultrasound to establish that the changes in appearance can be related to specific biological tissue changes. In addition, however, its high cost and lack of availability makes it at present unlikely to be used on a regular basis in the near future.

Assuming this study was a fair reflection of current practice there still appears to be a reluctance on behalf of practitioners to fully utilise diagnostic imaging as a adjunct to the clinical examination. Only a minority of subjects underwent any sort of diagnostic imaging prior to their inclusion in the study.

6.5. Recommendations

It was noted at the beginning of the thesis that science and scientists have yet to reach agreement upon the aetiology of chronic tendon pathology. Moving science forward is often a slow process particularly when examining new treatment regimes. With reference to the application of micro-current, this study, whilst relatively small in scale, has indicated that the application warrants further investigation. Whilst a wider scale trial would not necessarily further elucidate the reasons for the clinical findings a modification in the experimental methodology may clarify some of the biological mechanisms involved following the application of the micro-current therapy. It is known that fibroblasts respond to a stretch stimulus and this is possibly the reason why a programme of eccentric stretching exercises is the single most effective current conservative treatment for degenerative tendon pathology. *In-vitro* studies have also demonstrated that fibroblasts respond to an electrical stimulus.

Therefore in order to clarify the optimum treatment parameters for the micro-current therapy the following experiment could be conducted. The same subject entry and assessment criteria followed as the current study. The proposed study would have three study groups of subjects. Group X, receiving micro-current therapy only, Group Y receiving micro-current theraphy and eccentric stretching exercises and Group Z receiving eccentric stretching only. This would allow the researcher to evaluate whether it was the micro-current therapy in isolation that produced the improved functional outcome, the micro-current therapy and the stretching exercises or alternatively was the stretching exercise alone sufficient to produce an improvement in a significant proportion of the subjects. This is now a key area to be addressed in order to evaluate the potential of micro-current therapy for general clinical use.

It is noted that one of the limits of this study was the single application and standardisation of current intensity and frequency. It would be interesting to examine whether the alteration of these variables changes the prognosis of the pathology or the clinical outcomes.

The short-term objective of further *in-vitro* studies may be to establish the effect of different treatment parameters on fibroblast activity and subsequent collagen production, if indeed this is the reason for the clinical success. Long-term objectives should widen the scope and involve a more in-depth examination of the *in-vitro* behaviour of the tissue matrix of the growing normal and damaged cyto-skeleton and what effect the application of micro-current has upon it.

The reason for the reduction in intra-tendinous calcification, an unexpected finding in this study, may be found using the methods suggested above. Whilst not in possesion of a definitive proof the author feels the key to the biological working of micro-current simulation, altering the rates of cell proliferation, lies in the complex mechanisms of cell to cell signalling. Further investigation into this highly specialised area of cell biology would entail a detailed evaluation of the behaviour of the cell communication control systems.

It is recognised that this study effectively put one small area of current clinical practice under the microscope, but sadly it did highlight inadequacies in the health care system for dealing quickly with sport induced injuries. The introduction of a properly structured pathway to be followed by patients with sports injuries, would be useful. It is somewhat ironic that in some branches of medicine the imaging department is overused but for this, the area of sports induced injury, clinicians appears to allocate it a low priority. It is felt that it is not used sufficiently or appropriately to aid diagnosis. Until magnetic resonance imaging is more available, clinicians should use ultrasound more frequently. It is believed this will only happen if imaging departments promote the service and Radiographers and Radiologists become sufficiently proficient at musculo-skeletal imaging, in relation to clinical sports medicine, to instil faith in the clinicians dealing with the patients.

The final recommendation is to athletes: pain is present for a reason, do not ignore it and hope it will go away. Continuing to train to the same intensity and duration will ultimately increase the time it takes for an injury to heal.

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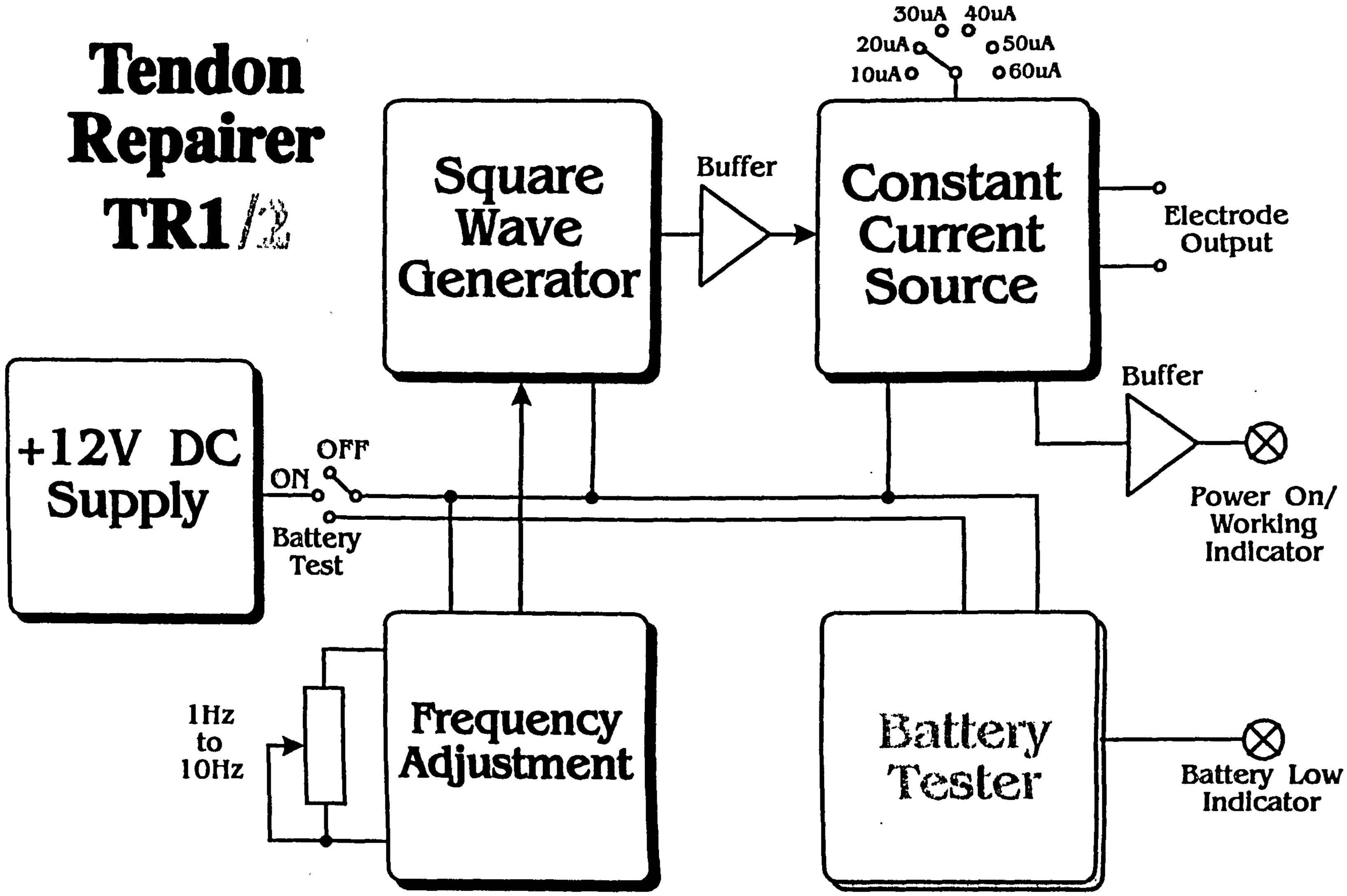
Comptes Rendus Societe Biologie 52: 1127

APPENDIX ONE

TENDON REPAIRER - CIRCUIT DIAGRAM

Tendon Repairer TR1/2



APPENDIX TWO

STATISTICAL CALCULATION DATA

Raw Data Cell Proliferation Rates

Control Fibroblasts

	0 days	3days	5days	7days
mean	3000	8300	55600	197000
mean-std	3000	7335.6349	41731.571	146667.77
mean+std	3000	9264.3651	69468.429	247332.23
stdev	0	964.36508	13868.429	50332.23

1uA Fibroblasts

	0 days	3days	5days	7days
mean	3000	4030	15000	32800
mean-std	3000	3593.4988	12206.555	24082.202
mean+std	3000	4466.5012	17793.445	41517.798
stdev	0	436.50124	2793.4447	8717.7979

40uA Fibroblasts

	0 days	3days	5days	7days
mean	3000	13340	120000	2230000
mean-std	3000	10338.884	102679.49	1549314.1
mean+std	3000	16341.116	137320.51	2910685.9
stdev	0	3001.1165	17320.508	680685.93

Control tenocytes

	0 days	3days	5days	7days
mean	3000	8100	51333	300000
mean-std	3000	7926.7949	47169.668	270000
mean+std	3000	8273.2051	55496.332	330000
stdev	0	173.20508	4163.332	30000

40uA tenocytes

	0 days	3days	5days	7days
mean	3000	9133.3333	120000	840000
mean-std	3000	8620.1732	90000	794174.24
mean+std	3000	9646.4935	150000	885825.76
stdev	0	513.16014	30000	45825.757

Both cell types

	0 days	3days	5days	7days
control F'blasts	3000	8300	55600	197000
1uA F'blasts	3000	4030	15000	32800
40uA F'blasts	3000	13340	120000	2230000
control T'cytes	3000	8100	51333	300000
40uA T'cytes	3000	9133	120000	840000

Collagen gel contraction

	3 hours	6 hours	12 hours	24 hours	48 hours
Well 1	3.5	3.2	3	2.8	2.8
Well 2	3.5	2.1	1.4	0.9	0.8
Well 3	3.1	2.4	1.9	0.8	0.7
Well 4	3.4	2.2	2	1.3	1
Well 5	3.2	2.6	1.7	1.4	0.6
Well 6	3.4	2.6	2	1.2	0.9

APPENDIX TWO

SUMMARY OF RAW DATA: PERIOD ONE

Left foot

PATIENT		G	GROUP	ULTRA	DF	PF	PAIN	STIFF	GA
1	1.00	2	0		19.0	43.0	83.0	15.0	1
2	1.00	1	0		21.0	44.0	82.0	10.0	1
3	1.00	2	0		21.0	51.0	56.0	10.0	3
4	1.00	1	7		22.0	49.0	57.0	10.0	3
5	1.00	2	9		17.0	51.0	83.0	15.0	1
6	1.00	1	3		27.0	42.0	32.0	10.0	3
7	1.00	1	0		23.0	55.0	54.0	10.0	3
8	1.00	2	0		17.0	44.0	81.0	15.0	1
9	1.00	2	0		25.0	49.0	84.0	15.0	1
10	1.00	2	0		18.0	54.0	82.0	15.0	1
11	1.00	1	0		18.0	45.0	30.0	5.0	5
12	1.00	1	0		12.0	60.0	32.0	15.0	3
13	1.00	1	0		24.0	50.0	58.0	10.0	3
14	1.00	1	9		21.0	47.0	57.0	10.0	3
15	1.00	2	0		25.0	50.0	.0	.0	7
16	1.00	2	7		21.0	51.0	82.0	10.0	1
17	1.00	1	0		24.0	49.0	.0	.0	7
18	1.00	2	9		24.0	50.0	56.0	10.0	1
19	1.00	2	0		21.0	52.0	83.0	10.0	1
20	1.00	1	0		24.0	51.0	57.0	10.0	3
21	1.00	1	7		18.0	45.0	54.0	15.0	3
22	1.00	1	7		23.0	53.0	29.0	5.0	4
23	1.00	2	0		25.0	55.0	83.0	10.0	1
24	1.00	2	0		17.0	54.0	83.0	15.0	1
25	1.00	1	0		25.0	48.0	57.0	10.0	3
26	1.00	2	0		17.0	52.0	99.0	15.0	1
27	1.00	2	0		23.0	49.0	.0	.0	7
28	1.00	1	7		23.0	47.0	56.0	10.0	3
29	1.00	2	9		23.0	47.0	57.0	10.0	3
30	1.00	2	0		25.0	48.0	.0	.0	7
31	1.00	1	0		24.0	50.0	32.0	5.0	3
32	1.00	1	0		24.0	49.0	56.0	10.0	3
33	1.00	1	0		23.0	49.0	82.0	10.0	1
34	1.00	2	0		22.0	50.0	81.0	82.0	1
35	1.00	1	7		23.0	48.0	28.0	5.0	3
36	1.00	2	9		24.0	49.0	28.0	10.0	3
37	1.00	2	9		19.0	49.0	57.0	15.0	3
38	1.00	1	0		22.0	49.0	56.0	10.0	3
39	1.00	2	0		21.0	46.0	83.0	15.0	1
40	1.00	1	9		23.0	49.0	56.0	10.0	3
41	1.00	1	0		19.0	47.0	82.0	15.0	1
42	1.00	1	0		23.0	50.0	56.0	10.0	3
43	1.00	2	0		24.0	51.0	.0	.0	7
44	1.00	2	9		22.0	50.0	82.0	10.0	1
45	1.00	1	3		24.0	51.0	31.0	10.0	3
46	1.00	1	0		23.0	49.0	.0	.0	7
47	1.00	2	0		24.0	50.0	31.0	10.0	3
48	1.00	2	0		25.0	51.0	.0	.0	7

Right foot

PATIENT		G	GROUP	ULTRA	DF	PF	PAIN	STIFF	GA
1	1.00	2	0		23.0	49.0	.0	.0	7
2	1.00	1	9		15.0	39.0	98.0	15.0	1
3	1.00	2	0		19.0	47.0	83.0	15.0	1
4	1.00	1	0		19.0	46.0	56.0	10.0	3
5	1.00	2	9		18.0	48.0	82.0	15.0	1
6	1.00	1	9		22.0	43.0	30.0	10.0	3
7	1.00	1	0		20.0	53.0	.0	.0	7
8	1.00	2	0		20.0	50.0	.0	.0	7
9	1.00	2	7		23.0	53.0	30.0	10.0	3
10	1.00	2	0		24.0	52.0	.0	.0	7
11	1.00	1	7		18.0	49.0	57.0	10.0	3
12	1.00	1	0		17.0	58.0	58.0	15.0	3
13	1.00	1	9		25.0	49.0	57.0	10.0	3
14	1.00	1	0		22.0	49.0	.0	.0	7
15	1.00	2	0		25.0	50.0	83.0	10.0	1
16	1.00	2	0		23.0	49.0	.0	.0	7
17	1.00	1	0		22.0	42.0	98.0	15.0	1
18	1.00	2	0		26.0	52.0	.0	.0	7
19	1.00	2	0		20.0	54.0	83.0	15.0	1
20	1.00	1	9		23.0	51.0	28.0	10.0	3
21	1.00	1	0		18.0	43.0	55.0	15.0	3
22	1.00	1	7		22.0	55.0	57.0	5.0	5
23	1.00	2	7		21.0	52.0	56.0	10.0	3
24	1.00	2	7		23.0	51.0	56.0	10.0	3
25	1.00	1	7		24.0	49.0	31.0	10.0	3
26	1.00	2	0		22.0	55.0	57.0	15.0	3
27	1.00	2	0		22.0	47.0	56.0	10.0	3
28	1.00	1	9		22.0	46.0	58.0	10.0	2
29	1.00	2	7		24.0	49.0	27.0	.0	5
30	1.00	2	0		20.0	49.0	57.0	10.0	3
31	1.00	1	0		25.0	51.0	28.0	5.0	5
32	1.00	1	0		24.0	48.0	55.0	10.0	3
33	1.00	1	0		24.0	51.0	56.0	10.0	3
34	1.00	2	0		23.0	50.0	10.0	10.0	1
35	1.00	1	0		21.0	46.0	57.0	10.0	1
36	1.00	2	4		23.0	51.0	57.0	10.0	1
37	1.00	2	9		21.0	47.0	57.0	10.0	3
38	1.00	1	0		23.0	50.0	.0	.0	7
39	1.00	2	0		24.0	50.0	.0	.0	7
40	1.00	1	9		22.0	49.0	57.0	10.0	3
41	1.00	1	1		23.0	49.0	56.0	15.0	3
42	1.00	1	9		21.0	47.0	55.0	10.0	3
43	1.00	2	0		17.0	46.0	82.0	15.0	1
44	1.00	2	0		23.0	49.0	.0	.0	7
45	1.00	1	0		24.0	49.0	.0	.0	7
46	1.00	1	0		17.0	47.0	83.0	15.0	1
47	1.00	2	0		26.0	51.0	.0	.0	7
48	1.00	2	9		24.0	50.0	55.0	10.0	2

Number of cases read: 96 Number of cases listed: 96

Table App.2 (1) A summary of the raw data collected for period one.

```
30  nonpar corr  gn with df pf pain stiff ultra/print=sig.

- - -  S P E A R M A N   C O R R E L A T I O N   C O E F F I C I E N T S  - - -

                    DF          PF         PAIN        STIFF       ULTRA

GA                .3765       .1467      -.8736      -.8182      -.6326
               N(   96)    N(   96)    N(   96)    N(   96)    N(   96)
               SIG .000    SIG .077    SIG .000    SIG .000    SIG .000

. . * IS PRINTED IF A COEFFICIENT CANNOT BE COMPUTED.
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Table App.2 (2) The Spearman correlation coefficients for period one. The left and right Achilles tendons functional assessment markers with the general assessment

APPENDIX TWO

SUMMARY OF RAW DATA: PERIOD FOUR

GROUP: 1 A

PAIN

Value Label	Value	Frequency	Percent	Valid Percent	Cum Percent
	.0	10	20.8	20.8	20.8
	15.0	2	4.2	4.2	25.0
	27.0	2	4.2	4.2	29.2
	28.0	3	6.3	6.3	35.4
	29.0	1	2.1	2.1	37.5
	30.0	1	2.1	2.1	39.6
	33.0	1	2.1	2.1	41.7
	34.0	1	2.1	2.1	43.8
	35.0	3	6.3	6.3	50.0
	36.0	5	10.4	10.4	60.4
	37.0	4	8.3	8.3	68.8
	58.0	1	2.1	2.1	70.8
	81.0	1	2.1	2.1	72.9
	82.0	7	14.6	14.6	87.5
	83.0	1	2.1	2.1	89.6
	97.0	1	2.1	2.1	91.7
	98.0	4	8.3	8.3	100.0
		Total 48	100.0	100.0	

Mean 47.333 Median 55.500 Std dev 33.238
Minimum .000 Maximum 98.000

Valid cases 48 Missing cases 0

STIFF

Value Label	Value	Frequency	Percent	Valid Percent	Cum Percent
	.0	14	29.2	29.2	29.2
	5.0	4	8.3	8.3	37.5
	10.0	16	33.3	33.3	70.8
	15.0	13	27.1	27.1	97.9
	83.0	1	2.1	2.1	100.0
		Total 48	100.0	100.0	

Mean 9.542 Median 10.000 Std dev 12.329
Minimum .000 Maximum 83.000

Valid cases 48 Missing cases 0

GROUP: 2 B

PAIN

Value Label	Value	Frequency	Percent	Valid Percent	Cum Percent
	.0	29	60.4	60.4	60.4
	4.0	1	2.1	2.1	62.5
	5.0	2	4.2	4.2	66.7
	27.0	4	8.3	8.3	75.0
	28.0	2	4.2	4.2	79.2
	29.0	3	6.3	6.3	85.4
	30.0	1	2.1	2.1	87.5
	32.0	1	2.1	2.1	89.6
	35.0	1	2.1	2.1	91.7
	36.0	2	4.2	4.2	95.8
	82.0	1	2.1	2.1	97.9
	83.0	1	2.1	2.1	100.0
	Total	48	100.0	100.0	

Mean 13.729 Median .000 Std dev 22.854
Minimum .000 Maximum 83.000

Valid cases 48 Missing cases 0

STIFF

Value Label	Value	Frequency	Percent	Valid Percent	Cum Percent
	.0	23	47.9	47.9	47.9
	5.0	15	31.3	31.3	79.2
	10.0	7	14.6	14.6	93.8
	15.0	2	4.2	4.2	97.9
	20.0	1	2.1	2.1	100.0
	Total	48	100.0	100.0	

Mean 4.229 Median 5.000 Std dev 5.355

Table App.2 (3) A summary of the raw data collected for period four.

--- SPEARMAN CORRELATION COEFFICIENTS --

	DF	PF	PAIN	STIFF	ULTRA
GA	.3765	.1467	-.8736	-.8182	-.6326
	N(96)	N(96)	N(96)	N(96)	N(96)
	SIG .000	SIG .077	SIG .000	SIG .000	SIG .000

" . " IS PRINTED IF A COEFFICIENT CANNOT BE COMPUTED.

Table App.2 (4) The Spearman correlation coefficients for period four. The left and right Achilles tendons functional assessment markers with the general assessment

	DF	PF	PAIN	STIFF	GA
ULTRA	-.3600	-.3608	.7674	.7561	-.7693
	N(190)	N(190)	N(190)	N(190)	N(190)
	SIG .000	SIG .000	SIG .000	SIG .000	SIG .000

" . " IS PRINTED IF A COEFFICIENT CANNOT BE COMPUTED.

12 Jun 96 SPSS Release 4.0 for HP9000/8xx
12:12:41 University of Surrey Central HP9000 Ser 870 HP-UX A.B8.0

Table App.2(5) Period one and four Spearman correlation coefficients, left and right Achilles tendon correlation's with ultrasound

The abbreviations refer to the following:
U- period, group - A or B, Ultra - ultrasound, DF - dorsi-flexion, PF - plantar-flexion, GA - general assessment.

APPENDIX TWO

SUMMARY OF RAW DATA

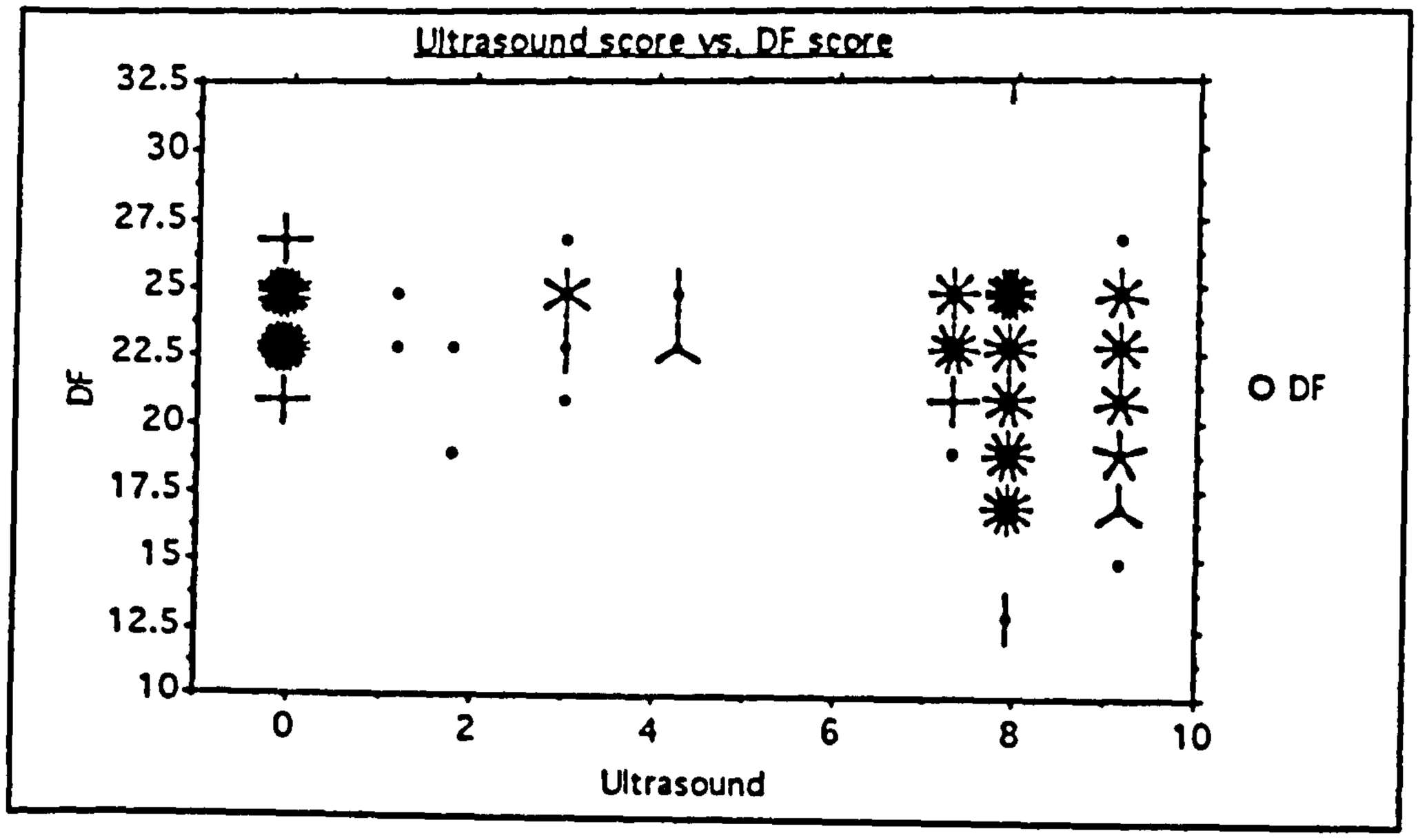

Table App.2 (6) A scatterplot of the dorsi-flexion score vs the ultraound score

DF Count	ULTRA.00	1.00	2.00	3.00	4.00	7.00	8.00	9.00	Row Total
-32.00							2		2 1.1
-27.00				1				1	2 1.1
-26.00	4								4 2.1
-25.00	8	1				4	5	2	20 10.5
-24.00	13			6	3	4	13	3	41 22.6
-23.00	17	1	1	1	3	6	5	3	37 19.5
-22.00	5			1		5	5	5	21 11.1
-21.00				1		4	7	7	19 10.0
-20.00	4						2		6 3.2
-19.00							5	3	8 4.2
-18.00			1			1	6	2	10 5.3
-17.00							11	1	12 6.3
-16.00							1	2	3 1.6
-15.00								1	1 .5
-12.00							2		2 1.1
Column Total	51 26.8	2 1.1	2 1.1	10 5.3	5 2.6	24 12.6	64 33.7	32 16.8	190 100.0

Table App.2 (7) The numerical distribution of the scatterplot in table (6)

The abbreviations refer to the following:
U- period, group - A or B, Ultra - ultrasound, DF - dorsi-flexion, PF - plantar-flexion, GA - general assessment.

APPENDIX TWO

SUMMARY OF RAW DATA

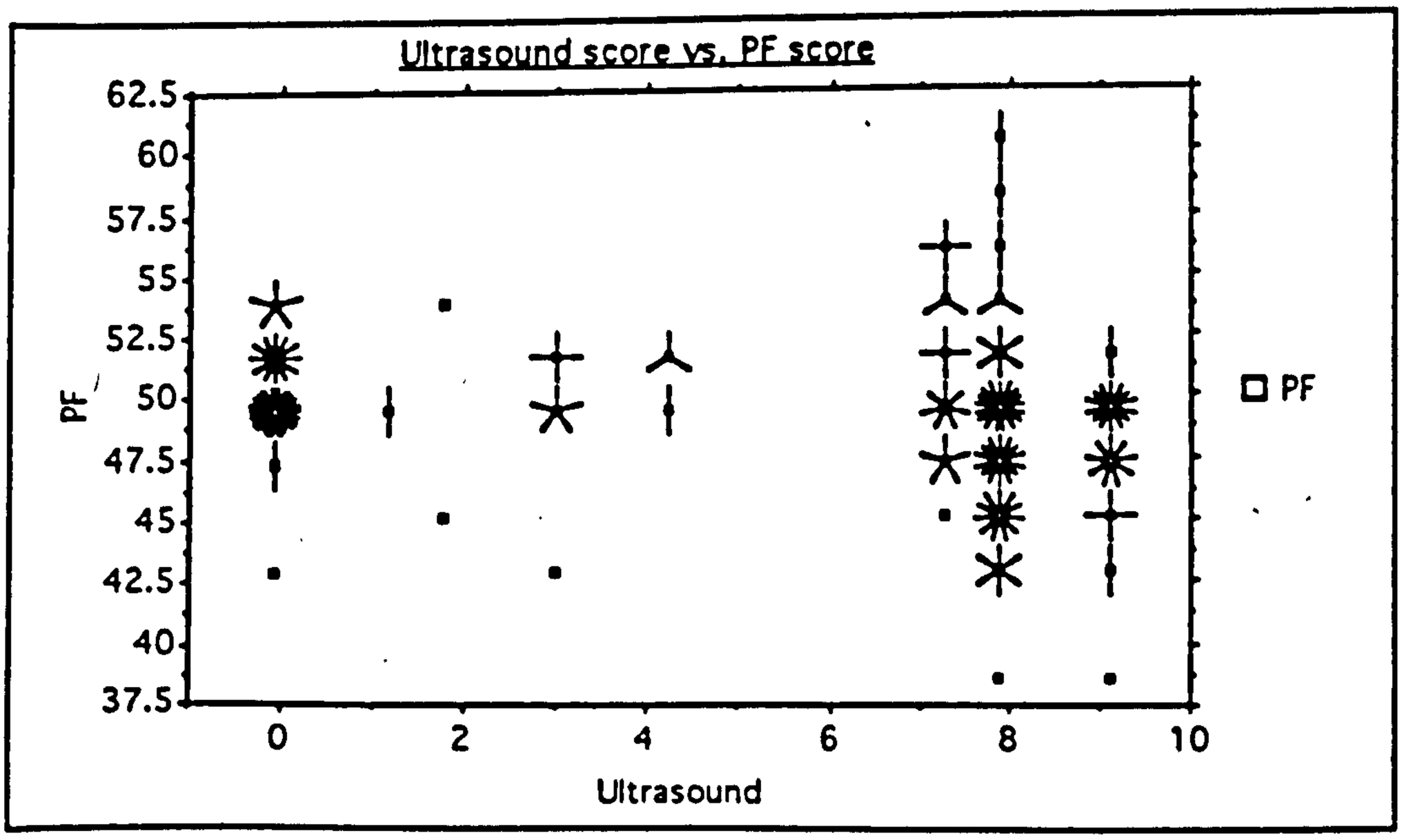

Table App.2 (8) A scatterplot of the plantar-flexion score vs the ultraound score

PF	ULTRA 00	1.00	2.00	3.00	4.00	7.00	8.00	9.00	Row Total
-60.00							2		2 1.1
-58.00							2		2 1.1
-55.00						4	2		6 3.2
-54.00	3						3		6 3.2
-53.00	2		1			3			6 3.2
-52.00	5					2	2		9 4.7
-51.00	7			4	3	2	4	2	22 11.6
-50.00	13	1		4	1	1	8	4	32 16.8
-49.00	18	1		1	1	6	9	10	46 24.2
-48.00	2					2	5	1	10 5.3
-47.00						3	9	8	20 10.5
-46.00						1	6	2	9 4.7
-45.00			1				3		4 2.1
-44.00							2	2	4 2.1
-43.00	1						3	1	5 2.6
-42.00				1			3	1	5 2.6
-39.00							1	1	2 1.1
Column Total	51 26.8	2 1.1	2 1.1	10 5.3	5 2.6	24 12.6	64 33.7	32 16.8	190 100.0

Table App.2 (9) The numerical distribution of the scatterplot in table (8)

	Patient	U	Group	Ultrasound	DF	PF	Pain	Stiffness	GenAss
1	1	1	2	8	19	43	83	15	1
2	2	1	1	8	21	44	82	10	1
3	3	1	2	8	21	51	56	10	3
4	4	1	1	7	22	49	57	10	3
5	5	1	2	9	17	51	83	15	1
6	6	1	1	3	27	42	32	10	3
7	7	1	1	8	23	55	54	10	3
8	8	1	2	8	17	44	81	15	1
9	9	1	2	8	25	49	84	15	1
10	10	1	2	8	18	54	82	15	1
11	11	1	1	8	18	45	30	5	5
12	12	1	1	8	12	60	32	15	3
13	13	1	1	8	24	50	58	10	3
14	14	1	1	9	21	47	57	10	3
15	15	1	2	0	25	50	0	0	7
16	16	1	2	7	21	51	82	10	1
17	17	1	1	0	24	49	0	0	7
18	18	1	2	9	24	50	56	10	1
19	19	1	2	8	21	52	83	10	1
20	20	1	1	8	24	51	57	10	3
21	21	1	1	2	18	45	54	15	3
22	22	1	1	2	23	53	29	5	4
23	23	1	2	8	25	55	83	10	1
24	24	1	2	8	17	54	83	15	1
25	25	1	1	8	25	48	57	10	3
26	26	1	2	8	17	52	99	15	1
27	27	1	2	0	23	49	0	0	7
28	28	1	1	7	23	47	56	10	3
29	29	1	2	9	23	47	57	10	3
30	30	1	2	0	25	48	0	0	7
31	31	1	1	8	24	50	32	5	3
32	32	1	1	8	24	49	56	10	3
33	33	1	1	8	23	49	82	10	1
34	34	1	2	8	22	50	81	10	1
35	35	1	1	7	23	48	28	5	3
36	36	1	2	9	24	49	28	10	3
37	37	1	2	9	19	49	57	15	3
38	38	1	1	8	22	49	56	10	3
39	39	1	2	8	21	46	83	15	1
40	40	1	1	9	23	49	56	10	3
41	41	1	1	8	19	47	82	15	1
42	42	1	1	8	23	50	56	10	3
43	43	1	2	0	24	51	0	0	7
44	44	1	2	9	22	50	82	10	1
45	45	1	1	3	24	51	31	10	3
46	46	1	1	0	23	49	0	0	7
47	47	1	2	8	24	50	31	10	3
48	48	1	2	0	25	51	0	0	7
49	1	2	2	0	23	49	0	0	7
50	2	2	1	9	15	39	90	15	1
51	3	2	2	8	19	47	83	15	1
52	4	2	1	8	19	46	56	10	3
53	5	2	2	9	18	48	82	15	1
54	6	2	1	9	22	43	30	10	3
55	7	2	1	0	20	53	0	0	7
56	8	2	2	0	20	50	0	0	7
57	9	2	2	7	25	53	30	10	3
58	10	2	2	0	24	52	0	0	7
59	11	2	1	7	18	49	57	10	3
60	12	2	1	8	17	58	58	15	3
61	13	2	1	9	25	49	57	10	3
62	14	2	1	0	22	49	0	0	7
63	15	2	2	8	25	50	83	10	1

The abbreviations refer to the following:
U- period, group - A or B, Ultra - ultrasound, DF - dorsi-flexion, PF - plantar-flexion, GA - general assessment.

	Patient	U	Group	Ultrasound	DF	PF	Pain	Stiffness	GenAss
64	16	2	2	8	23	49	8	8	7
65	17	2	1	8	32	42	98	15	1
66	18	2	2	8	26	52	8	8	7
67	19	2	2	8	20	54	83	15	1
68	20	2	1	9	23	51	29	10	3
69	21	2	1	8	18	43	55	15	3
70	22	2	1	7	22	55	57	5	5
71	23	2	2	7	21	52	56	10	3
72	24	2	2	7	23	51	56	10	3
73	25	2	1	7	24	49	31	10	3
74	26	2	2	7	22	55	57	15	3
75	27	2	2	8	22	47	56	10	3
76	28	2	1	9	22	46	58	10	2
77	29	2	2	7	24	49	27	0	5
78	30	2	2	8	20	49	57	10	3
79	31	2	1	8	25	51	29	5	5
80	32	2	1	8	24	48	55	10	3
81	33	2	1	8	24	51	56	10	3
82	34	2	2	8	23	50	83	10	1
83	35	2	1	8	21	46	57	10	1
84	36	2	2	4	23	51	57	10	1
85	37	2	2	9	21	47	57	10	3
86	38	2	1	8	23	50	0	0	7
87	39	2	2	0	24	50	0	0	7
88	40	2	1	9	22	49	57	10	3
89	41	2	1	1	23	49	56	10	3
90	42	2	1	9	21	47	55	10	3
91	43	2	2	8	17	46	82	15	1
92	44	2	2	0	23	49	0	0	7
93	45	2	1	0	24	49	0	0	7
94	46	2	1	8	17	47	83	15	1
95	47	2	2	0	26	51	0	0	7
96	48	2	2	9	24	50	55	10	2
97	1	3	2	7	22	47	0	5	5
98	2	3	1	9	21	44	82	10	1
99	3	3	2	0	23	51	0	0	7
100	4	3	1	8	24	49	28	5	5
101	5	3	2	3	23	50	0	5	5
102	6	3	1	9	27	42	28	10	3
103	7	3	1	8	17	47	98	15	1
104	8	3	2	8	19	47	28	5	4
105	9	3	2	7	25	49	32	5	4
106	10	3	2	•	21	54	56	10	3
107	11	3	1	8	18	45	30	5	4
108	12	3	1	8	12	60	57	15	3
109	13	3	1	8	24	50	58	10	3
110	14	3	1	9	21	47	57	10	2
111	15	3	2	8	25	50	0	0	7
112	16	3	2	3	22	51	0	5	5
113	17	3	1	0	24	49	0	0	7
114	18	3	2	3	24	50	0	0	7
115	19	3	2	0	22	52	55	10	3
116	20	3	1	9	19	47	82	15	1
117	21	3	1	8	18	45	56	15	3
118	22	3	1	7	23	53	0	0	7
119	23	3	2	7	25	55	0	5	5
120	24	3	2	3	21	51	28	10	3
121	25	3	1	0	23	48	82	15	1
122	26	3	2	0	22	52	0	5	5
123	27	3	2	0	23	49	0	0	7
124	28	3	1	9	21	47	82	10	1
125	29	3	2	0	24	50	27	0	5
126	30	3	2	0	25	49	0	0	7

	Patient	U	Group	Ultrasound	DF	PF	Pain	Stiffness	GenAss
127	31	3	1	9	24	49	57	10	1
128	32	3	1	8	24	49	56	10	3
129	33	3	1	4	23	50	27	0	5
130	34	3	2	9	18	44	83	15	1
131	35	3	1	7	23	48	55	10	2
132	36	3	2	7	24	49	27	5	4
133	37	3	2	9	21	49	29	10	3
134	38	3	1	8	16	46	83	15	1
135	39	3	2	3	24	49	0	5	5
136	40	3	1	8	24	48	28	5	4
137	41	3	1	0	24	48	0	0	5
138	42	3	1	9	19	47	82	15	1
139	43	3	2	0	22	50	0	0	7
140	44	3	2	3	24	50	4	5	5
141	45	3	1	4	23	51	56	10	2
142	46	3	1	0	23	49	0	0	7
143	47	3	2	1	25	50	0	5	5
144	48	3	2	0	25	51	0	0	7
145	1	4	2	0	23	49	0	0	7
146	2	4	1	8	17	39	98	15	1
147	3	4	2	3	24	50	0	0	7
148	4	4	1	7	22	46	54	10	3
149	5	4	2	0	24	51	0	0	5
150	6	4	1	0	24	43	0	0	5
151	7	4	1	0	20	53	0	0	7
152	8	4	2	0	20	50	0	0	7
153	9	4	2	7	25	53	30	5	4
154	10	4	2	•	24	.52	0	0	7
155	11	4	1	9	16	49	97	15	1
156	12	4	1	8	17	58	82	15	1
157	13	4	1	9	25	49	57	10	3
158	14	4	1	0	22	49	0	0	7
159	15	4	2	0	25	50	0	0	7
160	16	4	2	0	23	49	0	0	7
161	17	4	1	8	32	42	98	15	1
162	18	4	2	0	26	52	0	0	7
163	19	4	2	0	23	54	56	10	3
164	20	4	1	9	22	49	56	10	3
165	21	4	1	8	18	43	56	15	3
166	22	4	1	7	21	55	0	0	7
167	23	4	2	7	24	52	0	0	7
168	24	4	2	0	24	54	0	0	7
169	25	4	1	8	22	49	82	15	1
170	26	4	2	0	23	54	0	0	7
171	27	4	2	8	22	47	29	5	5
172	28	4	1	9	16	46	98	15	1
173	29	4	2	4	24	49	28	10	3
174	30	4	2	8	17	42	82	15	1
175	31	4	1	9	24	50	33	10	3
176	32	4	1	8	24	48	55	10	3
177	33	4	1	4	24	51	27	0	5
178	34	4	2	0	23	50	0	0	5
179	35	4	1	8	21	46	55	10	2
180	36	4	2	7	23	50	29	5	4
181	37	4	2	7	21	47	27	5	5
182	38	4	1	0	23	50	0	0	7
183	39	4	2	0	24	50	0	0	7
184	40	4	1	8	24	49	29	5	4
185	41	4	1	0	23	49	0	0	5
186	42	4	1	8	17	47	83	15	1
187	43	4	2	3	24	51	27	5	5
188	44	4	2	0	23	49	0	0	7
189	45	4	1	0	24	49	0	0	7

	Patient	U	Group	Ultrasound	DF	PF	Pain	Stiffness	GenAss
198	46	4	1	8	21	47	81	18	1
191	47	4	2	8	26	51	8	8	7
192	48	4	2	8	25	50	8	5	5

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Patient No	Group	Sex	Age	1-D-F Lt	1-D-F Rt	1-P-F Lt	1-P-F Rt	1-Pain Lt	1-Pain Rt	1-Stiffness Lt	1-Stiffness Rt	1-Gen Ass Lt	1-Gen Ass Rt	1-Ultrasound Lt	1-Ultrasound Rt	2-Pain Lt	2-Pain Rt
1	B	Male	41	19	23	43	49	83	0	15	0	Poor	Excellent	c,g 3,h:1	a	55	0
2	A	Female	23	21	15	44	39	82	98	10	15	Poor	Poor	c,g 2	c,g 2	82	96
3	B	Male	38	21	19	51	47	56	83	10	15	Fair	Poor	c,i	g 3,h 2,i	27	30
4	A	Male	33	22	19	49	46	57	56	10	10	Fair	Fair	e	h 1,g,e	27	30
5	B	Female	34	17	18	51	48	83	82	15	15	Poor	Poor	d,g 1,i	d,i	30	30
6	A	Male	46	27	22	42	43	32	30	10	10	Fair	Fair	g 1	g 2,d	30	29
7	A	Male	38	23	20	55	53	54	0	10	0	Fair	Excellent	h 1	a	82	0
8	B	Male	36	17	20	44	50	81	0	15	0	Poor	Excellent	b,g,h 3	a	55	0
9	B	Male	29	25	25	49	53	84	30	15	10	Poor	Fair	c,e	e	30	28
10	B	Male	43	18	24	54	52	82	0	15	0	Poor	Excellent	c,e,g 4	a	56	0
11	A	Male	38	18	18	45	49	30	57	5	10	Good	Fair	e,c	g e	57	97
12	A	Male	32	12	17	60	58	32	58	15	15	Fair	Fair	c,g 2	f,g 4,h:4	82	81
13	A	Male	29	24	25	50	49	58	57	10	10	Fair	Fair	c,e,g 2	d g 1	58	57
14	A	Male	36	21	22	47	49	57	0	10	0	Fair	Excellent	e,d	a	57	0
15	B	Female	33	25	25	50	50	0	83	0	10	Excellent	Poor	a	g 3,h 2	0	27
16	B	Male	69	21	23	51	49	82	0	10	0	Poor	Excellent	g 3,i	a	31	0
17	A	Male	37	24	32	49	42	0	98	0	15	Excellent	Poor	a	h 3,g 3,f	0	98
18	B	Male	31	24	26	50	52	56	0	10	0	Poor	Excellent	d,g 2	a	28	0
19	B	Male	27	21	20	52	54	83	83	10	15	Poor	Poor	c,k	c,k	83	83
20	A	Female	43	24	23	51	51	57	29	10	10	Fair	Fair	c,g 1,h:2	d g 1	57	29
21	A	Male	32	18	18	45	43	54	55	15	15	Fair	Fair	g	c,i	54	55
22	A	Female	18	23	22	53	55	29	57	5	5	Fair/Good	Good	g,f	e	29	55
23	B	Male	34	25	21	55	52	83	56	10	10	Poor	Fair	c,i,g 2	e,g 1	55	30
24	B	Male	33	17	23	54	51	83	56	15	10	Poor	Fair	c,e,g 2	e	no ass	no ass
25	A	Male	28	25	24	48	49	57	31	10	10	Fair	Fair	e,c	a,e	55	30
26	B	Male	32	17	22	52	55	99	57	15	15	Poor	Fair	h 1,i,e	e	56	31
27	B	Male	48	23	22	49	47	0	56	0	10	Excellent	Fair	a	c,h 2,g 2,i	0	28
28	A	Male	42	23	22	47	46	56	58	10	10	Fair	Fair/Poor	b,e,g 2	d	54	56
29	B	Male	45	23	24	47	49	57	27	10	0	Fair	Good	d,g 2	e	27	27
30	B	Male	48	25	20	48	49	0	57	0	10	Excellent	Fair	a	c,e,g 3	0	83
31	A	Female	28	24	25	50	51	32	29	5	5	Fair	Good	c,g 1	k	32	31
32	A	Female	29	24	24	49	48	56	55	10	10	Fair	Fair	c,k	c	55	55
33	A	Male	44	23	24	49	51	82	56	10	10	Poor	Fair	g 2,h:2	g 2,h:2	0	0
34	B	Female	34	22	23	50	50	81	83	10	10	Poor	Poor	c,g 1	c,g 2,h:2	30	30
35	A	Female	44	23	21	48	46	28	57	5	10	Fair	Poor	b,e	c,g 1	56	57
36	B	Male	41	24	23	49	51	28	57	10	10	Fair	Poor	d,g 2	b,g 2	30	29
37	B	Female	46	19	21	49	47	57	57	15	10	Fair	Fair	d,h 2	d	30	27
38	A	Male	48	22	23	49	50	56	0	10	0	Fair	Excellent	g 2,h:2,i	a	56	0
39	B	Female	55	21	24	46	50	83	0	15	0	Poor	Excellent	b,h 2,g 2	a	30	0
40	A	Male	33	23	22	49	49	56	57	10	10	Fair	Fair	d	d	56	57
41	A	Male	36	19	23	47	49	82	56	15	10	Poor	Fair	c	b	97	54
42	A	Male	46	23	21	50	47	56	55	10	10	Fair	Fair	c,g 3	d,g 3	30	30
43	B	Male	27	24	17	51	46	0	82	0	15	Excellent	Poor	a	b,g 2,h:2	0	31
44	B	Male	56	22	23	50	49	82	0	10	0	Poor	Excellent	d,h 3,g 3,i	a	55	0
45	A	Female	37	24	24	51	49	31	0	10	0	Fair	Excellent	b,g 1	a	31	0
46	A	Male	44	23	17	49	47	0	83	0	15	Excellent	Poor	a	c,f,g 4	0	84
47	B	Male	33	24	26	50	51	31	0	10	0	Fair	Excellent	c	a	30	0
48	B	Female	30	25	24	51	50	0	55	0	10	Excellent	Poor/Fair	a	d,g 2	0	27

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2-Stiffness Lt	2-Stiffness Rt	2-Ultrasound Lt	2-Ultrasound Rt	3-Pain Lt	3-Pain Rt	3-Stiffness Lt	3-Stiffness Rt	3-Ultrasound Lt
5	0 g 3	a		28	0	5	0 e	
10	15 no u/s	no u/s		82	96	10	10 no u/s	
5	5 i	g 3 h 1 i		0	0	0	0 a	
0	10 e	h 1 g e		30	54	0	10 e	
5	5 g 1	a		30	29	5	5 no u/s	
5	5 no u/s	no u/s		30	29	10	5 d g 1	
15	0 g h 2 i	a		97	0	15	0 g ix3 b	
10	0 g h 2 b	a		30	0	5	0 g h 1 b	
10	10 c e	e		29	27	5	5 c e	
10	0 c e g 4	a		56	0	10	0 no u/s	
10	15 e c	g d e		57	97	10	15 e c	
15	15 no u/s	no u/s		82	81	15	15 c g 3	
10	10 no u/s	no u/s		58	57	10	10 no u/s	
10	0 no u/s	no u/s		57	0	10	0 e d	
0	5 a	g 1		0	0	0	5 a	
5	0 no u/s	no u/s		29	0	5	0 g 1	
0	15 a	h 3 g 3 f		0	98	0	15 a	
5	0 g 1	a		0	0	5	0 g 1	
10	10 d	d		30	30	5	5 a	
10	10 no u/s	no u/s		82	56	10	10 no u/s	
15	15 no u/s	no u/s		54	55	15	15 g e	
5	10 no u/s	no u/s		0	0	0	5 e	
10	10 e g 1	i e		0	5	0	5 no u/s	
no ass	no ass	no u/s	no u/s	4	0	10	0 g 1	
5	5 no u/s	no u/s	no u/s	58	57	10	10 d e	
10	10 no u/s	no u/s	no u/s	30	29	10	10 e i	
0	5 a	c h 2 g 2		0	28	0	5 a	
10	10 b e g 2	d g 1		81	81	10	10 b g 2 h 2	
5	0 g 2	g 3 c		28	55	5	10 g 1	
0	10 no u/s	no u/s		0	57	0	10 a	
10	10 no u/s	no u/s		29	28	10	10 c g 1	
10	10 no u/s	no u/s		55	55	15	15 no u/s	
0	0 g 2	g 2		29	30	5	5 g 2	
5	5 no u/s	no u/s		83	30	15	5 b g 2 h 2	
10	10 no u/s	no u/s		56	57	10	10 b e g 2	
5	5 g 2 d	g 2 b		27	29	5	5 g 2 e	
10	10 no u/s	no u/s		29	27	10	10 c	
10	0 g 2 h 2 i	a		83	0	15	0 g 3 h 2 ix3	
10	0 no u/s	no u/s		28	0	5	0 g 1	
10	10 d	d		56	57	10	10 no u/s	
10	10 no u/s	no/us		97	54	10	10 no u/s	
5	5 no u/s	no u/s		56	56	10	10 c g 3	
0	10 a	g 2 h 1		0	30	0	5 a	
10	0 h 1 g 2	a		4	0	5	0 g 2 i	
10	0 no u/s	no u/s		56	0	10	0 d g 2	
0	15 a	c f g 4		0	82	0	15 a	
10	0 no u/s	no u/s		27	0	5	0 b	
0	5 a	g 1		0	0	0	5 a	

3-Ultrasound Rt	4-Pain Lt	4-Pain Rt	4-Stiffness Lt	4-Stiffness Rt	4-Gen Ass Lt	4-Gen Ass Rt	4-D-F Lt	4-D-F Rt
a	0	0	5	0 Good	Excellent	22	23	
no u/s	82	98	10	15 Poor	Poor	21	17	
g 1	0	0	0	0 Excellent	Excellent	23	24	
h 1 g e	28	54	5	10 Good	Fair	24	22	
no u/s	0	0	5	0 Good	Good	23	24	
d g 2	28	0	10	0 Fair	Good	27	24	
a	98	0	15	0 Poor	Excellent	17	20	
a	28	0	5	0 Fair/Good	Excellent	19	20	
e	32	30	5	5 Fair/Good	Fair/Good	25	25	
no u/s	56	0	10	0 Fair	Excellent	21	24	
g d e	30	97	5	15 Fair/Good	Poor	18	16	
f g 4 h 4	57	82	15	15 Fair	Poor	12	17	
no u/s	58	57	10	10 Fair	Fair	24	25	
a	57	0	10	0 Fair/Poor	Excellent	21	22	
g 1	0	0	0	0 Excellent	Excellent	25	25	
a	0	0	5	0 Good	Excellent	22	23	
h 3 g 3 f	0	98	0	15 Excellent	Poor	24	32	
a	0	0	0	0 Excellent	Excellent	24	26	
c	55	56	10	10 Fair	Fair	22	23	
no u/s	82	56	15	10 Poor	Fair	19	22	
c i	56	56	15	15 Fair	Fair	18	18	
e	0	0	0	0 Excellent	Excellent	23	21	
no u/s	0	0	5	0 Good	Excellent	25	24	
a	28	0	10	0 Fair	Excellent	21	24	
d e	82	82	15	15 Poor	Poor	23	22	
e	0	0	5	0 Good	Excellent	22	23	
c g 1	0	29	0	5 Excellent	Good	23	22	
d g 1	82	98	10	15 Poor	Poor	21	16	
g 2 c	27	28	0	10 Good	Fair	24	24	
e g 3 h 3	0	82	0	15 Excellent	Poor	25	17	
k	57	33	10	10 Poor	Fair	24	24	
no u/s	56	55	10	10 Fair	Fair	24	24	
g 2	27	27	0	0 Good	Good	23	24	
g 1 h 1	83	0	15	0 Poor	Good	18	23	
c g 1	55	55	10	10 Fair/Poor	Fair/Poor	23	21	
g 2 e	27	29	5	5 Good/Fair	Fair/Good	24	23	
c	29	27	10	5 Fair	Good	21	21	
a	83	0	15	0 Poor	Excellent	16	23	
a	0	0	5	0 Good	Excellent	24	24	
no u/s	28	29	5	5 Fair/Good	Fair/Good	24	24	
no u/s	0	0	0	0 Good	Good	24	23	
c g 3	82	83	15	15 Poor	Poor	19	17	
g 1	0	27	0	5 Excellent	Good	22	24	
a	4	0	5	0 Good	Excellent	24	23	
a	56	0	10	0 Poor/Fair	Excellent	23	24	
c f g 4	0	81	0	10 Excellent	Poor	23	21	
a	0	0	5	0 Good	Excellent	25	26	
g 1	0	0	0	5 Excellent	Good	25	25	

4-P-F Lt	4-P-F Rt	4-Ultrasound Lt	4-Ultrasound Rt
47	49 e	a	
44	39 d g 3	c g 3	
51	50 a	g 1	
49	46 b h 2	g e j	
50	51 g 1	a	
42	43 d g 1 j	a	
47	53 h 2 ix3 g e	a	
47	50 g c	a	
49	53 e	e	
54	52 no u/s	no u/s	
45	49 e c	g d e	
60	58 c g 3	f g 4 h 4	
50	49 c e g 2	d g 1	
47	49 d e	a	
50	50 a	a	
51	49 g 1	a	
49	42 a	h 3 g 3 f	
50	52 g 1	a	
52	54 a	a	
47	49 d g 3	d g 2	
45	43 g c	c i	
53	55 e	e	
55	52 i	e	
51	54 g 1	a	
48	49 c g 2	c g 2	
52	54 a	a	
49	47 a	c g 1	
47	46 d g 2	d g 2 h 2	
50	49 a	b g 2	
49	42 a	e g 3 h 3	
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APPENDIX THREE

DIAGNOSTIC ULTRASOUND - THE APPEARANCE OF THE ACHILLES TENDON FOLLOWING SURGERY

Radiography (1996) **2**, 27–41

ULTRASOUND

DIAGNOSTIC ULTRASOUND: THE APPEARANCE OF THE ACHILLES TENDON FOLLOWING SURGERY

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(Received 16 June 1995; accepted 18 September 1995)

Purpose: To describe the sonographic appearance of the Achilles tendon following surgery. The images presented are from a selection of patients screened for inclusion in a wider study undertaken to evaluate the efficacy of a micro-current treatment regime, contrasted with current conservative management, for the Achilles tendon presenting with chronic pathology. Twenty per cent of the patients studied reported no change or a worsening of their original symptoms following surgical intervention. All subjects underwent an initial clinical and imaging assessment to ascertain their level of functional ability and the degree of deviation from normal sonographic appearance.

Methods: Sixteen of the 60 subjects required for the research programme had previously undergone surgical intervention. Failure to respond to conservative management was the consistent reason for surgery. Patients were scanned in the prone position, employing a standard technique, using real-time sonography with a 10 MHz transducer. Longitudinal and transverse scans were performed.

Scans were undertaken at initial assessment, 6 months and 1 year post-presentation.

Results: Surgical intervention can significantly affect the ultrasound appearance of the Achilles tendon. The disturbed tendon can present as enlarged, with a lesser or greater degree of anatomical variation, with residual or new pathology resulting in pain and/or functional disability.

Conclusions: Real-time sonography of the Achilles tendon can make a contribution to post-surgical assessment. It can evaluate accurately the success of a procedure and reduce the 'sit and wait' time, when patients are often subjected to further bouts of conservative treatment in an attempt to relieve post-surgical symptoms.

Key words: treatment; chronic pathology; musculo-skeletal; functional.

INTRODUCTION

This paper describes the sonographic appearance of the Achilles tendon following surgery. It should be emphasized that the patients examined presented for inclusion in a clinical research trial which was undertaken to evaluate the efficacy of a micro-current treatment regime as following surgery they were still having functional disability and/or pain. There are therefore no pre-operative images.

The sonographic appearance of the Achilles tendon with and without pathology is well documented [1–4]. However there appears to be a lack of documentation on the appearance of the Achilles tendon following surgery undertaken for chronic pathology.

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Ultrasound was used to assist in the assessment process, to confirm the diagnosis and to identify the type of tissue alteration. Magnetic resonance scanning would also be a suitable modality but ultrasound was immediately available and could be used to perform dynamic examinations at low cost. The parameters considered were the size of the tendon, changes to the echogenic pattern, surgical sequelae and the presence of residual or new pathology.

The normal anatomical appearance is described in order to place the post-surgical appearance in context and to make a visual distinction between pathology and surgery.

METHODS

A standard ultrasound technique was employed utilizing a 10 MHz transducer with a water stand-off.

Longitudinal and transverse real-time scans were taken. It is imperative to ensure that the surface of the probe is placed parallel to the tendon. If the beam is oblique in relation to the tendon an artificial hypoechogenic pattern, mimicking pathology, can result [3,8].

Transverse sections enable an accurate assessment of the tendon's size and establish any degree of tendon thickening. The greater diameter of the elliptical transverse section is orientated forward and medially.

To enable an evaluation of functional anatomy the patients were also scanned whilst in dorsi-flexion and plantar-flexion, stressed and unstressed. This provided valuable information about the tendon's response during movement.

Ultrasound scan was performed at initial assessment and then at 16-monthly intervals.

DISCUSSION

Normal ultrasound appearance

The normal tendon anatomy is briefly reviewed in order to put the post-surgical appearance in context. Figure 1 illustrates the normal anatomical appearances, viewed as a sagittal section. Figure 2 demonstrates the longitudinal appearance of the tendon. Anterior to the tendon at the os-calcis is the triangular area of adipose tissue, Kager's triangle, which is less echogenic than the tendon itself. Anterior to the tendon lies the soleus muscle (at the superior part of the tendon), flexor hallucis longus, digitorum longus and the posterior tibial tendon. The transverse section is shown in Fig. 3. The tendon is oval, having a greater transverse than antero-posterior diameter.

Consistent with other work [1–4] the average antero-posterior diameter of the normal tendon has been found to be 5.0 ± 0.5 mm, measured at 1 and 4 cm above the insertion.

Ultrasound appearance—post-surgery

Post-operatively the tendon may appear oedematous and may thus be demonstrated as enlarged, sonography should not be used until this has stabilized. The minimum time after which a patient was scanned following surgery was 5 months, taking this into account, the tendons examined are generally enlarged with anatomical variation, showing abnormal anterior deviation and post-surgical adhesions.

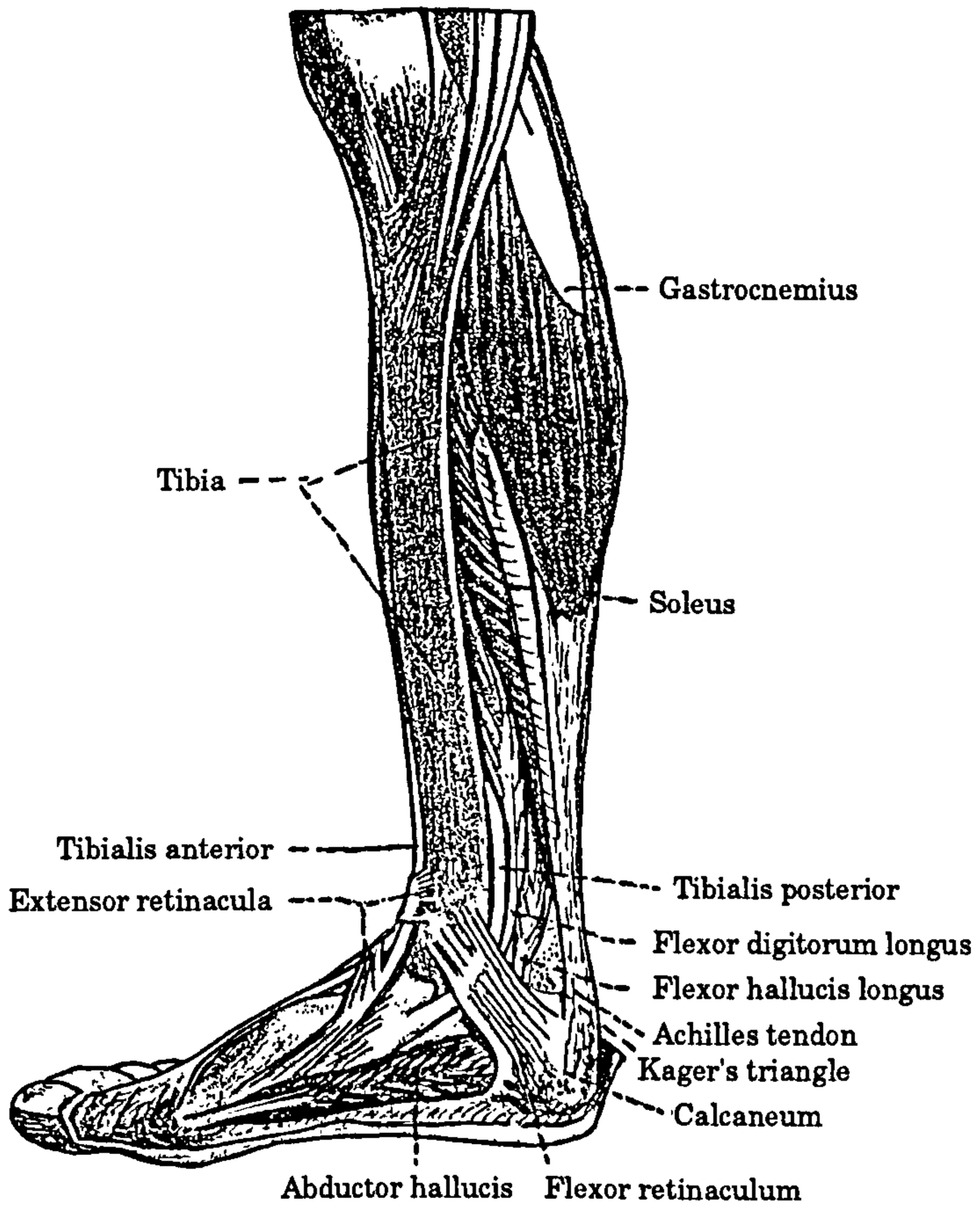
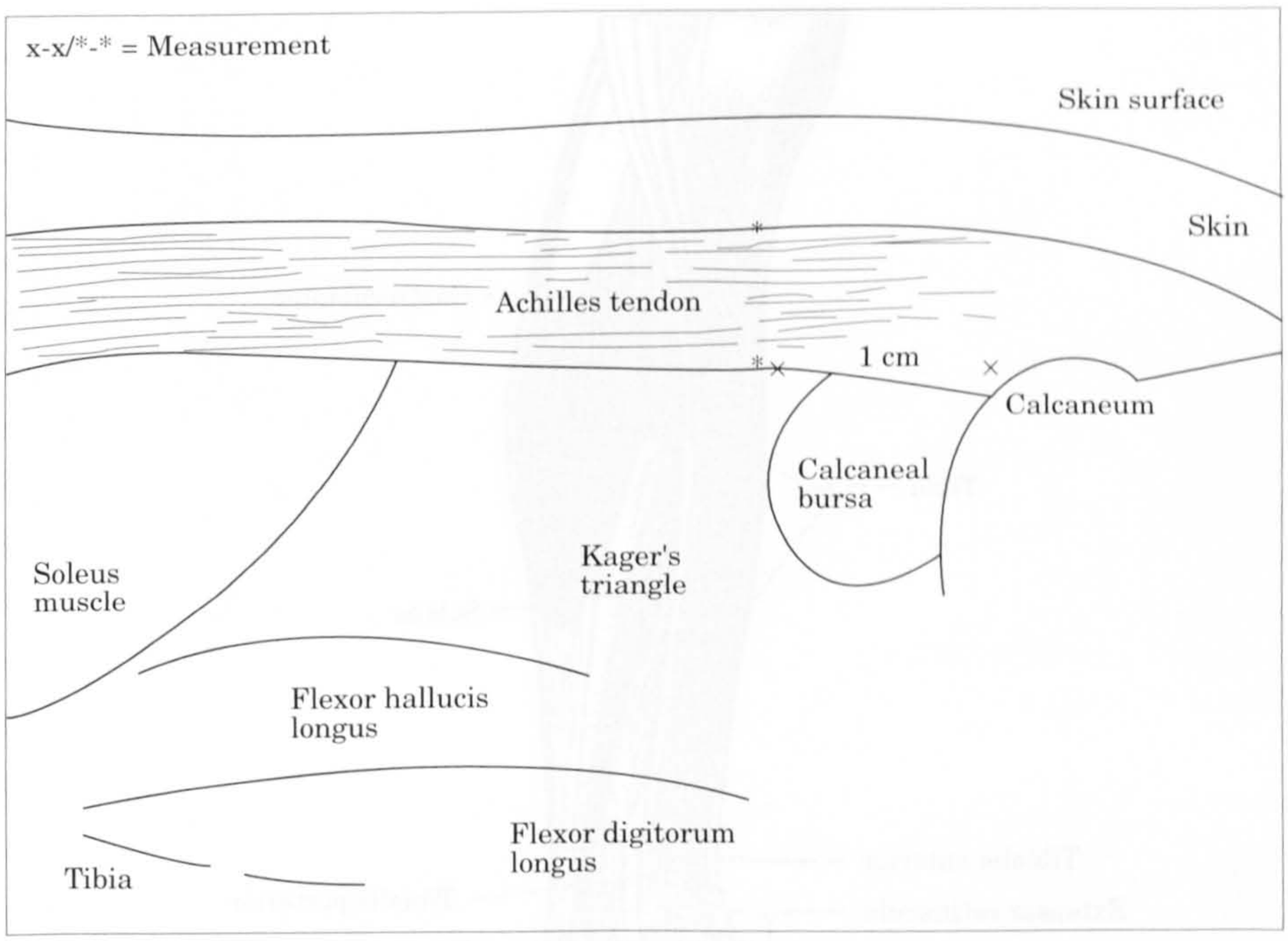


Figure 1. Anatomical appearance of the lower leg: medial aspect.

Williams [5] has highlighted how poor surgical technique, for example a tunnel mouth stenosis caused when the paratenon is cut straight as opposed to obliquely, results in pain caused by bunching of the fibrillar bundles on movement (Fig. 4). Residual and new pathologies, such as collagenous scarring and calcification(s), have been noted as resulting in functional disability and/or pain.

Patient 1. Figures 5 to 8 show the tendon of Patient 1, a 27-year-old athlete, of international standard, who underwent a bi-lateral decompression for chronic tendonitis following unsuccessful conservative management which included therapeutic ultrasound and massage.

Figure 5 demonstrates the longitudinal appearance of the right Achilles tendon, superior to the insertion at the os calcis. The solid arrow indicates the incision of the paratenon with the fibrillar tendon tissue lying abnormally inferiorly and posteriorly. When the foot is plantar-flexed the bunching of the fibrillar bundles inferior to the paratenon show constriction preventing normal movement of the tendon within the paratenon. This may have been responsible for the area of fibrillar disintegration (dotted area on the diagram), with a longitudinal length of 0.7 cm (between the crosses). Superiorly from posterior to anterior there are two distinct bands, shown in Fig. 6. The



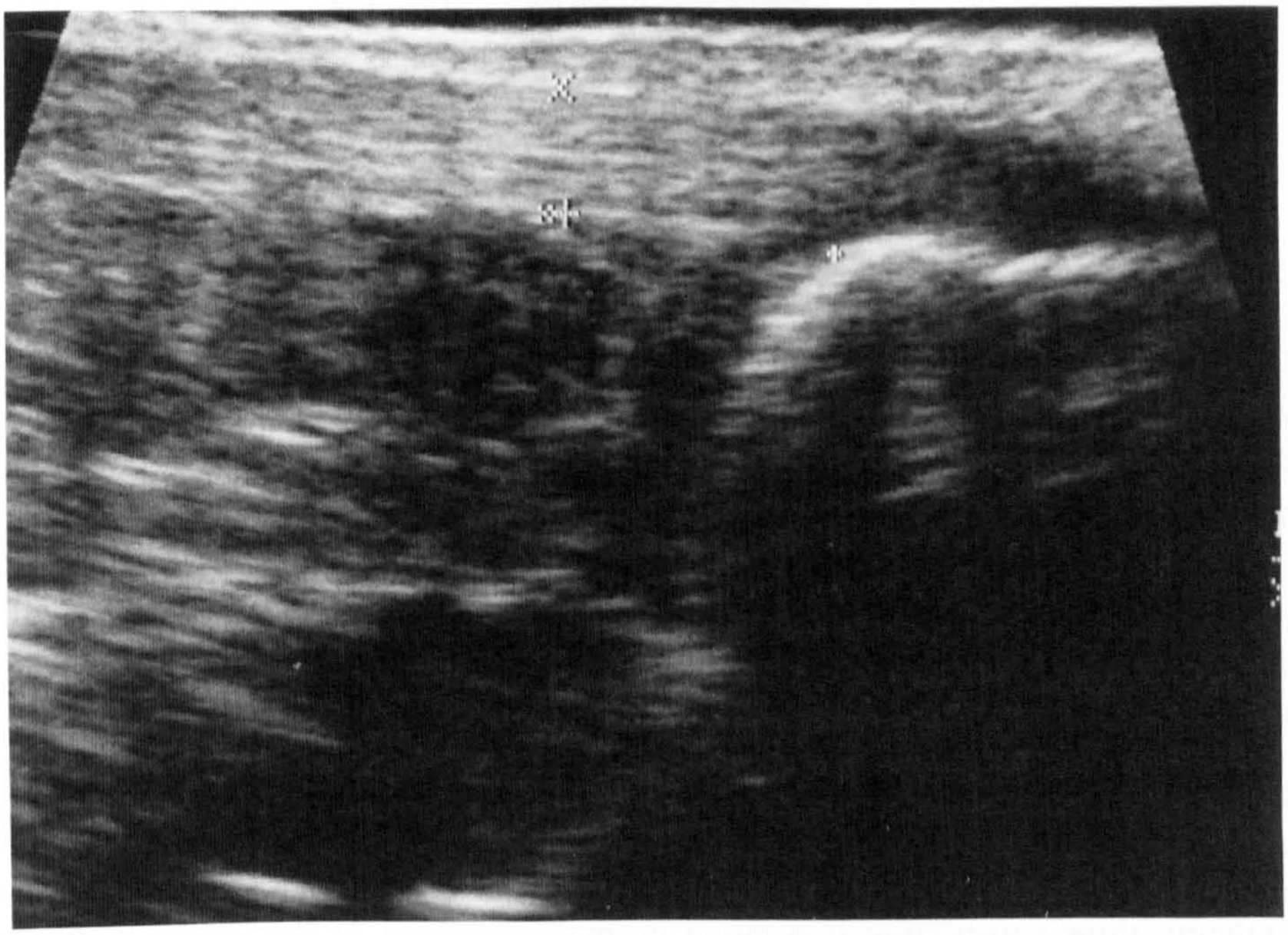
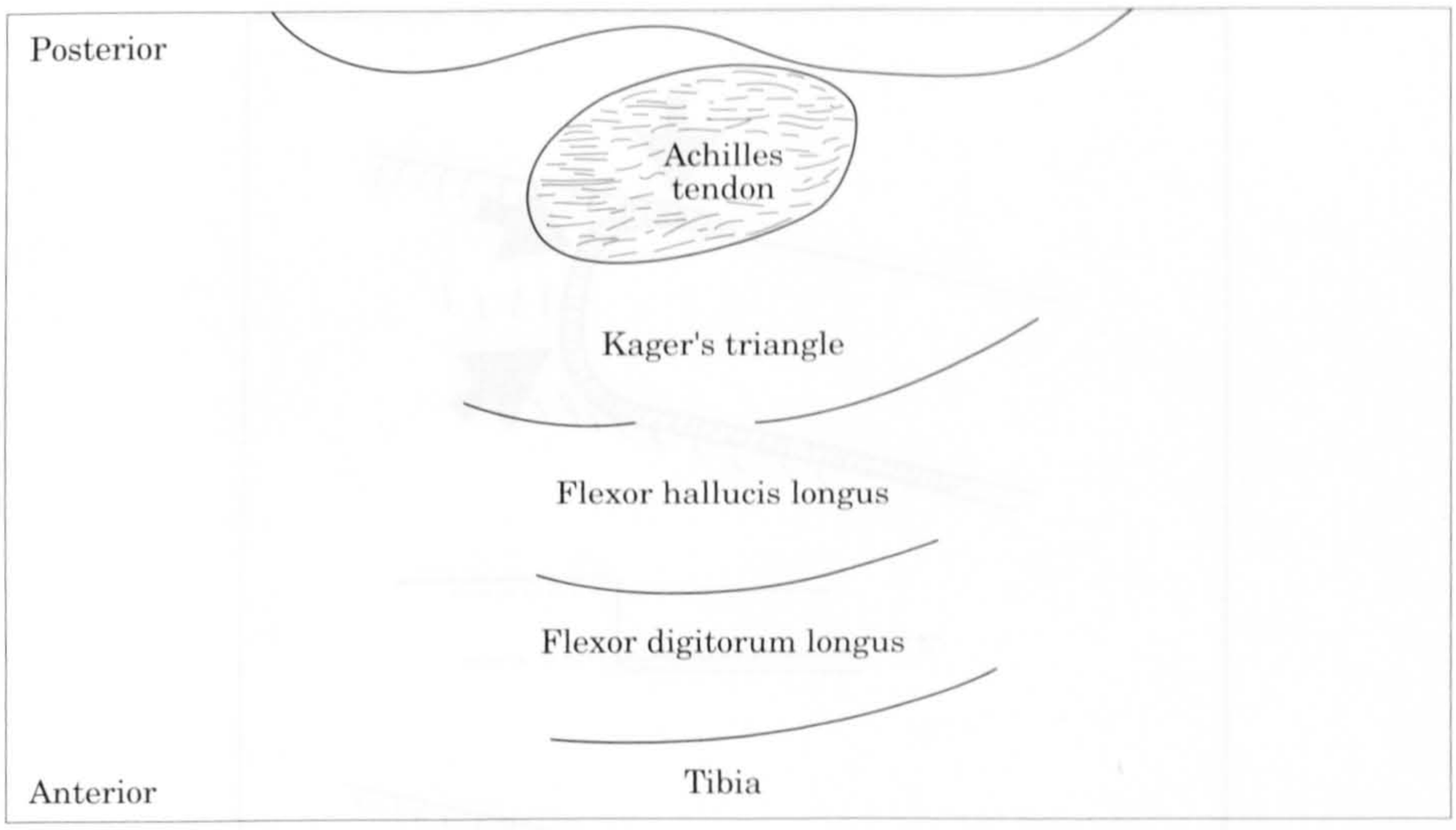


Figure 2. Normal Achilles tendon: longitudinal section.



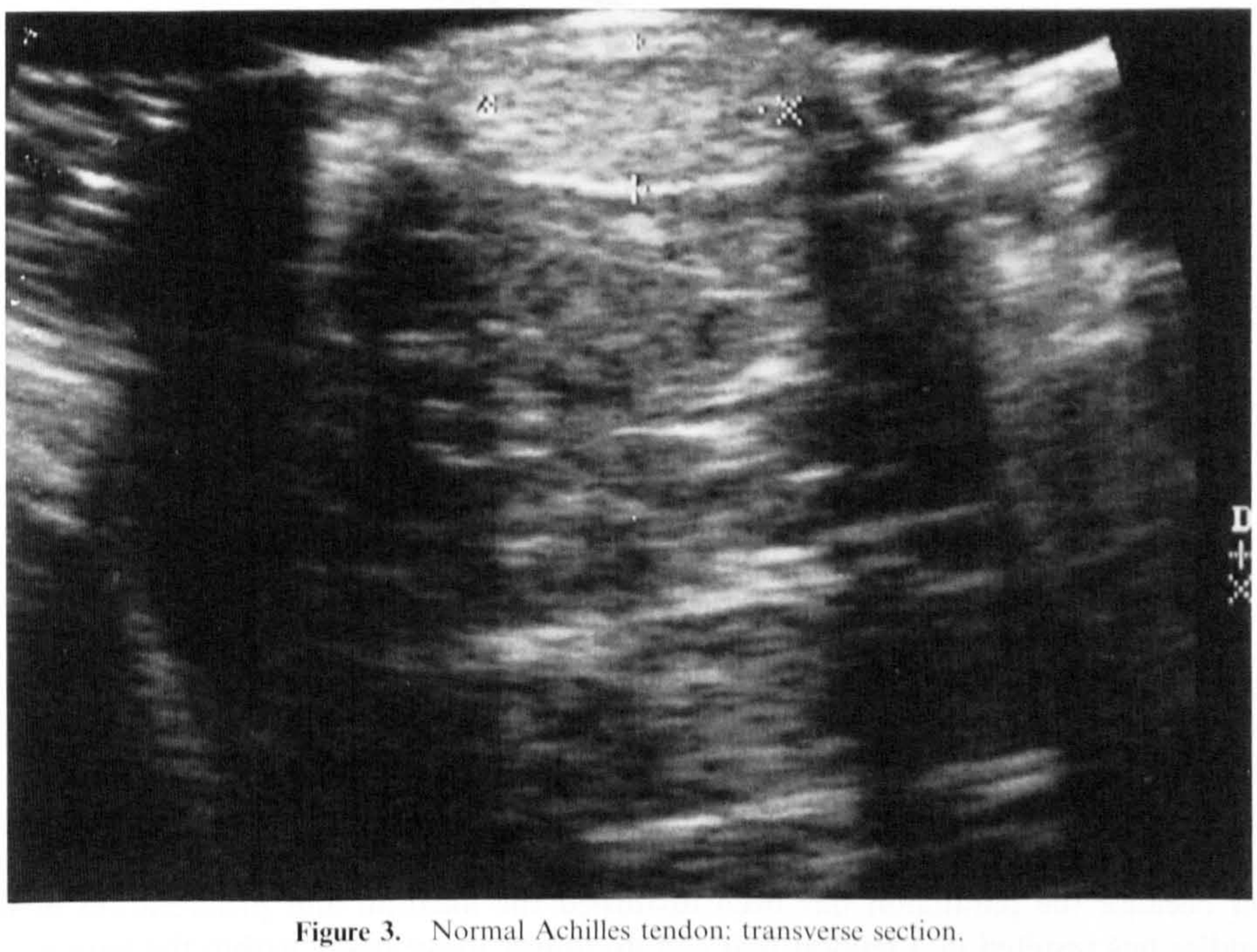


Figure 3. Normal Achilles tendon: transverse section.

anterior band measuring 0.5 cm shows the normal ribbon-like appearance with a suggestion of fibrous scarring (solid arrow) at the intratendinous qastrocnemius/soleus interface. Posteriorly, there is an area of regular echogenicity, this is the opened paratenon. This region also has an area of fibrous tissue (open arrow).

The normal tendon has a hypoechogenic linear pattern consistently described as ribbon-like, contained within two thin and regular echogenic bands, the paratenon [1,2].

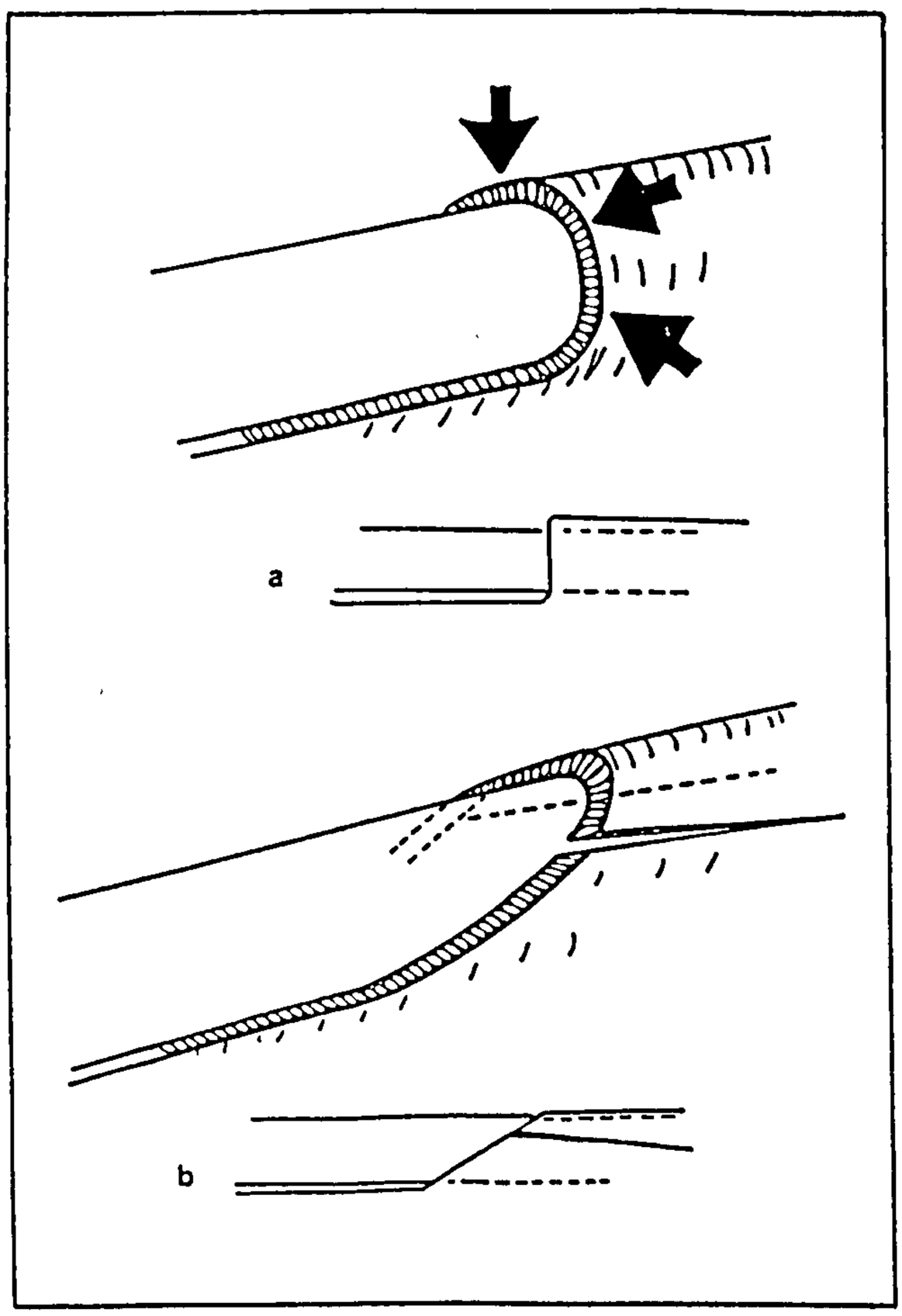
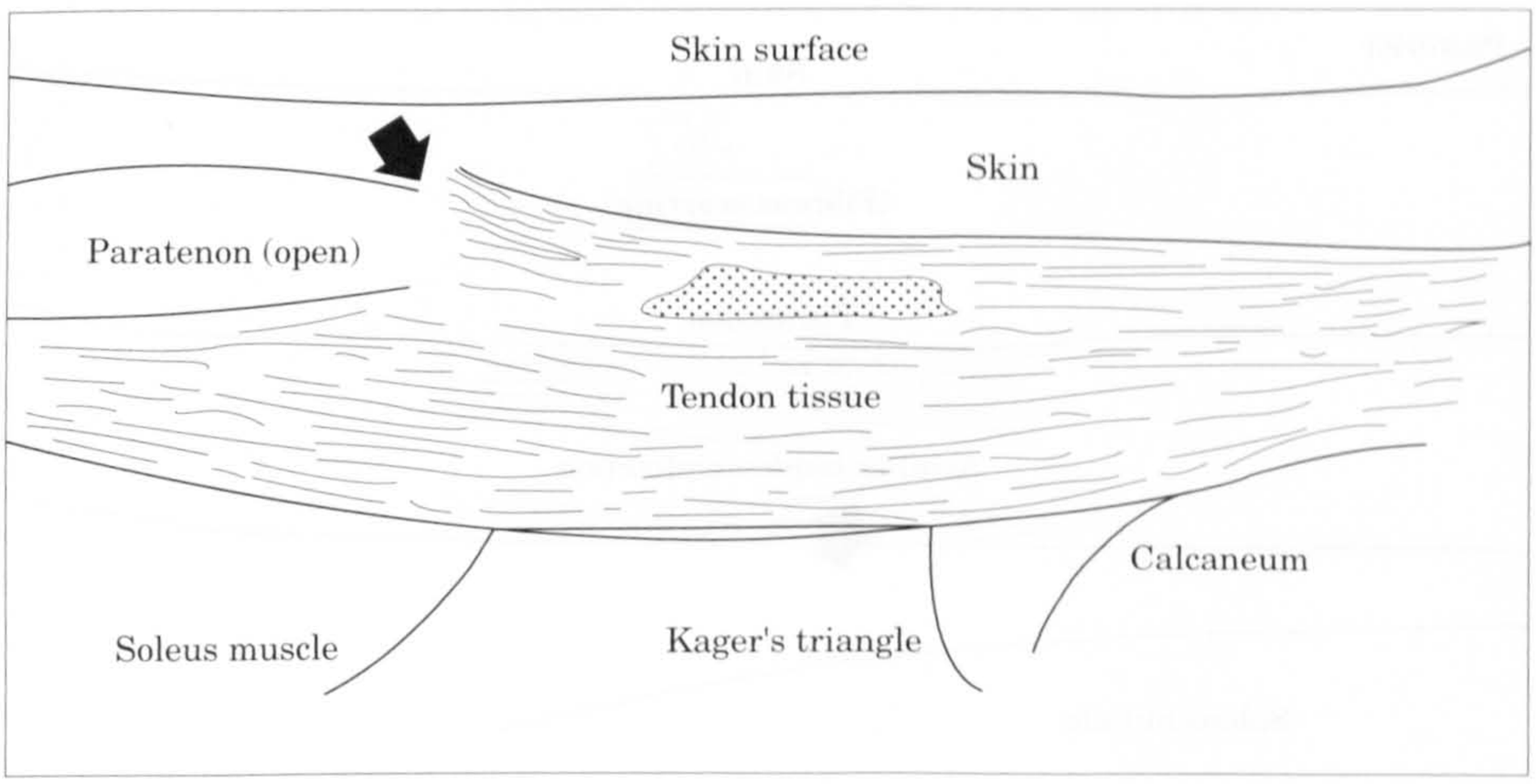


Figure 4. Surgical tunnel mouth stenosis [5]. (a) Straight cut; (b) oblique cut.

The left tendon has a similar appearance to the right. Figure 7 demonstrates how the tendon, instead of running parallel to the skin surface, as is seen in normal anatomy, deviates anteriorly. The white crosses represent measurement callipers, at the point where the tendon starts its deviation. This situation is exacerbated when the foot is plantar-flexed. The mid-portion of the tendon lies 1.0 cm more anteriorly to the skin surface than would be expected. Here the fibrillar bundles have become disorientated and because the paratenon has been disturbed the location and proliferation of the bundles has resulted in a tendon that can no longer move freely within the paratenon.

The transverse section of both tendons shows what I describe as a 'hamburger' appearance. Two fibrous bands run through the centre (Fig. 8). The surgical technique employed leaves the incised crural fascia on both sides of the tendon open, resulting in this appearance. This technique is described by Kvist and Kvist [6]. The tendon is round instead of the normal more oval appearance. Fibrillar bundles now lie above the level of undisturbed paratenon. The two white lines on the image in the mid-portion of the tendon are the paratenon distal to the excision.



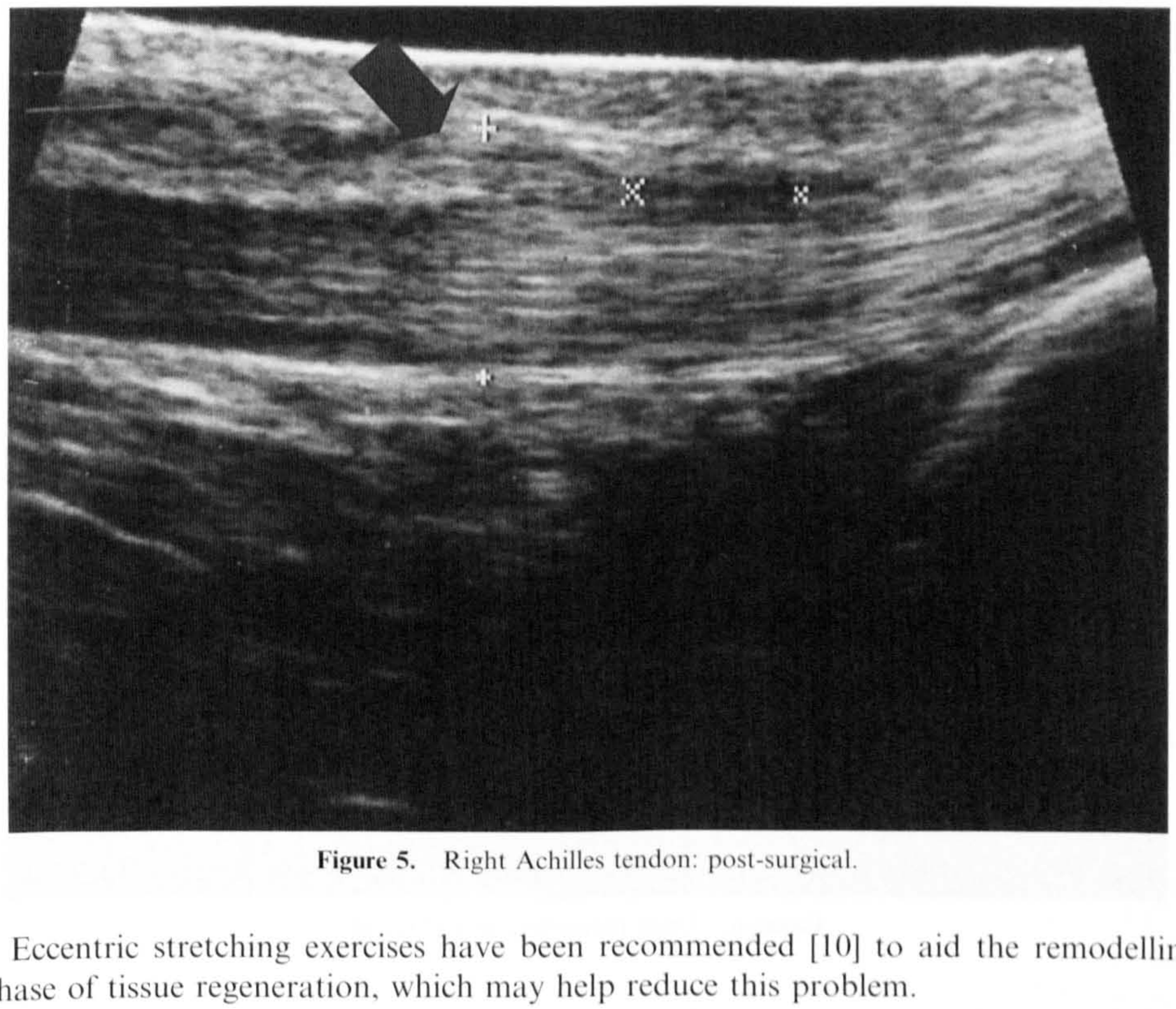
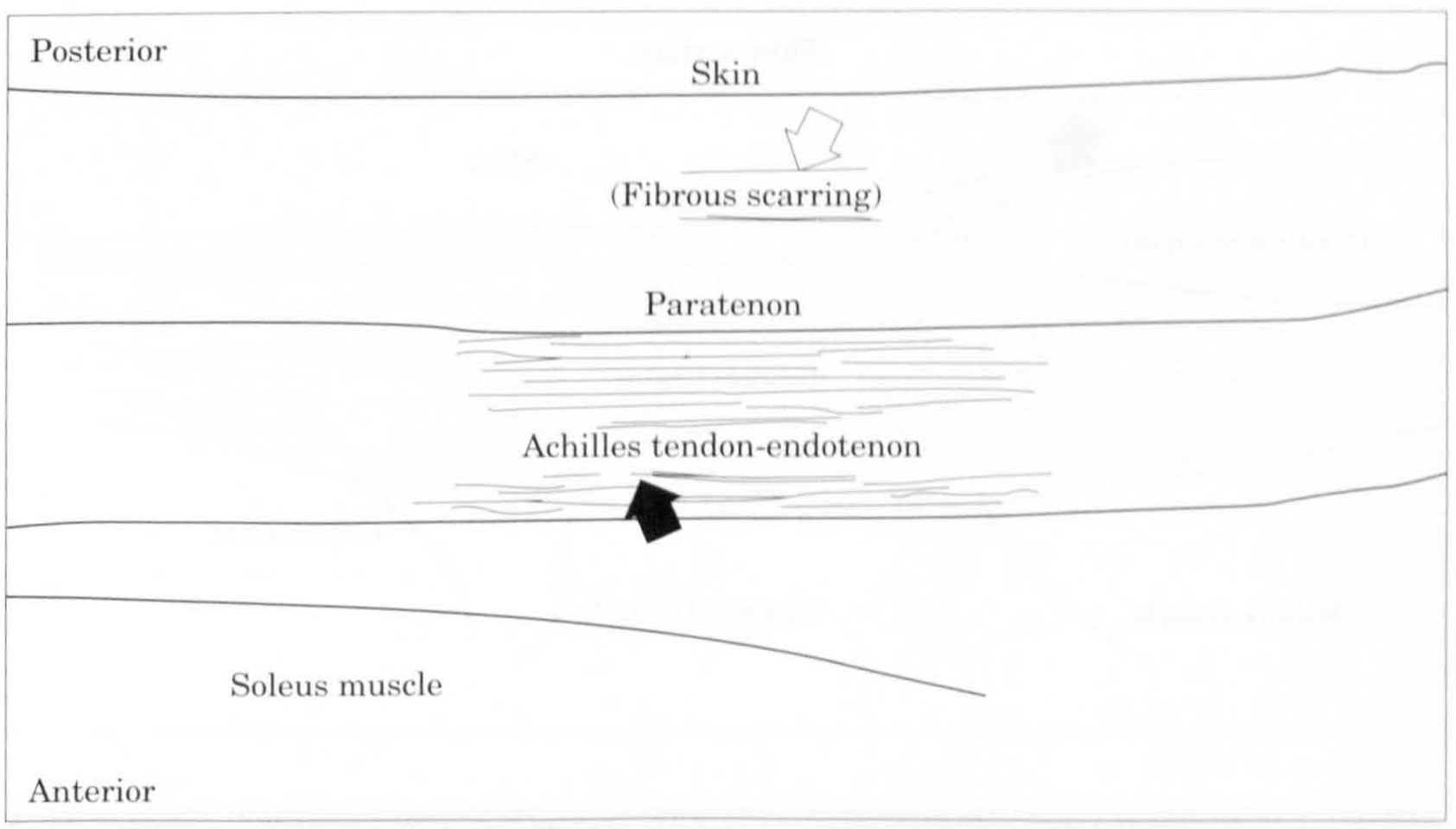


Figure 5. Right Achilles tendon: post-surgical.

Eccentric stretching exercises have been recommended [10] to aid the remodelling phase of tissue regeneration, which may help reduce this problem.

Patient 2. A lack of enlargement of a tendon evidently does not always indicate a lack of pathology. Following bi-lateral explorations and a tenosynovectomy Patient 2, also an athlete (aged 30 years), reported little improvement in his symptoms. Any stress to the tendon, for example prolonged driving, gentle jogging or wobble board exercises caused the tendon to flare up. Sonography showed the tendon was not greatly enlarged



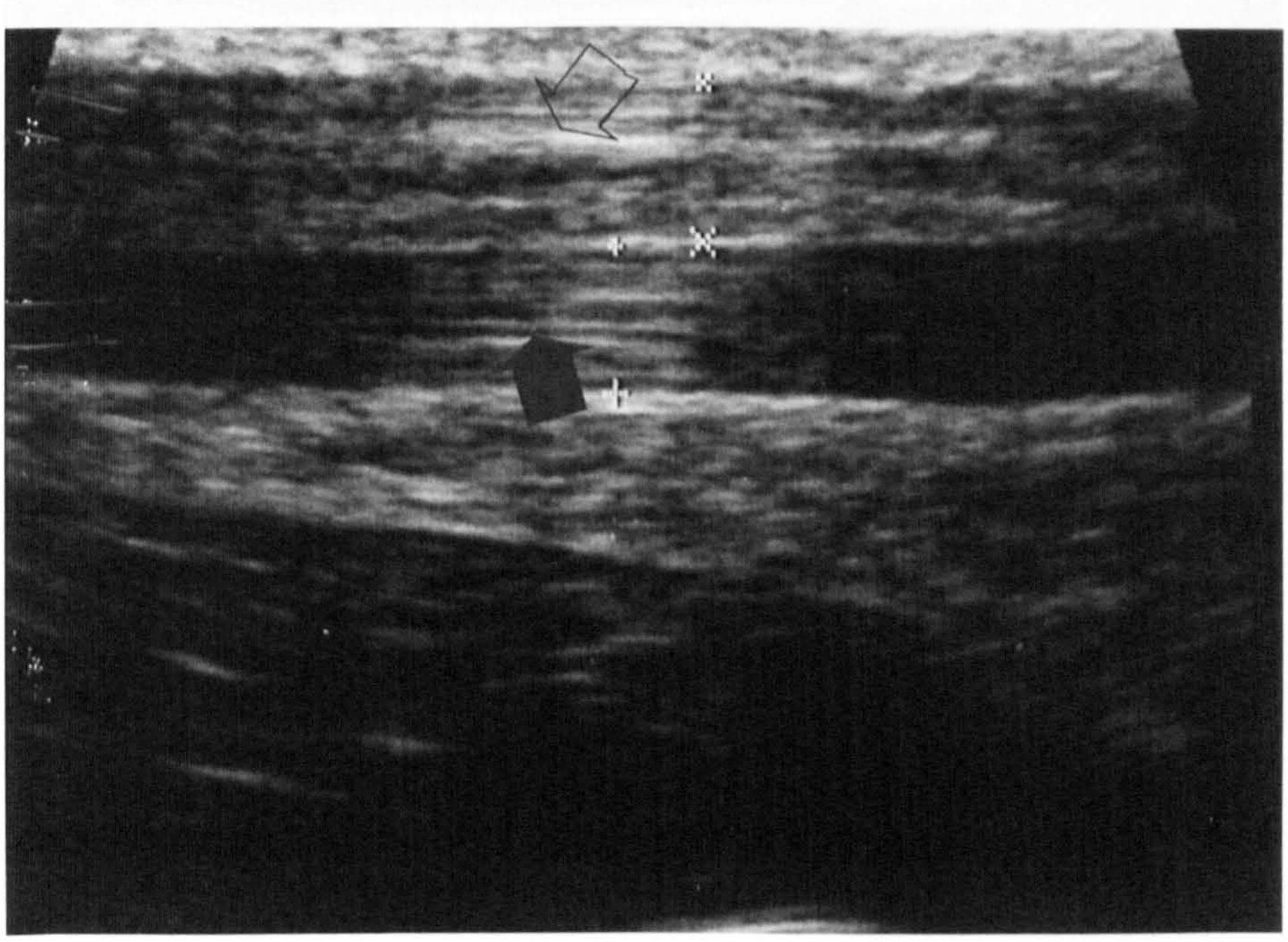


Figure 6. Open paratenon: post-surgical.

but showed micro-calcification adjacent to the insertion, arrows in Fig. 9. This is possibly the cause of the inflammatory bouts and subsequent pain which the patient experiences. The patient was also diagnosed as having a grade two partial rupture, hollow arrows, Fig. 10. Whether there is a causal link between these pathologies is difficult to conclude. The use of soft-tissue radiography was of no benefit to this patient. The calcification was of insufficient density to be demonstrated on a radiograph.

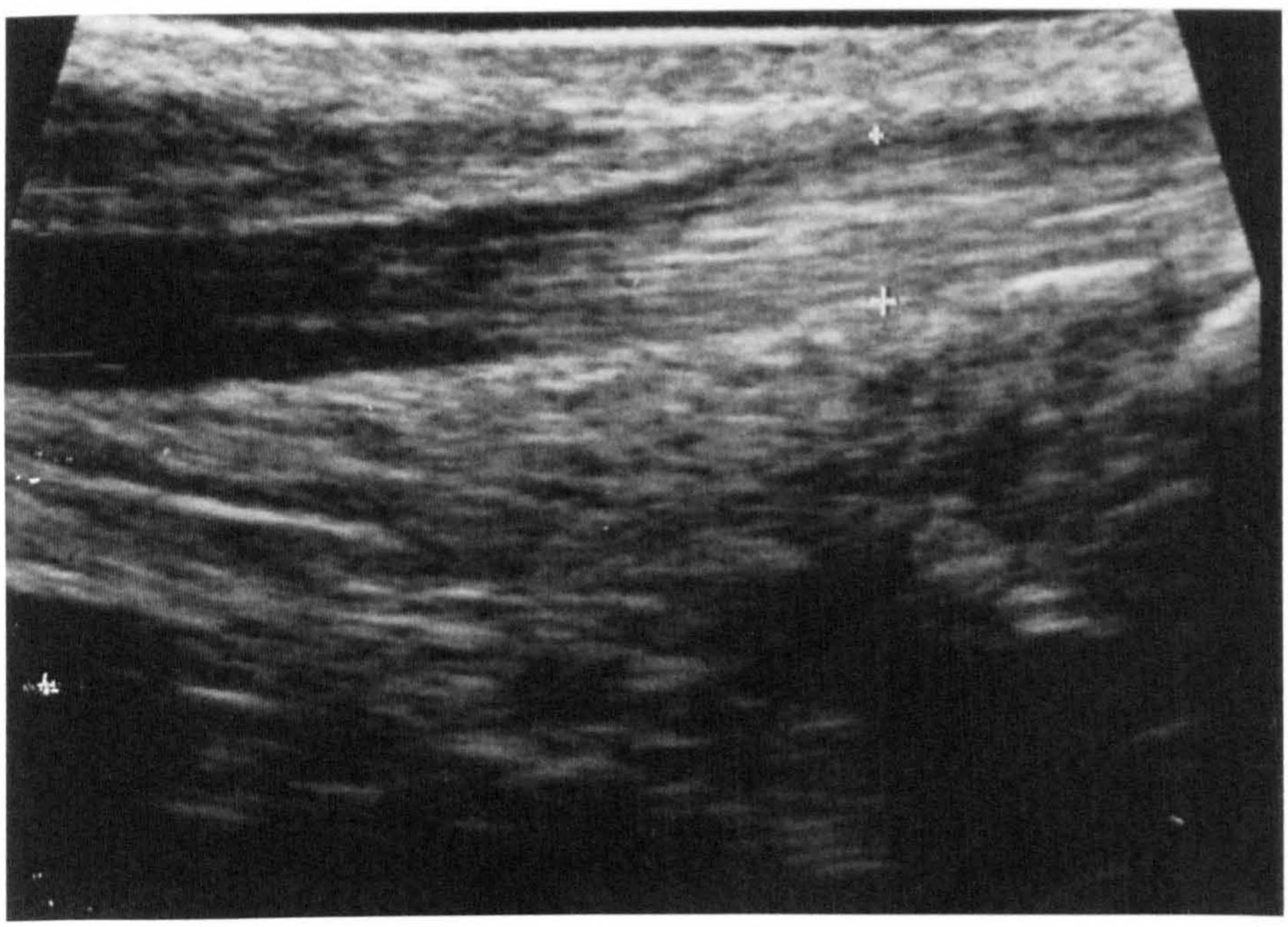


Figure 7. Anterior tendon deviation: post-surgical.

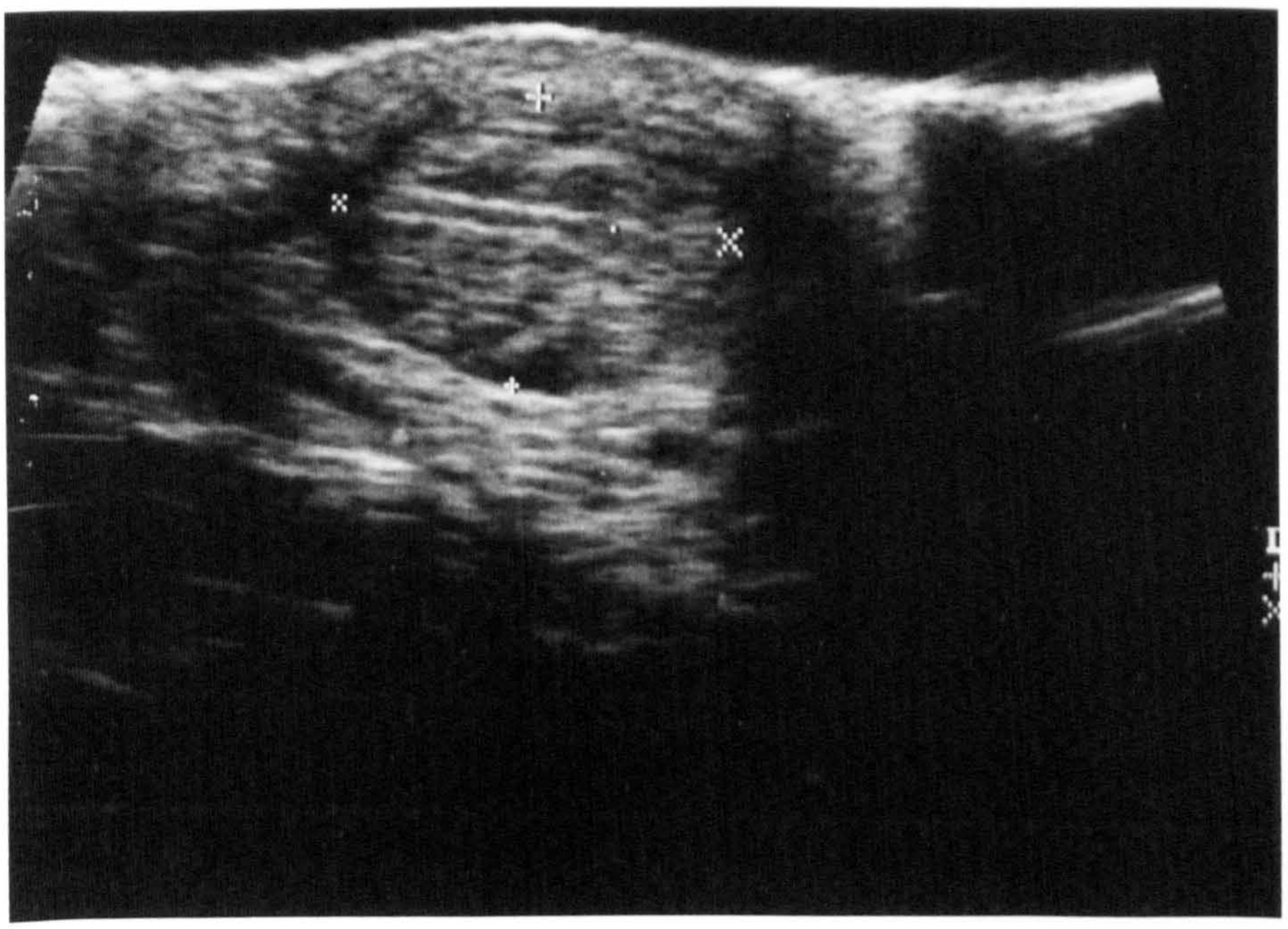


Figure 8. 'Hamburger appearance': transverse section.

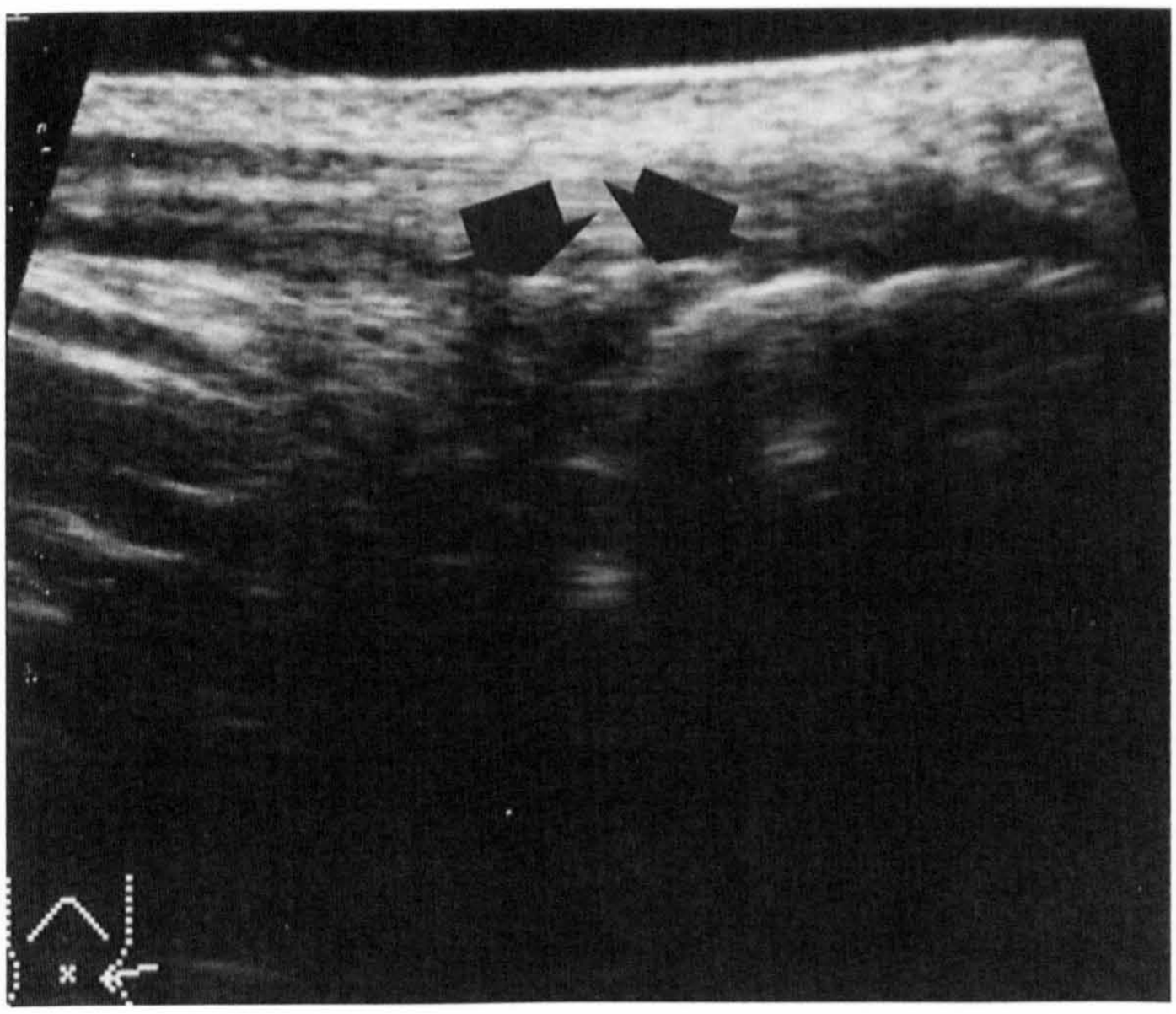


Figure 9. Micro-calcification: longitudinal section.

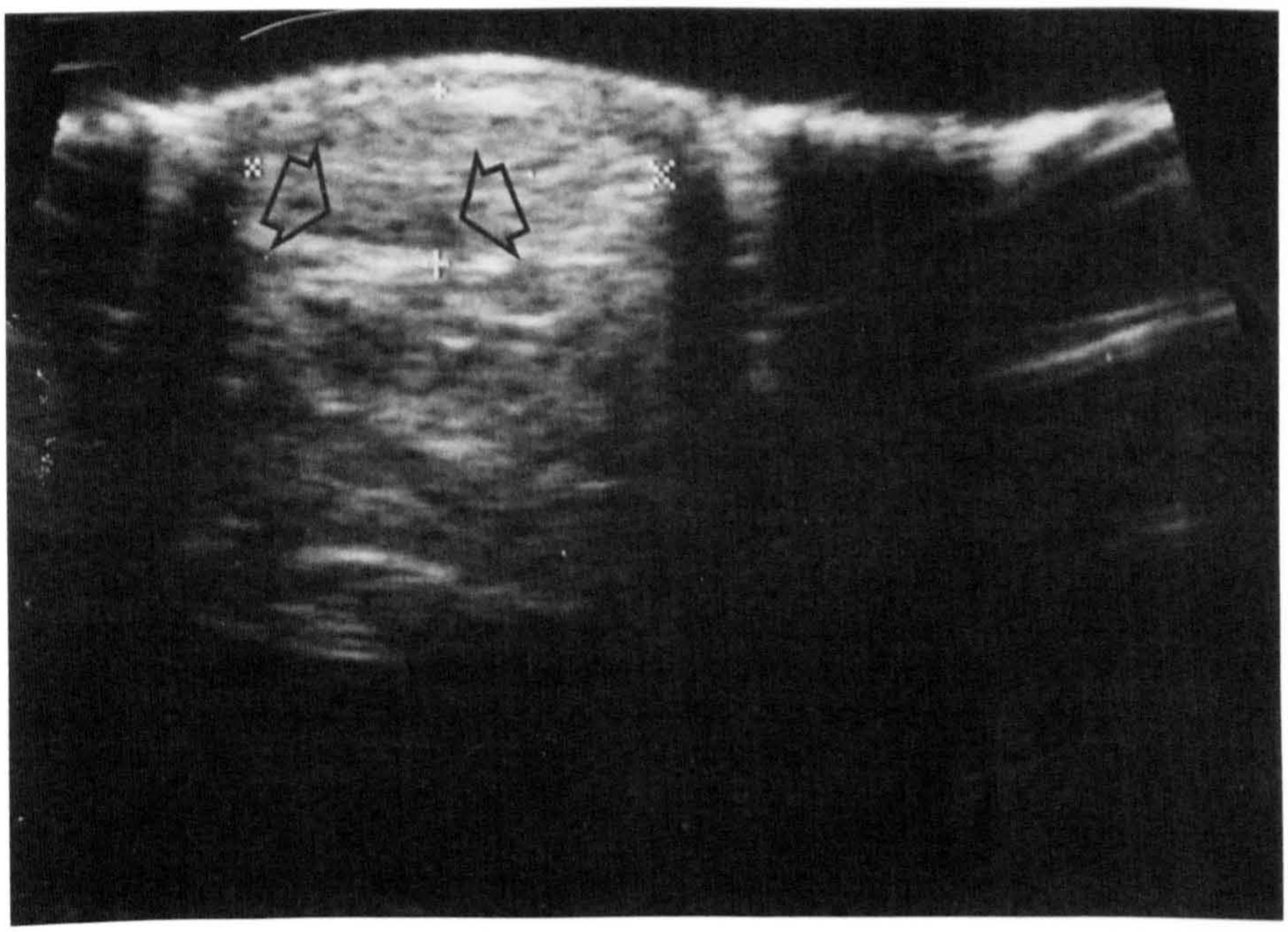


Figure 10. Partial rupture: transverse section.

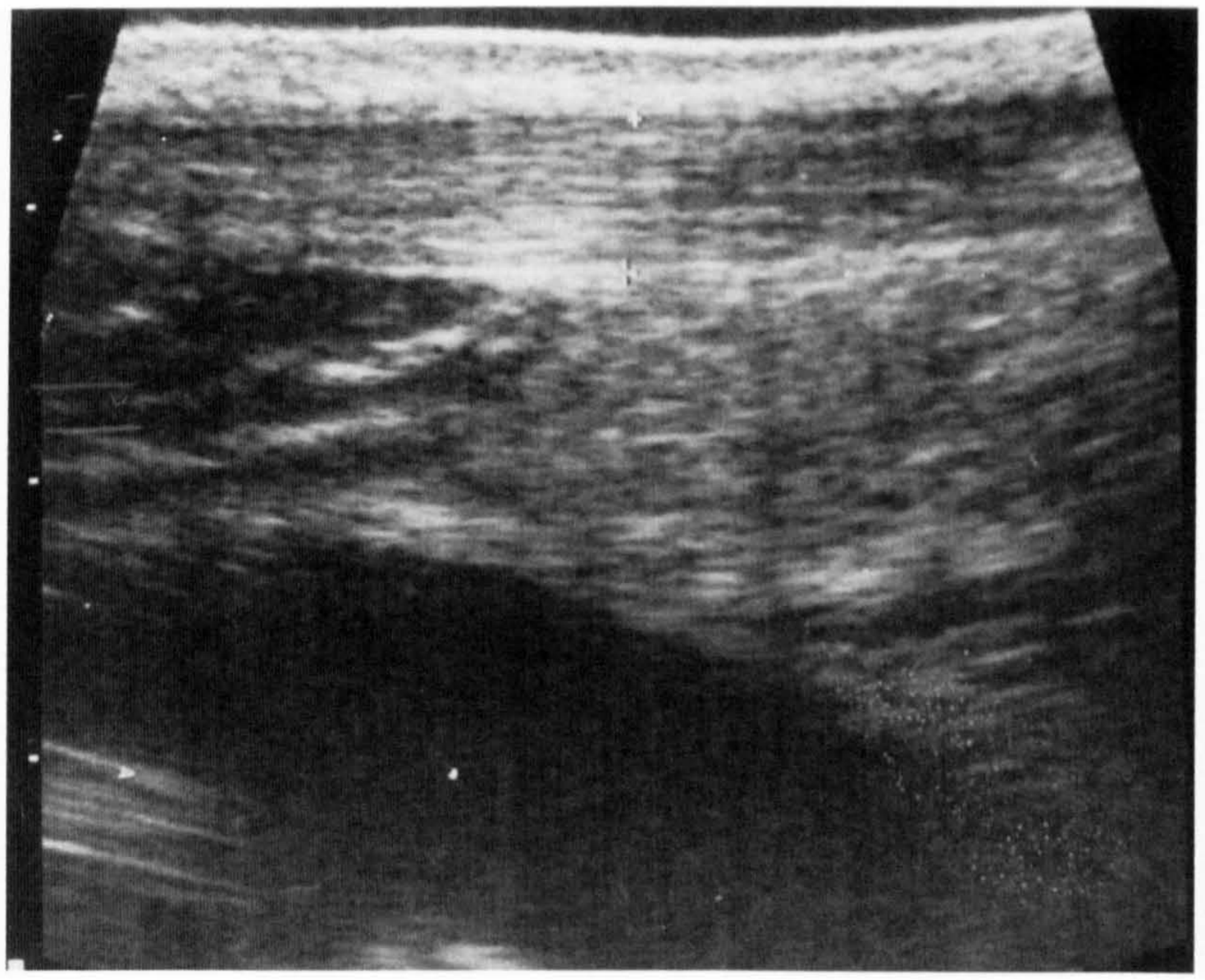


Figure 11. Partial rupture: longitudinal section.

Ultrasound has played a significant role in the patient's clinical management. Following the removal of the calcification using the new treatment regime the patient has reported a marked reduction in symptoms and has resumed normal athletic activity without having to resort to further surgery.

Patient 3. A full rupture to the tendon may be managed surgically or non-surgically. Many authors [5, 11–15] will argue the case for and against with equal conviction and evidence. Two months after a local injection of cortisone into the tendon Patient 3 experienced a full rupture of the tendon. This presents interesting images and demonstrates the importance of considering the appearance of the longitudinal and transverse sections. Figure 11, the longitudinal image of the right tendon, shows a relatively normal appearance. The corresponding transverse section, Fig. 12, shows grossly abnormal anatomy which is believed to be the result of pathology and the subsequent surgical technique employed. On clinical examination the patient had a markedly reduced degree of normal dorsi-flexion (more than 5° from the contra-lateral side [15]), which indicates a shortened tendon. The large hypoechogenic area in the anterior portion of the tendon (bold arrow, Fig. 12) is the soleus muscle, in a more inferior position than one would expect. In addition the loss of normal functional ability has led to adhesions to the paratenon. The prognosis may have been improved if imaging of the tendon had been undertaken post-surgery at the time when the patient showed no improvement. He has impaired functional ability and constant pain, the patient was scanned at 3-monthly intervals for a year, during which time he was prescribed anti-inflammatory drugs and stretching exercises. A small, but insignificant, degree of improvement was noted subjectively by the patient.

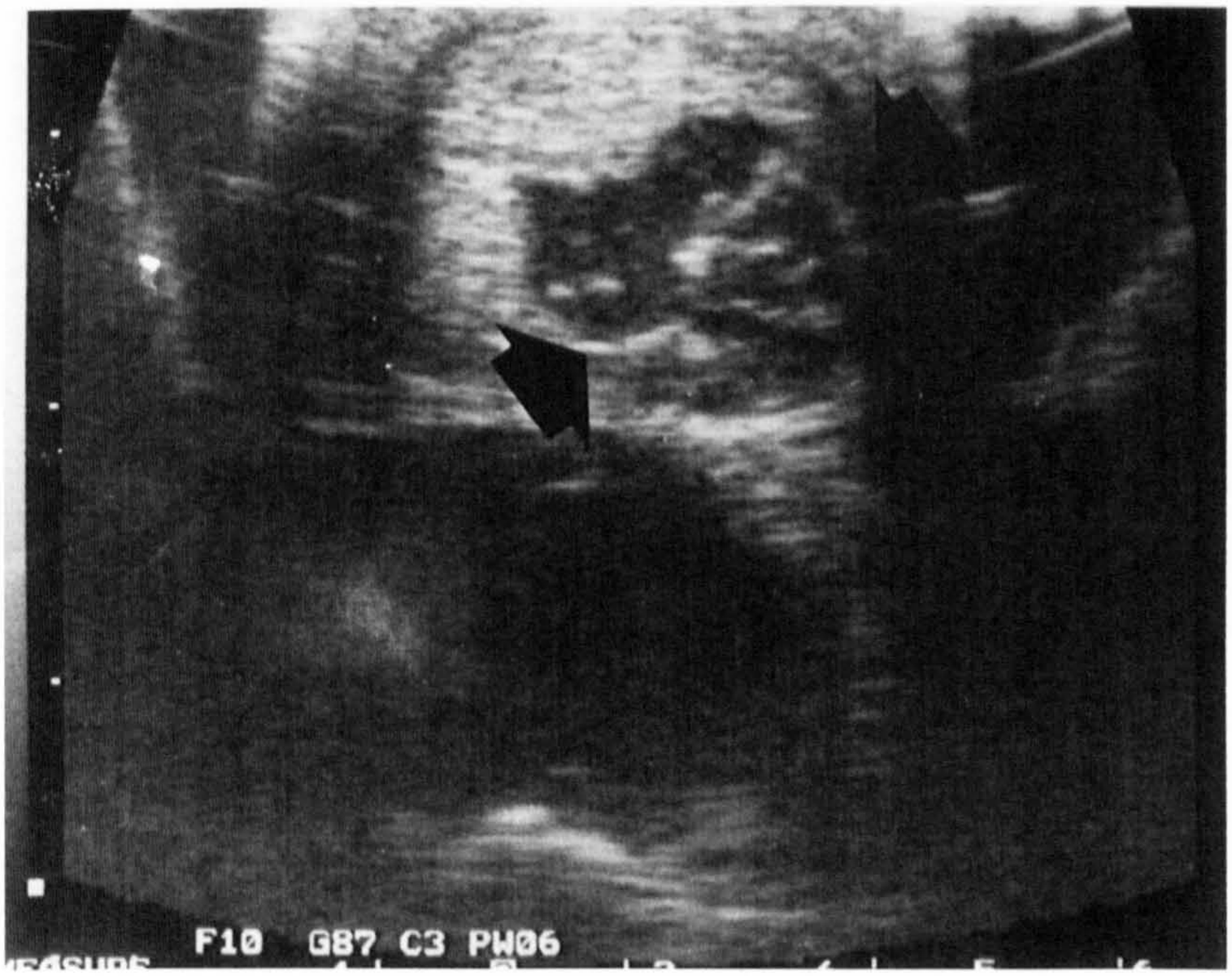


Figure 12. Shortened tendon.

Patient 4. Chronic pathology is at times mismanaged, Patient 4, a club marathon runner, was initially diagnosed as having chronic paratenonitis. Following a period of conservative treatment, which included a cortisone injection into the tendon which failed to deliver any tangible improvement, he was referred for surgery. The patient presented 6 months post-surgery, with severely impaired functional ability, and in a fair degree of pain. An isometric plantar-flexion test showed a reduced power output of 50 per cent and any exercise was impossible. Figure 13 shows the longitudinal section of the right tendon. The tendon deviates severely anteriorly when the foot is in the 'neutral' position. Superiorly the tendon lies 0.7 cm anterior to the skin surface, with the paratenon adhered to the endotenon itself, with inflammatory changes. Each dorsi-flexion and plantar-flexion movement of the foot presumably causes further irritation. It is particularly useful to scan whilst the patient goes through these movements. This allows assessment of the movement of the endotenon in the paratenon. Figure 14, the transverse section, demonstrates an enlarged tendon, 1 × 1.5 cm with a large hypoecho-genic area covering almost two-thirds of the tendon's cross-sectional area. The patient was given no post-surgical after-care, or exercises. On follow-up scan at 3 months the area was slightly larger and the likelihood of a complete rupture of the tendon high. The reasons for these appearances are as follows—a tunnel mouth stenosis has occurred superior to the calcaneum resulting in the deviation of the tendon anteriorly. It appears that the crural fascia has been left open and this may have had the effect of impairing venous circulation. In normal anatomy when the foot is in plantar flexion the fascia is pulled proximally along with the covering skin and this 'milks' venous blood towards the heart [16]. The impairment of circulation may have resulted in the grade 3 partial rupture.

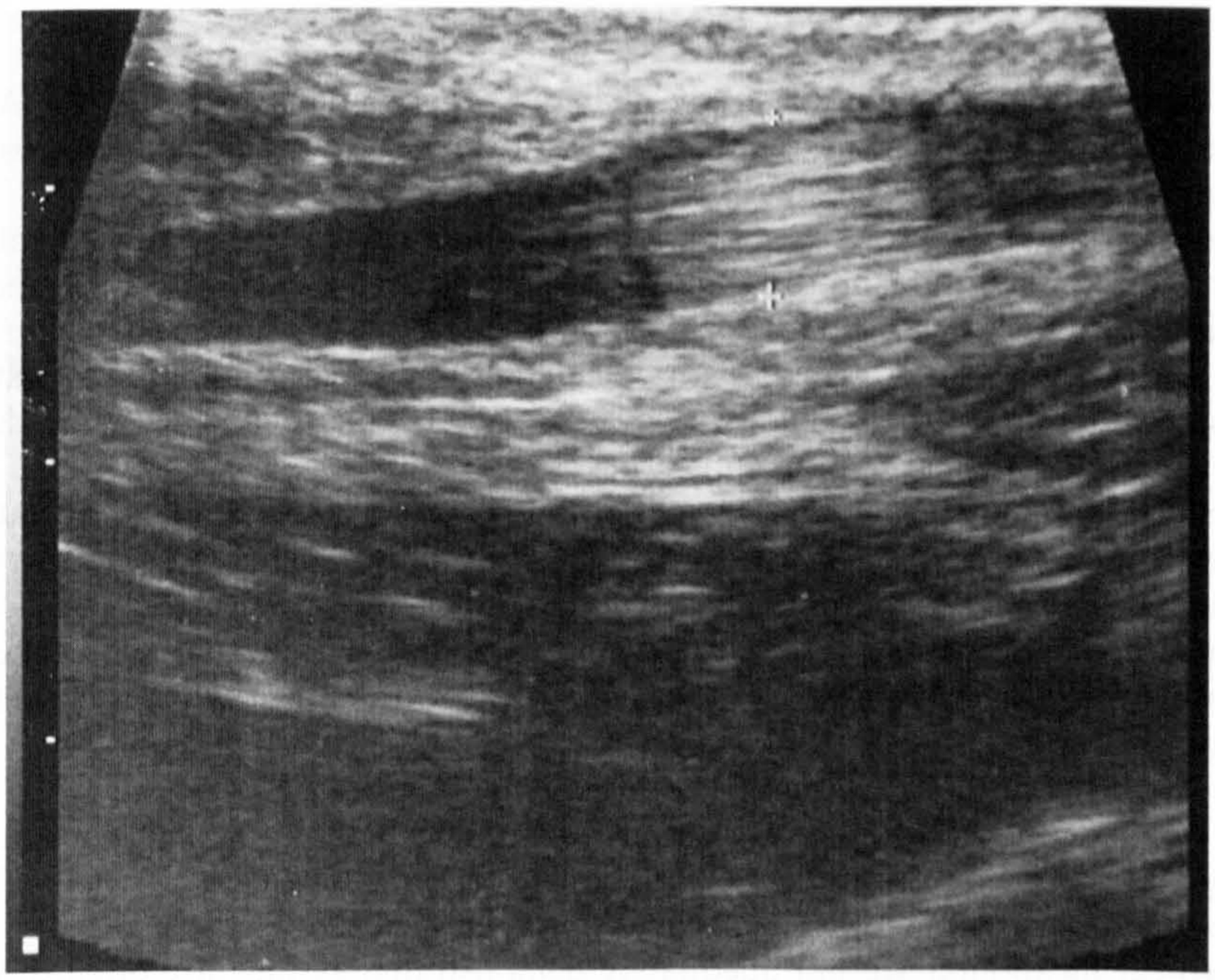


Figure 13. Longitudinal section: anterior deviation.

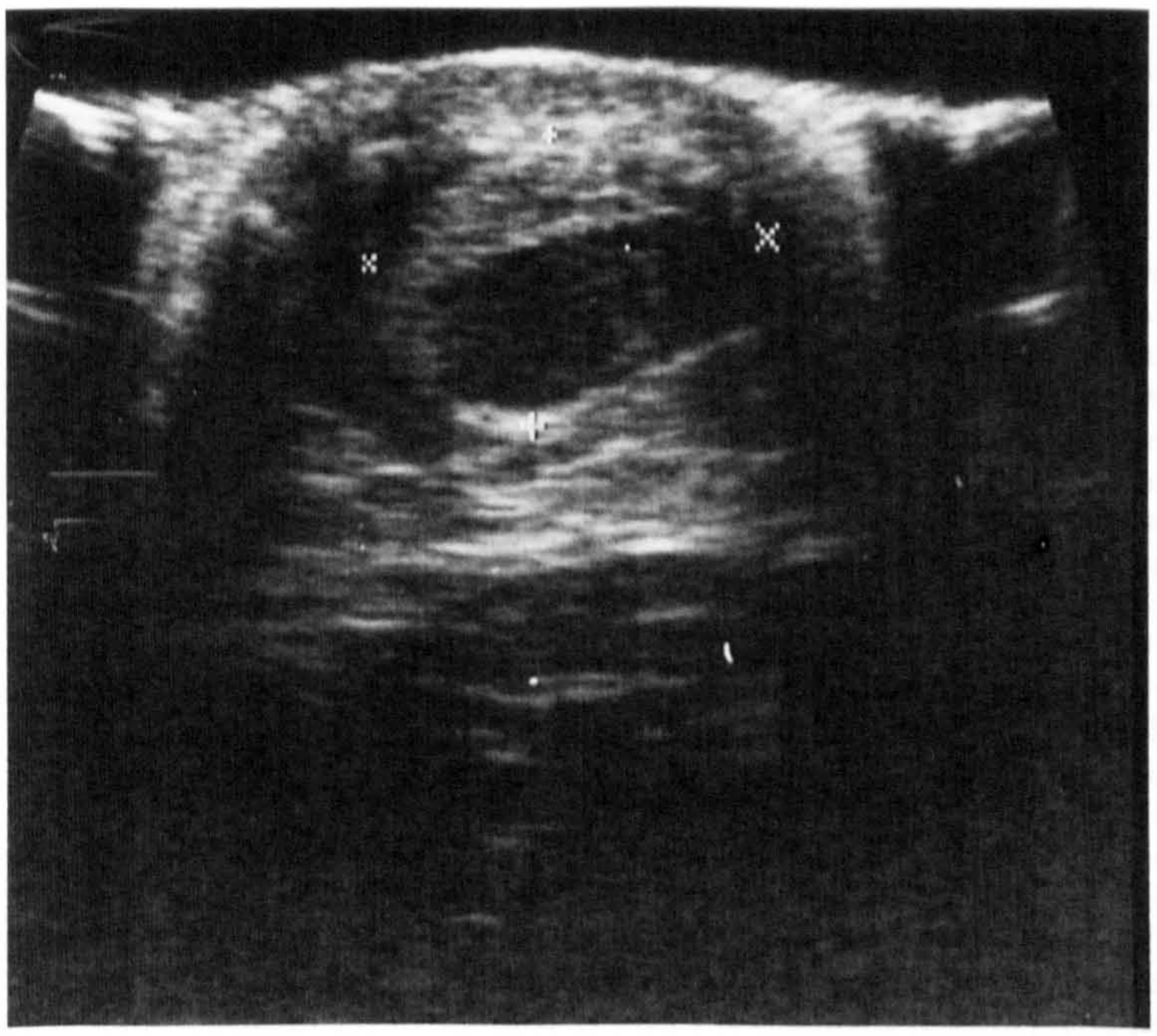


Figure 14. Grade 3 partial rupture: transverse section.

CONCLUSION

It has become clear through this study, that the surgical management of the Achilles tendon presenting chronic pathology, does not always leave the patient symptom free and there is potential for similar cases to present in the future.

Magnetic resonance scanning is becoming more common and has the advantage of soft tissue discrimination, and the ability to evaluate both adjacent soft tissue and bony structures. However, ultrasound does have the distinct advantages of greater availability, the ability to perform dynamic examinations easily and at low cost. Any imaging of anatomy with pathology or post-surgical changes make diagnosis difficult, for as has been demonstrated the appearances can be diverse.

Several authors agree [17–21] that more often than not surgical management is the treatment of choice and diagnostic ultrasound can make a significant contribution to post-surgical assessment of the Achilles tendon, and can help to evaluate the success of a surgical procedure more accurately. It can also reduce the 'sit and wait' time when patients are subjected to further bouts of conservative treatment whilst they still have symptoms.

Soft tissue radiography has limited value for the following reasons

- the Achilles tendon can only be demonstrated adequately in the lateral projection
- only gross anatomy can be seen in relation to Kager's triangle
- intratendinous pathology e.g. fibrillar disintegration will not be visualized
- micro-calcification(s) are not adequately demonstrated as they are often of insufficient density to be visible.

Acknowledgements

The author would like to particularly thank Dr Greg Papas who assisted in the scanning of the subjects. Dr Cherian Thomas for his opinions and assistance and Mrs Pat Ball and Tina Wells of Chase Farm Hospitals Trust.

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APPENDIX FOUR

SUBJECT QUESTIONNAIRE

&

PATIENT CONSENT FORM

QUESTIONNAIRE

PERSONAL DETAILS

Subjects Name		Subject Group	A	B

Date of Initial Consultation	

Clinical History:

CLINICAL PROGRESS

The following set of statements relate to the progression of your achilles tendon condition ***SINCE*** the initial consultation.
(subjects with both tendons affected please indicate this by placing a right or left adjacent to your responses)

This section is divided into three sections:

1 - General condition

2 - Treatments received

3 - Level of training/activity

1: General condition

In your opinion, is your achilles tendon condition:

Better		Worse		Unchanged	

Please indicate your response with a tick.

If better or worse please briefly explain how it has changed under the following headings:

- Pain

- Stiffness

- General flexibility/movement

2: Treatment(s) received since initial consultation

Group A subjects only:

- Have you received any treatments for the condition?

Yes:	No:

- What are/were the treatments?

- How often are/were they prescribed/given?

- How would you describe the effects of the treatment(s)?:

- short term (immediately post treatment, one - two weeks)

- long term

Group B Subjects only:

Date of treatment: start:
finish:

- following your treatment how would you describe the effects of the treatment?

- short term (immediately post treatment, one - two weeks)

- long term

3: Level of training / activity

Please state the type, level and duration of training you currently undertake by responding to the following table. Please place a number in the appropriate box corresponding to the number of sessions undertaken per week and the level of intensity for the particular activity form the key below:

a = low level of effort

b = moderate level

c = high level of effort

FOR EXAMPLE

If you run 3 times a week at a moderate level place 3b in the running box.

I do not need a complete diary of your training for the last three months, rather an indication of how much stress/work your tendon will take.

Types of training/activity	Level of activity/duration
Running	
Cycling	
Swimming	
Weights	
Other	

Thank you for your time and co-operation. I will be in contact soon.

RESEARCH STUDY -

The Application of Micro-Current to the

Achilles Tendon Presenting with Pathology

PATIENT INFORMATION SHEET

The Purpose of the study and a brief description of the procedure to be carried out.

The main purpose of the study is to examine whether it is possible to improve healing in tendon injuries using a very small electric current.

If you agree to take part in the study your particular problem will be clinically assessed to establish whether it is consistent with the study's protocol.

Willing and suitable subjects will then be randomly selected to receive either only the standard treatment available or, the new treatment regime involving the application of a small electrical current to the injured area. Neither you, nor your doctor or referring practitioner will know in advance which treatment protocol you will be allocated.
Subjects undergoing both treatment schedules will be then monitored at three monthly intervals for a period of one year.

The new treatment will last for fifteen to thirty minutes daily for two weeks.
The levels of electricity are very small, you will therefore feel nothing when the electricity is being applied.
Subjects may cease involvement in the study at any time if they wish to do so.

David Chapman-Jones - Research Investigator

CONSENT FOR PARTICIPATION IN RESEARCH

To be completed by the research investigator

A patient has the legal right to grant or withhold consent prior to examination or treatment.

Patients should be given sufficient information, in a way they can understand, about the proposed treatment and the possible alternatives. Patients must be allowed to decide whether they agree to treatment. They may refuse or withdraw consent to treatment or investigation at any time.

The patients consent to treatment will be recorded on this form, (further guidance is given in HC(90)22(Guide to Consent for Examination or Treatment).

PATIENT DETAILS

Hospital No:

Surname:

First Names:

Date of Birth:

Referring Consultant/Practitioner:

TYPE OF INVESTIGATION/ TREATMENT

NON-INVASIVE MICRO-CURRENT APPLICATIONS

TO THE ACHILLES TENDON.

I confirm I have explained the investigation and treatment this research will entail and the options available if they do not wish to participate.

Signature: .....

Name:.....

Date:.....

PATIENTS: *PLEASE READ THIS CAREFULLY*

Consultant/Referring Practitioner:

Research Investigator: **David Chapman-Jones**

You have the right to refuse to participate in this research programme without this adversely affecting your care and treatment. It is the responsibility of the investigator and your consultant/referring practitioner to explain the investigation and treatment and what the alternatives are.

1. If there is anything you do not understand about the explanation or you would like further information, please ask.
2. Please check that all the information on the form is correct. Once you are happy with it please sign and date it.

I am the patient.

I agree to what is proposed and has been explained to me.

I understand the information that has been given to me concerning the investigation and treatment.

I therefore agree to take part in this study.

Signature of Patient:

.....

Surname:

.....

First Names:

.....

Address:

.....

.....

Date.....