STIFFNESS IN HUMAN JOINTS

by

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A Thesis submitted in fulfilment of the requirements of the
Degree of Doctor of Philosophy, University of Leeds.

September 1993

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ABSTRACT

Articular stiffness is an important symptom in most arthritic diseases and appears to be a useful marker of disease activity in rheumatoid arthritis. Attempts to obtain a reliable objective measure of articular stiffness span the last 30 years but a meaningful measure of this symptom remains elusive. A number of reasons have been suggested to explain the discrepancy between objective and subjective stiffness in arthritis and these can be summarised as: a semeiological confusion, aberrant mechano-receptor thresholds and concurrent muscle wasting. This thesis examines each of these hypotheses.

Some patients may confuse pain and stiffness or may wish to use other words to describe their joint symptoms. A questionnaire was developed which enabled patients to express their joint symptomatology using a wide range of descriptors. No differences were found between health professionals and patients in their definition of each of the descriptors. The questionnaire discriminated clearly between groups of patients with rheumatoid arthritis, ankylosing spondylitis and non-articular rheumatism.

Movement perception threshold was measured in the finger but it was found that subjects relied on cutaneous information. Vibration perception threshold was used as an alternative measure of mechano-receptor thresholds: no abnormalities were found in 50 patients with rheumatoid arthritis.

Muscle cross-sectional area was calculated from anthropometric data and the results compared with measurements obtained from computed tomographic scans. A significant decrease in forearm muscle cross-sectional area was found in rheumatoid

arthritis but the decrease was not sufficient to explain the reduction in grip strength observed, some of the variation being explained by deformity and pain in the joints. From this study it was possible to make a correction for muscle wasting in previously published stiffness data, revealing significant increases in metacarpo-phalangeal joint stiffness in rheumatoid arthritis. This result was confirmed in new data based on the resonant frequency of the wrist. Further data on the qualitative aspects of muscle were obtained by relating dynamic angular wrist stiffness to level of contraction of forearm muscles. Although arthritic subjects differed significantly from normals at maximum activation, when the results were expressed in terms of absolute grip strength no differences were found, suggesting inhibition of muscle activation in rheumatoid arthritis.

It is concluded that symptomatic stiffness is objectively quantifiable in arthritis providing measurements are made in relationship to the equilibrium position of the joint and providing a correction is made for muscle wasting.

List of Figures

List of Plates

SECTION 1

CHAPTER 1

INTRODUCTION

Stiffness is an important symptom in most arthritic diseases. As a symptom, it headed the list of the 1959 American Rheumatism Association diagnostic criteria for rheumatoid arthritis (Ropes et al, 1959) and it still takes pride of place in the new revised diagnostic criteria (Arnett et al, 1988). Stiffness, as measured by the duration of morning stiffness in minutes, appears to be a useful marker of disease activity. It is responsive to treatment with anti-inflammatory and disease-modifying drugs and correlates with laboratory indices of inflammation and other clinical indicators of disease activity (Rhind et al, 1987). Moreover, it is easy to understand why patients with rheumatoid arthritis feel stiff; the synovial proliferation and inflammation, the low viscosity synovial fluid, the periarticular oedema and the inflammation in other periarticular structures such as synovial sheaths could all cause pain and decreased compliance in the articular structures.

Not surprisingly engineers, familiar in their field with stiffness as a reflection of the physical properties of simple and complex materials, were keen to quantify this dimension in arthritic disease. Yet, not withstanding the ingenuity of the physical devices used to measure stiffness, until recently conflicting results have been obtained. More recently, measuring joint stiffness by appropriate devices in diseases in which stiffness is a prominent symptom, several studies have been unable to demonstrate any increase in the physical stiffness of joints (Yung et al, 1986, Helliwell et al, 1987, Walsh et al, 1989). Even the usefulness of the

symptom of stiffness is now questioned: duration of early morning stiffness has been found to be a poor discriminator between inflammatory and non-inflammatory conditions (Hazes et, 1993) and stiffness may be a synonym for pain (Rhind et al, 1987) relieved by simple analgesics (Emery et al, 1986).

This discrepancy between subjective and objective assessments could occur for several reasons (Helliwell, 1987). Firstly, it may be that the lay interpretation of the word stiff does not accord with the professional interpretation. In describing the symptoms in their joints, patients may be confusing pain with stiffness or may be referring to a limited range of movement. In fact, a wide variety of descriptors are used when patients are invited to give unaided descriptions of the sensations arising from their joints (Rhind et al, 1987). Secondly, it may be that the sensation of stiffness is real and yet the sensory information necessary for this perception, being a synthesis of signals from a number of peripheral mechano receptors in joint capsule, ligament and muscle, is somehow aberrant as a result of the chronic inflammatory state. Thirdly, muscle wasting associated with the rheumatic disease may be masking true increases in articular stiffness. If significant changes of opposite magnitude occur in different tissues all of which contribute to total joint stiffness then measured stiffness may remain unchanged or decreased. In rheumatoid arthritis there is significant muscle atrophy: subclinical polymyositis has been reported in up to 85% of patients (Steinberg and Wynn Parry, 1961), and grip strength is reduced in value to 25% of normal (Helliwell et al, 1987). It is difficult to say exactly what is the contribution of muscles and tendons to total torque in the joint in normals, but it has been shown that forearm muscles account for half the resistance to movement of the DIP joint in its mid-range (Barnett and Cobbold,

1969). The relative decrease in muscle contribution to total torque may well offset any increase seen in articular and periarticular structures. This idea was suggested originally by Wright and Plunkett (1966) and revived by the Durham group (Yung et al, 1986), but surprisingly they could find no evidence of a decrease in forearm muscle girth in their patients with rheumatoid arthritis.

The contents of this thesis pursue these themes. In Chapter 2, following a historical review of the measurement of joint stiffness, the results and conclusions of my DM thesis (The measurement of stiffness and strength in the rheumatic hand, Oxford University, 1987) will be presented together with suggestions for future research arising from that thesis. In Section II, Chapters 3-6, further experimental data will be presented. Since each of these chapters represents a new direction for investigation the structure of each chapter will include a concise survey of the literature, Methods, Results and Discussion. Chapter 3 reports an investigation into the semeiology of stiffness. Using a newly designed descriptive questionnaire two questions are explored. Firstly, do patients with arthritic disease share with health professionals the same concept of the word 'stiff'? Secondly, do patients with different forms of arthritis use different words, both in quantity and quality, to describe the sensations arising from their joints?

In Chapter 4 the results of experiments designed to measure mechanoreceptor thresholds are presented. The measurement of movement perception threshold is described using a modification of the Leeds microprocessor controlled arthrograph. Having obtained unreliable results using this technique, a study of vibration perception thresholds in rheumatoid arthritis is described.

Chapter 5 describes an investigation into the relationship between grip strength and forearm muscle cross-sectional area. Cross-sectional area is measured from forearm circumference, skin and subcutaneous thickness and from previously recorded bone dimensions. A close correlation between estimated and actual (from CT scan) cross-sectional areas is obtained. The relationship between anatomical cross-sectional area, grip and other variables in normal subjects and in rheumatoid arthritis is described.

An exploration of the relationship between grip, muscle cross-sectional area and wrist stiffness is presented in Chapter 6. Wrist stiffness in this case is determined by an indirect technique based on the resonant frequency of a perturbed structure - the hand grasping a strain-gauged dynamometer. These experiments permit the use of a correction factor (for muscle wasting) when comparing wrist stiffness in normals and in patients with arthritis.

Chapter 7 in Section III reviews the results of these new experimental data in the context of the preceding work and presents new information as a result of re-analysis of experimental data from the DM thesis. Finally, Chapter 8 includes Conclusions, Summary and suggestions for future research.

CHAPTER 2

THE MEASUREMENT OF JOINT STIFFNESS; SURVEY OF LITERATURE

Section A - The arthrographs

Metacarpo-phalangeal joints

Knee joint

Ankle joint

Hip joint

Elbow joint

Discussion

Section B - Indirect Measures of Joint Stiffness

Section C - DM Thesis

Stiffness in rheumatoid arthritis

Stiffness in other rheumatic diseases

Circadian variation

Serial changes in joint stiffness following:

Ibuprofen:

Intra-articular steroids:

Intravenous methyl prednisolone:

Physiotherapy:

Arthroplasty

Conclusions

Summary

Section A - the arthrographs

Introduction

An arthrograph is a device which measures passive resistance to imposed motion at a joint. Its purpose is to define the rheological properties of the tissues in and around the joint. A number of devices have been developed to measure joint stiffness in this manner, the most frequently studied joint being the second metacarpo-phalangeal (MCP) joint. Generally, sinusoidal wave forms are imposed at a frequency of 0.5-1 cycles per second with varying amplitudes of displacement (and therefore varying angular velocities). During these tests the patient is expected to sit or lie comfortably with the muscles around the joint completely relaxed. Surface or needle electro-myographic recordings show the muscles to remain silent during measurements, and experiments under anaesthesia have revealed no significant difference in stiffness values (Ingpen and Hume-Kendall, 1968, Helliwell, 1987).

Stiffness is measured in terms of elasticity, viscosity, inertia, friction, and plasticity. In practical terms the only significant contributions to total stiffness at rest come from elasticity and viscosity (Wright and Johns, 1960). Continuous measurement of resistive torque while imparting sinusoidal displacement produces a hysteresis loop that, for the purposes of analysis, can be divided into an elastic and a viscous component. In simple terms the slope of the loop (measured as either the peak-to-peak slope or a straight line fitted to the loop) represents the elastic torque and the area of the loop represents the work done when moving the joint. Sometimes the standard engineering concept of hysteresis is calculated: hysteresis is the ratio of the area of the loop to the area of a triangle fitted to the loop. The ratio is multiplied

by 100 and the hysteresis expressed as a percentage. (Fig 2.1)

It is important to measure the stiffness of a joint using the equilibrium position of the joint as a datum. The equilibrium position is the position a joint would assume if no gravitational or active muscle forces were present. Thus, in the equilibrium position, passive resistance elements acting across the joint are balanced. The equilibrium position is not the same as the neutral position which is the datum position from which displacement angles are measured. These have been standardised for all joints by the American Academy of Orthopaedic Surgeons (Heck et al, 1966). For the MCP joint the neutral position occurs when the proximal phalanx is in line with the metacarpal bone in both sagittal and coronal planes. The equilibrium position of the MCP joint varies from person to person but is about 20° flexion and 5° ulnar deviation from the neutral position.

Unless measurements are taken with reference to the equilibrium position, misleading data on joint stiffness may occur. This is illustrated in Figure 2.2 in which two rheologically identical static torque displacement curves are drawn. These curves are constructed, not by imposing sinusoidal wave-forms, but by successively moving the joint from position to position over the entire range of movement and measuring the static torque at each position in sequence. Since these are not dynamic measurements no hysteresis is apparent. The only difference between the two curves in Figure 2.2 is the point at which they intersect the displacement axis. It can be seen that over the mid-range of motion the relationship between the static torque and the angular displacement is linear but towards the limit of anatomical motion there is a sharp increase in the slope of the curve as a result

Figure 2.1

Typical hysteresis loop derived from the finger arthrograph.

Area of loop = A_1

Area XYZ = A_2

Slope of loop = XY

$(A_1/A_2) \times 100$ = hysteresis
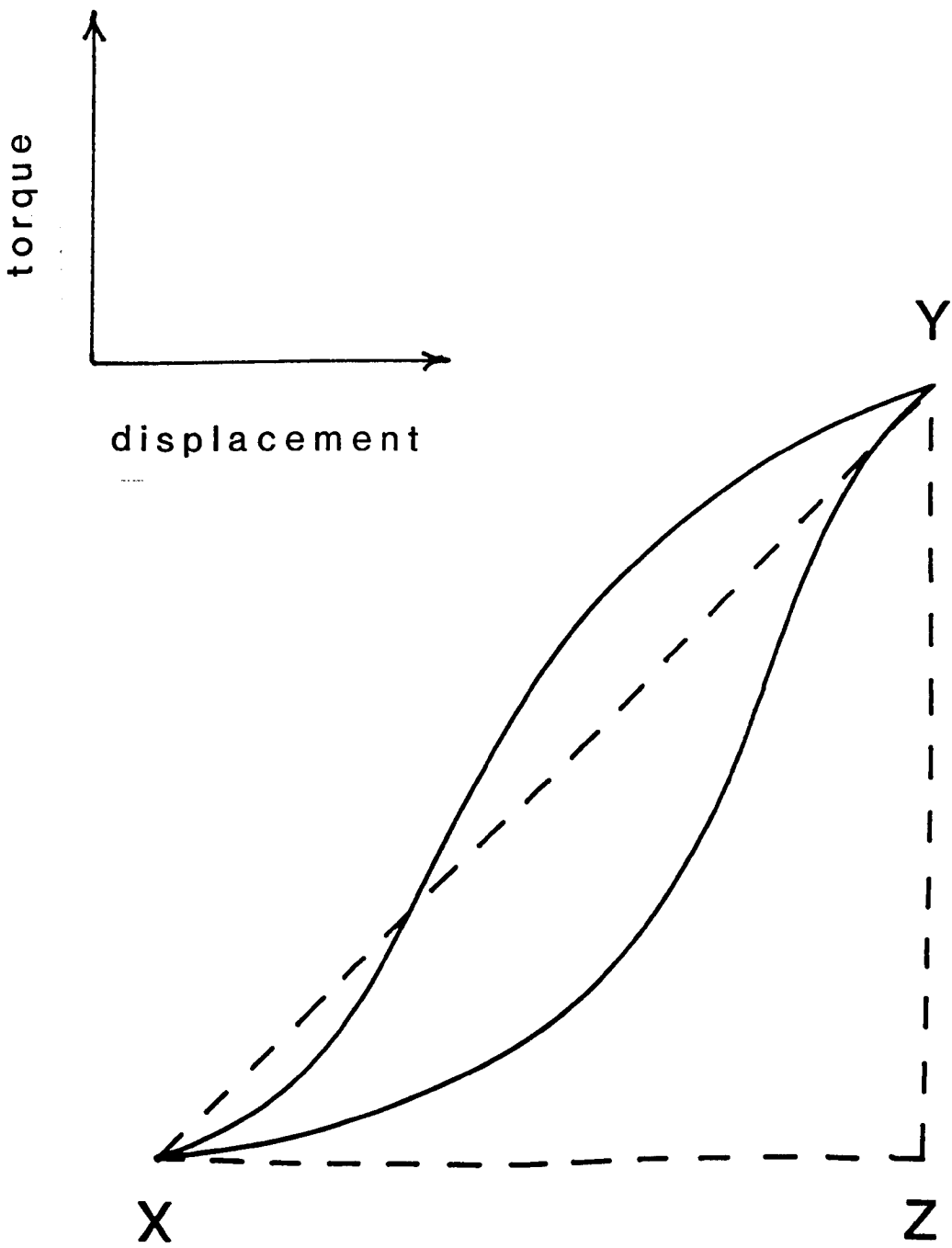
Figure 2.1

Figure 2.2

Two rheologically similar curves.

EP1 and EP2: equilibrium position of first and second curves respectively.

NP: neutral position.

If stiffness measurements are taken at a fixed range of angular displacement, such as AB, then different, and misleading, results are obtained.
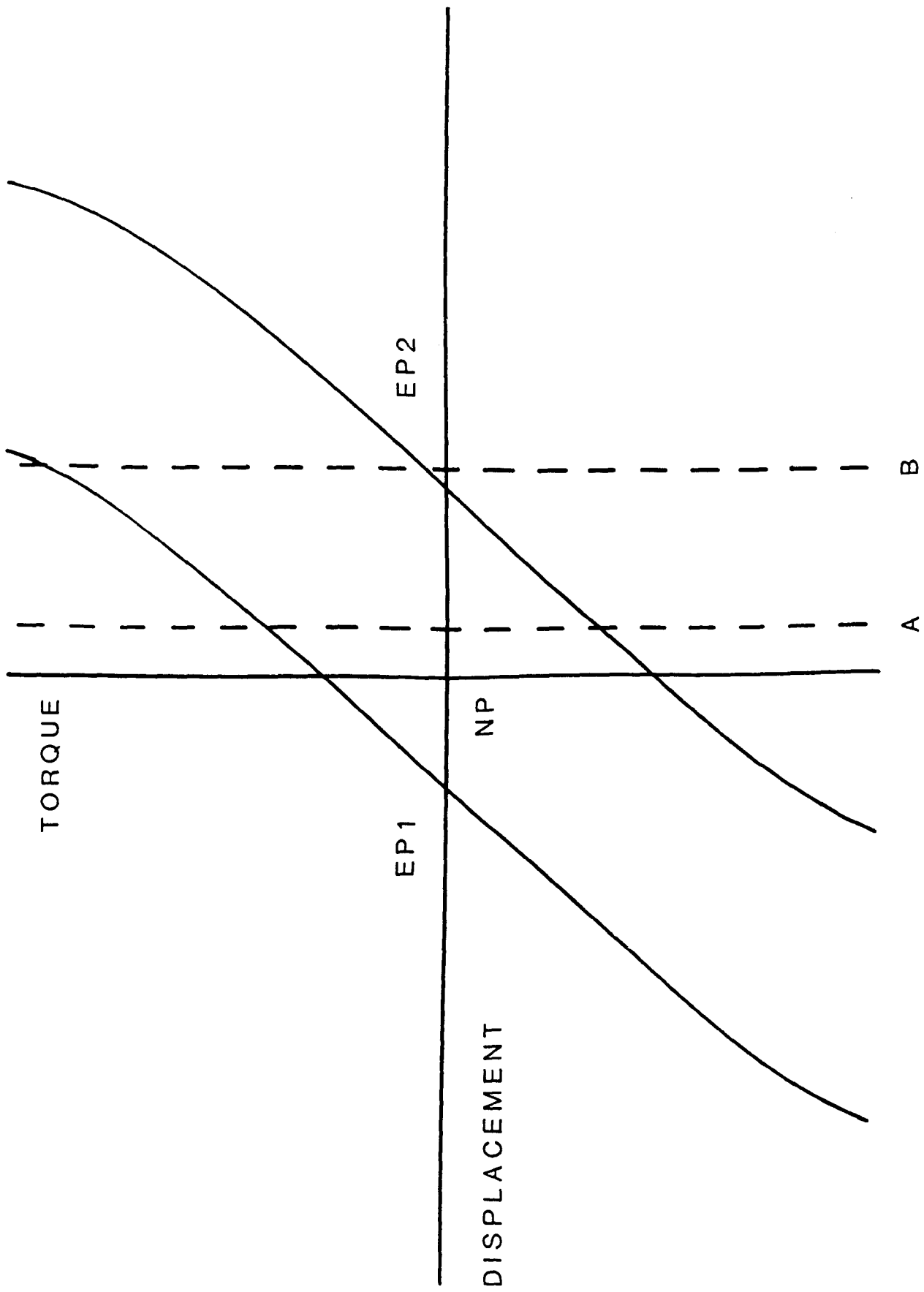
Figure 2.2

of incongruity of joint surfaces and taut restraining ligaments. If stiffness measurements are taken at a fixed range of angular displacement (such as A-B in Figure 2.2), then different, and misleading results could be obtained.

Stiffness at the metacarpo-phalangeal joint - flexion extension

Wright and Johns studied stiffness in the second MCP joint using a prototype arthrograph design (Wright and Johns, 1960a, Wright and Johns, 1960b, Wright and Johns, 1961, Johns and Wright 1964). Sinusoidal motion was applied to the joint by means of a heavy pendulum that rotated a shaft to which the finger was attached by a lever. The maximum peak-to-peak amplitude of motion imposed was 60° and frequencies varied from 0.05 to 1.0 Hz by altering the pendulum length. Torque was measured by strain gauges bonded to the lever and amplitude by a low torque potentiometer attached to the pendulum shaft. Results were presented on a dual beam cathode ray oscilloscope which from hysteresis loops could be photographed and measured. In later experiments these authors derived sinusoidal motion from a variable speed motor and mechanical coupling. The first few traces obtained were discarded, and thereafter the loops were reproducible. Analysis of the loops was laborious: measurement of the area of the loop was done either by planimetry or by weighing the loop after cutting it out of the photographic paper. These authors were able to show that in normal subjects elastic stiffness contributed 90% to total stiffness, viscous stiffness at maximum velocity 9%, and frictional stiffness less than 1%. Although no figures were quoted the initial experiments suggested that stiffness increased with age, cooling, venous occlusion and arterial occlusion. In six subjects with inactive rheumatoid arthritis five had increased stiffness and one subject with active rheumatoid arthritis had increased elastic stiffness. Maximum stiffness at full

flexion for 31 normal males (females) was 3.92 x 10^{-3} (2.60 x 10^{-3}) Nm/deg and at extension 5.10 x 10^{-3} (2.90 x 10^{-3}) Nm/deg. The elastic stiffness over the whole range (60°) for a normal subject was 4.68 x 10^{-3} Nm/deg, and for a subject with 'a badly damaged joint', 7.19 x 10^{-3} Nm/deg).

These articles provided the earliest objective assessment of joint stiffness and represent a major attempt to quantify symptomatology. However, the results obtained must be viewed with some caution partly because the mechanical system used may have led to inaccuracies and partly because of the small number of subjects able to be tested with an inevitably cumbersome technique. No attempt was made to define the equilibrium position of the joint and the range of motion imposed may well have encroached upon the limits of linear stiffness, particularly in the arthritic joints.

Backlund and Tiselius (1967) used an almost identical apparatus to that of Wright and Johns in measuring MCP stiffness in 16 patients with rheumatoid arthritis and 10 normal subjects. Over a 60 degree range they obtained a value of 0.35 x 10^{-3} Nm/deg at midpoint for normal females and 0.93 x 10^{-3} Nm/deg at midpoint for normal males. A single arthritic patient had a stiffness value of 2.16 x 10^{-3} Nm/deg.

Further studies at the MCP joint in flexion/extension were suspended for a number of years while other joints were measured. In 1981 a new version of the flexion/extension finger arthrograph was devised (Jobbins et al. 1981) but this noisy, rather cumbersome apparatus had no facility for mathematical analysis of traces, differentiation between subjects relying on visual inspection. The first micro-

processor controlled finger arthrograph was developed by the Durham group (Unsworth et al, 1981, Unsworth et al, 1982, Yung et al, 1984, Yung et al, 1986). Unsworth altered finger arthrograph design by measuring the index finger in flexion/extension in the horizontal plane. The patient grasps a mahogany post, approximately 2 inches in diameter, between the thumb, middle, ring and little fingers, thus leaving the index finger free. The motor of the arthrograph is linked by a scotch yoke mechanism to the drive arm which travels to a point above the patient's finger where it is attached to the proximal phalanx. This was the first arthrograph to provide instantaneous analysis of hysteresis loop and to measure and define stiffness in relation to the equilibrium point of the joint. Because of the comparative ease with which this test could be conducted a large number of normal subjects and patients with arthritis were tested in addition to studies on circadian variation and the effect of physiotherapy. Patients with rheumatoid arthritis appeared to be no stiffer than normal controls as measured by the mid-position torque at fixed angular displacements from the equilibrium position. These torques were similar to those obtained by Backlund and Tiselius: normal male mid-position torque at 20° flexion 15.3 x 10^{-3} Nm, normal female at 20° flexion 13.9 x 10^{-3} Nm, arthritic male at 20° flexion 17.2 x 10^{-3} Nm and arthritic female at 20° flexion 16.1 x 10^{-3} Nm.

Byers (1985) used a motor driven finger arthrograph very similar to the one originally described by Wright and Johns using a fixed speed, fixed displacement device measuring torque at peak flexion and at peak extension. She was interested in the effect of exercise on morning stiffness and mobility in patients with rheumatoid arthritis and did not study any normal subjects. The angular stiffness

she obtained for 30 patients with rheumatoid arthritis was similar to that obtained by Wright and Johns: 10.40 x 10^{-3} Nm/deg.

In a major break from tradition Howe et al (1985) measured stiffness at the third MCP joint using side to side motion (strictly speaking this is abduction/abduction). Another original feature was the use of a printed DC servo motor with integral tachometer feedback and amplifier obviating the need for scotch yoke mechanical linkage since it is possible to move the motor armature in phase with an electrical waveform fed into the amplifier. On line micro-processor controlled test characteristics and analysis are provided. The standard test consists of a sinusoidal displacement of 8° peak-to-peak amplitude and a frequency of 0.2 Hz: the test is carried out around the equilibrium position of the joint. Since the test was easy and quick to perform a large number of normal subjects were measured: angular stiffness for males was found to be 10.4 x 10^{-3} Nm/deg and for females 5.9 x 10^{-3} Nm/deg. An important feature of this paper was the clear relationship between an anthropometric measurement (finger circumference) and stiffness variables, this dimension explaining variability between males, females and the young and old. In a later study, Helliwell et al (1988a) measured elastic and viscous torques in 135 patients with rheumatoid arthritis and found no difference between these measurements and those for the normal group when corrected for finger circumference.

The various measures of stiffness obtained at the MCP joint are collated and compared in Table 2.1. The Table has been divided into two parts because of the

variation in presentation of results. However, some valid comparisons can be made.

1. Mid-range stiffness in the third MCP joint in abduction/abduction is probably no different to mid-range stiffness in flexion/extension in the second MCP joint.

2. The greater the angular displacement the higher the peak torques recorded. It must be noted that both Wright and Johns (1961) and Unsworth et al (1984) emphasised that they were measuring peak torques within the central linear part of the torque displacement curve.

3. Where the equilibrium position is used as a datum there is no difference in stiffness between patients with rheumatoid arthritis and normal controls.

4. It is difficult to explain the differing results obtained by Wright and Johns (1961) and Backlund and Tiselius (1967). These authors were using the same device with minor modifications and the same angular displacement.

5. The results of Yung et al (1986) are of a similar magnitude to those obtained by Backlund and Tiselius (1967): both groups found stiffness in normal subjects to be less than that found in normal subjects by other groups. The reason for this is not clear, although it must be remembered that some of the figures in Table 2.1 are derived, and it may be that direct comparison is invalid.

Table 2.1 Summary of previous arthrographs using McP joint.

+ F/E = Flexion/extension
A/A = Abduction/abduction

* 0 = Equilibrium position not used as a datum
1 = Equilibrium position used as reference datum

AUTHORS	END POINT STIFFNESS x 10^{-3} Nm		MID RANGE STIFFNESS x 10^{-3} Nm/deg		DIRECTION	EQUILIBRIUM POSITION
	NORMAL	RHEUMATOID ARTHRITIS	NORMAL	RHEUMATOID ARTHRITIS		
WRIGHT & JOHNS (1961)			4.68 (60 deg)	7.19 (60 deg)	F/E	0
BACKLUND & TISELIUS (1967)			F: 0.35 M: 0.93	2.16	F/E	0
YUNG, UNSWORTH, HASLOCK (1986)	F: 13.9 M: 15.3 (20 deg flexion)	F: 16.1 M: 17.2 (20 deg flexion)			F/E	1
BYERS (1985)				10.40 (60 deg)	F/E	0
HOWE, THOMPSON, WRIGHT (1985)			F: 5.9 M: 10.4 (8 deg.)		A/A	1
HELLIWELL, HOWE, WRIGHT (1988a)				7.3 (8 deg)	A/A	1

Knee joint stiffness

In the late 1960's an attempt was made to measure knee stiffness with the lower leg supported in a vertical position (Goddard et al, 1969, Such et al, 1975). Again, sinusoidal motion was applied to the joint by an electrical motor applied through a scotch yoke mechanism. Because of problems with the size and weight of the leg, displacement cycles extending from full flexion to full extension were not obtained: rather small amplitude cycles were recorded at different angular displacements. Angular stiffness over 22° about a knee flexion angle of 90° was 159×10^{-3} Nm/deg for males and 91×10^{-3} Nm/deg for females. However, it became apparent that the major problem with the vertically driven arthrograph was the counter balance system necessary to offset the mass of the lower limb. Nevertheless it was suggested that compared to normal individuals patients with rheumatoid arthritis had increased stiffness. It was interesting that Such et al related elastic and viscous stiffness to age, thigh circumference and sex, but made no attempt to control for these variables.

In an attempt to overcome the mass of the lower limb, a horizontally driven knee arthrograph was designed (Thompson, 1978 and Thompson et al, 1978). Multiple small hysteresis loops were measured at varying angular displacements and the equilibrium point of the knee joint was defined from the line of elastic resistance through the centroids of the individual hysteresis loops. Elastic stiffness was measured as the sum of the mid-position torques and viscous stiffness as the sum of the areas of the individual hysteresis loops. In rheumatoid arthritis both elastic and viscous stiffness were decreased compared to normal subjects. However, a major drawback with this device was the awkward position patients had to adopt resulting in a prolonged uncomfortable posture during the test. Stiffness at mid-

range for normal males was given as 65 x 10^{-3} Nm/deg and for normal females 44 x 10^{-3} Nm/deg. Thompson was also able to adapt his device for measuring elbow stiffness and, in one normal subject, measured an angular stiffness of 25 x 10^{-3} Nm/deg over a 70° range.

Despite the aforementioned theoretical problems with the vertical knee arthrograph, a similar model to the one used by Such et al was recently employed in a study of knee stiffness before and after immobilisation following knee surgery (Heerkens, 1986, Heerkens et al, 1986, Heerkens et al, 1987). These studies involved mainly young adults and confirmed previous observations that stiffness measurements correlate with anthropometric data such as leg length, thigh circumference and body weight. The differences found between males and females could be explained on this basis. These authors found that the effect of immobilisation on the knee was a change in the equilibrium position towards extension, an increase in elastic stiffness which returned to normal within a month and a marked decrease in viscous stiffness which took much longer to return to normal. They attributed these changes to wasting within the thigh muscles following immobilisation.

More recently torque/displacement at the knee has been measured as a function of passive hamstring compliance (Gajdosik et al, 1990). The normal subjects in this study were measured with the leg in the horizontal position but a precise description of passive mechanical properties of the system was not carried out. Stiffness, derived from the published curves, was 405 Nm/deg for males, 211 Nm/deg for females. These figures do not represent true mid-range stiffness but the angles from which they were derived, between 50° and 70° knee flexion, are not so far removed

from the usual equilibrium position of the joint.

Ankle joint

Siegler and Moskowitz (1984) measured the passive and active components of the internal moment around the ankle joint during ambulation. These authors were interested in the relative contribution of passive and active components and established that in normal walking the active component far exceeded the passive component (113 Nm active 6.7 Nm passive). Hysteresis loops were obtained and from these an approximate value of stiffness for the ankle joint about the neutral position was 200×10^{-3} Nm/deg.

More extensive measurements have been taken by a group in Montreal (Weiss et al, 1986, Kearney et al, 1990, Weiss et al, 1990). This group encased the foot in a customised polyurethane cast and measured viscous and elastic stiffness by exerting a series of random, small (maximum peak-to-peak amplitude 5.5°) perturbations about a predefined ankle position: ten such measurements were made in all separated by about 6°. These authors allowed creep to take place before testing. In normal subjects they found total range of motion of 56.7°, an equilibrium position of 30.8° plantar flexion from the neutral and an elastic torque of 279×10^{-3} Nm/deg at the equilibrium position. The viscous torque at the equilibrium position, 3.49×10^{-3} Nm seconds/deg was much less than the elastic torque. These authors measured peak and range torques of 1361×10^{-3} Nm at maximum plantar flexion and 2531×10^{-3} Nm at maximum dorsiflexion. Although not discussed in their papers it is possible to relate their stiffness measurements to body weight of their subjects, a correlation coefficient of 0.7 being obtained. No subjects with arthritis were measured.

Hip joint

Yoon and Mansour (1982) have measured the passive elastic moment at the hip with the subject lying on the side and the knee extended. They found the neutral position to be about 12° flexion and over the range of movement between 5° extension to 65° flexion, the approximate stiffness during the linear mid-phase was 454 x 10^{-3}Nm/deg.

Elbow joint

Hayes and Hatze (1977) have measured the passive viscoelastic properties of the structures spanning the elbow. In 3 normal subjects they plotted torque/displacement curves of the elbow at speeds of less than 3°per second. As with other joints they found a linear mid-phase with a steep rise in torque towards the extreme ranges of movement. The slope of the linear mid-range was 24.4 x 10^{-3}Nm/deg.

MacKay et al (1986) using a device called a 'manipulandum' - essentially a horizontal torque-driven arthrograph - determined the slope of the mid-range at the elbow to be 26.53 x 10^{-3} Nm/deg. the viscosity about 9% of this figure.

Discussion

Table 2.2 presents the measured and derived stiffness from a range of human joints and these are illustrated in Figure 2.3. Generally speaking there is an increase in mid-range elastic stiffness with joint size, the possible exception to this rule being the knee and ankle joints. The wide variation in stiffness for the knee joint is probably explained by the different methodology used: of the two horizontal

Table 2.2

COMPARISON OF MID-RANGE ANGULAR STIFFNESS BY JOINT

* measured at 90° flexion

Authors	Angular Stiffness at Mid-range (x 10^{-3}, Nm/deg)	Joint
Helliwell, Howe and Wright (1987)	M 10.4 F 5.9	McP3
Such 1972 *	M 159 F 91	Knee
Thompson, Wright and Dowson (1978)	M 72 F 44	
Gajdosik et al (1990)	M 405 F 211	
Hayes and Hatze (1977)	24.4	Elbow
Thompson (1978)	25.0	
McKay et al (1986)	26.5	
Seigler and Moskowitz (1984)	230	Ankle
Weiss, Kearney and Hunter (1986)	279	
Yoon and Mansour (1982)	454	Hip

Figure 2.3

Histogram of stiffness in humans measured in different joints, (derived from Table 2.2).

Figure 2.3

Axis labels: logK (Nm/deg x 10-3); categories: McP, Elbow, Ankle, Knee, Hip; values 0, 0.5, 1, 1.5, 2, 2.5, 3

measurements the figures recorded by Thompson (1978) are more reliable since Gajdosik et al (1990) used a hand held dynamometer to measure torque and did not define the equilibrium position of the joint.

In terms of joint circumference alone we would expect successive increments in stiffness from MCP to hip joint and, generally speaking, with increasing joint circumference there is an increase in the number and size of muscles acting across the joint. However, mid-range elastic stiffness will depend on a number of factors including absolute joint size, capsular and restraining ligaments, and periarticular structures, particularly the surrounding muscles. The ankle joint complex possesses a number of tough inter-osseous ligaments which may increase the stiffness of this joint compared with the knee.

What conclusions can we draw from the comparative studies of joint stiffness in normal and rheumatoid arthritis subjects? There is a clear difference between the results of earlier studies and later studies and this is illustrated in Table 2.1. As has already been discussed it is clear that some of these differences result from differences in arthrographic design and analysis of results. Unless stiffness measurements are made with reference to the equilibrium position of the joint misleading results may be obtained. It is clear from earlier studies that the equilibrium position was not defined and this may have led to erroneous results. Close reading of the earlier papers by Wright and Johns and Backlund and Tiselius, however, reveals that measurements were probably taken around a datum that was not very far from the equilibrium point for this joint.

A number of other factors may be responsible for the discrepancy:

1. Because of wide inter-individual variability it is important to study sufficient numbers of patients. This criticism may be particularly applied to the work of Wright and Johns (1961) and Backlund and Tiselius (1967).

2. Most studies have shown there are age and sex differences in stiffness variables (the sex difference can be seen in Table 2.2). It is not clear whether this is due to intrinsic differences in the tissues, for example collagen, or whether it is directly related to the different anthropometric characteristics of men and women. The studies by Thompson (1978) and by Howe et al (1985) suggest the latter. This will be discussed further in Chapters 5 and 6.

3. There is symptomatic circadian variation in stiffness and pain (Bellamy et al, 1991). Therefore it is important to standardise the time of day the measurements are made. Stiffness is most prominent in the early morning in arthritis and one study has demonstrated this phenomenon in normal people using an arthrograph (Yung et al, 1984). In a further study patients with longstanding rheumatoid arthritis did not show such variation (Helliwell et al, 1986).

4. Since anti-inflammatory drugs relieve the symptom of stiffness it is important to take any measurements when the effect of these drugs may be minimal or at least to make comparative measurements at a similar time after drug administration.

5. Rheumatoid arthritis is in general a chronic progressive disease of the joints. At presentation the joints are swollen with an acute inflammatory synovitis. As the disease progresses cartilage and bone erosion may occur. The capsule

and periarticular ligaments of the joint become weakened. The disease may be arrested at any time leading to healing by fibrosis and secondary osteoarthritis. Unchecked progression may lead to a dislocated, destroyed and useless articulation. Periarticular structures such as muscles may waste markedly in acute arthritis but may recover some bulk during rehabilitation. Clearly the physical properties of the joint tissues will vary according to the pathological stage of the disease and any attempt to measure joint stiffness must therefore take this spectrum of pathology into account. The study by Helliwell et al (1988) showed that patients with acute active rheumatoid arthritis differed from subjects with inactive rheumatoid arthritis and subjects with dislocated joints (see later in this chapter). It may, therefore, be that discrepancies found between authors are due to measurements being taken on different sub-populations of patients.

6. Earlier arthrographs used relatively large angular displacements to measure joint stiffness. If the imposed angular displacements encroached on the limits of joint range then, because of the non-linearity of the torque/ displacement curve at these extremes, a misleading impression of mid-range elastic torque would be obtained (see Figure 2.2). This is particularly liable to occur in rheumatoid arthritis in which it is likely that the range of movement over which the torque/displacement curve is linear is diminished compared to normals (Helliwell, 1987).

Section B - Indirect measures of joint stiffness

Some idea of elastic stiffness in the joint can be obtained either by applying a standard force and measuring displacement or by applying a standard displacement and measuring the resistive torque. Scott (1960) measured the diurnal variation in displacement by applying a standard extension force to the second MCP joint in normals and in rheumatoid arthritis. Loebl (1972) applied angular displacement in abduction/abduction to the index and middle fingers with the MCP joint held at 90° flexion. With this technique he was able to show age related and sex differences. Dorso-volar movement in response to a hand-held pressure sensitive rod that incorporated a gravity goniometer has also been investigated (Wagner and Drescher, 1984). Alternatively, Rasker et al (1986) applied a standard displacement to the finger over a period of 2 seconds and then measured the resistive torque. Although this group was interested in the influence of weather on stiffness they demonstrated an increase in stiffness in rheumatoid arthritis, although a wide scatter of results was obtained.

All these methods fail to give a true and comparable indication of joint stiffness since measurements were not made in reference to the equilibrium position of the joint. Furthermore, even within-subject longitudinal measurements may be misleading because changes in the equilibrium position (without any change in joint stiffness) may occur.

An alternative indirect measure of joint stiffness was devised by Hickling et al (1967). Measurement was made by enclosing the index finger in a sleeve to which was attached a weighted lever approximately 30cms long. The time taken for the

tip of the lever to fall through a pre-defined arc was measured, either by the use of a photo-electric cell (Hickling et al, 1967), or by an electronic timer triggered as the finger commenced its fall (Ingpen and Hume-Kendall, 1968, Ingpen, 1968). Some attempt was made to standardise the starting position with the wrist dorsiflexed and the MCP joint flexed so that the finger started in the horizontal plane, but no reference was made to the equilibrium position of the joint. These authors provided a simple, inexpensive, portable and acceptable method with which they could assess many patients with relative ease. They found the fall time to be constant irrespective of age, sex or body size and 97% of normal observations were between 70-82 milliseconds. In rheumatoid arthritis, although results were rather vaguely stated ('over 200 readings obtained') fall times varied from normal to 120 milliseconds and treatment with anti-inflammatory drugs and intra-articular steroid reduced fall times significantly.

From the rheological point of view it is hard to know exactly what Ingpen, Hume-Kendall and Hickling were measuring. The displacement is provided by the effect of gravity on the finger and attached lever. Since viscous stiffness is velocity dependent, increased fall times (which were observed in patients with rheumatoid arthritis) should reflect increased viscous stiffness in the joint. The contribution of elastic forces to the fall time is less clear, particularly since the relationship of the finger at the start of the fall to the equilibrium position of the joint was not known. We have designed a device similar to that of Ingpen and Hume-Kendall (Jolly and Malone, 1987). In young normal subjects the fall time over an arc of 10° was between 66 and 76 milliseconds, very similar to that obtained by Ingpen and Hume-Kendall. Furthermore, Joy and Malone could find no relationship between the

physical properties of the finger (length, volume and circumference) and fall time. However, we found that patients with rheumatoid arthritis were difficult to accommodate in the device despite making modifications to allow for joint disease.

Walsh has been interested in measuring the mechanical properties of the wrist as a reflection of forearm muscle physiology (Lakie et al, 1979a, Lakie et al, 1979b, Lakie et al, 1979c, Lakie et al, 1984 and Walsh et al, 1989). The wrist is held horizontally halfway between pronation and supination and oscillated in flexion/ extension over small amplitudes of displacement. This group used a printed motor similar to that used by Howe et al (1985): in this case the movement of the wrist is governed by the strength and frequency of current entering the printed motor: the response in this case being the movement at the wrist rather than the torque. For a given current (and hence torque) the amplitude of displacement has a maximum value - the resonant frequency. By changing the strength of the current and sweeping through the frequencies it is possible to plot a graph of resonant frequency against torque. Resonant frequency was shown to be higher at lower torques thus demonstrating increased stiffness with smaller pertabations, but following transient larger displacements this disappeared, an example of thixotropy. In a series of measurements on patients with long-standing rheumatoid arthritis they found a lower resonant frequency for a given applied torque (i.e. decreased stiffness) and the thixotropic effect was found to be similar in both normal subjects and patients.

An ingenious indirect method of measuring joint stiffness was devised in a series of experiments by Barnett and Cobbold (Barnett and Cobbold, 1962, Barnett and

Cobbold, 1968, Barnett and Cobbold, 1969, Barnett 1971). These authors, one an anatomist, employed the anatomical quirk in which the effect of the long flexor profundus tendon on the distal phalangeal joint can be eliminated by flexion of the proximal interphalangeal joint to 90° keeping the metacarpo- phalangeal joint in the neutral position. Alternatively extending both distal interphalangeal and proximal interphalangeal joints while flexing the metacarpo-phalangeal joint to 90° allows full control of the distal phalanx. Their experimental arrangement required the subject to sit with the hand supinated and the middle finger flexed at either the proximal or metacarpo-phalangeal joint. A pendulum was attached to the finger via a loop of metal and the rate of decay of the swinging pendulum was used to calculate the joint stiffness ('coefficient of resistance'). These authors were able to record decreases in the rate of decay (and hence increase 'stiffness') with age. By engaging the flexor profundus tendon the measured coefficient of resistance doubled. This device provides an indirect measure of viscous and frictional torques at the DIP joint. Since the energy expended in stretching the elastic element is recovered on correcting the deformation the rate of decay of the swinging pendulum would be independent of elastic torque. No experiments were performed in subjects with rheumatic disease.

Section C - DM Thesis 'The measurement of stiffness and strength in the rheumatic hand'

With the development of the horizontal finger arthrograph Helliwell (1987) was able to measure MCP joint stiffness in a large number of patients both with rheumatoid arthritis and other rheumatic diseases and to correlate these changes with subjective symptoms of stiffness in situations where these symptoms would be expected to

change. Table 2.3, taken from that thesis, details the number of patients with rheumatoid arthritis and their stiffness variables compared to the normal group derived by Howe et al, 1985. It was felt that an important step in measuring joint stiffness in rheumatoid arthritis was to define the state of the disease locally. Since there is a linear relationship between stiffness and finger circumference disease sub-groups were compared using finger circumference as a co-variant and these results, again reproduced from the thesis, are presented in Table 2.4. and are illustrated in Figure 2.4. Summarising the results:

1.   In rheumatoid arthritis although the relationship between mean slope, area and hysteresis with finger circumference was not as good as for the normal group, none of the differences were statistically significant.

2.   Clear differences emerged between the patient sub-groups after adjusting the mean for finger circumference. The inactive RA group was stiffer than normal. The active RA group showed no difference in elastic stiffness but a reduction in viscous stiffness. The groups containing patients with subluxed joints and arthroplasties appeared similar, both demonstrating a decrease in mean slope, area and hysteresis.

3.   The observations were explained in the following way. In some respects it was felt that the measured stiffness reflected the pathological changes at the joint. Active rheumatoid arthritis causes swelling and laxity in both capsule and periarticular ligaments, whereas inactive rheumatoid arthritis results in fibrosis and scar tissue. Subluxation of the joint results in complete dissolution of the articular structure and periarticular ligaments.

4.   To reconcile the discordance between objective and subjective stiffness in active rheumatoid arthritis it was suggested that in relative terms patients

Table 2.3

COMPARISON OF PATIENT GROUPS WITH NORMALS: (after Helliwell, 1987)

* $p < 0.001$: + $p < 0.01$; # $p < 0.05$

	MEAN SLOPE vs FINGER CIRCUMFERENCE				HYSTERESIS vs FINGER CIRCUMFERENCE			
	F (slope)	Adjusted Variables (x 10^{-3} Nm/deg)			F (slope)	Adjusted Variables %		
		Disease	Normal	t		Disease	Normal	t
All RA	4.00+	7.6	7.7	0.03	2.88	32.4	36.3	2.62+
Active RA	2.14	7.5	7.9	0.6	1.32	31.5	36.2	2.64+
Inactive RA	0.02	10.9	7.7	3.5*	1.5	31.5	36.6	2.17#
Subluxed McP	2.16	6.3	7.8	1.60	1.4	33.1	36.3	1.44
Ankylosing Spondylitis	3.34	10.5	8.2	2.6+	2.2	32.3	35.9	1.53
Hypermobility	0.89	6.8	7.5	0.6	0.01	34.9	36.7	0.7

Table 2.4

SUMMARY OF STIFFNESS VARIABLES IN RHEUMATOID ARTHRITIS (MEAN VALUES) - NORMALS GIVEN FOR COMPARISON
(after Helliwell, 1987)

	n	Finger Circum-ference (mm)	Mean Slope x 10^{-3} Nm/deg	Area x 10^4	Hysteresis %	Equilibrium Position (deg. ulnar deviation)
All RA	135	57.3	7.3	831	32.6	5.6
Active RA	66	58.3	7.3	800	31.8	3.8
Inactive RA	32	56.3	9.7	1089	32.4	3.4
Subluxed McP	32	56.5	5.3	668	33.9	12
Arthroplasty	5	56.8	5.1	653	35.0	5
Normals	128	59.5	8.2	1180	36.0	3.2

Figure 2.4

Individual stiffness values for patients with rheumatoid arthritis, superimposed on normal regression lines (after Helliwell, 1987)
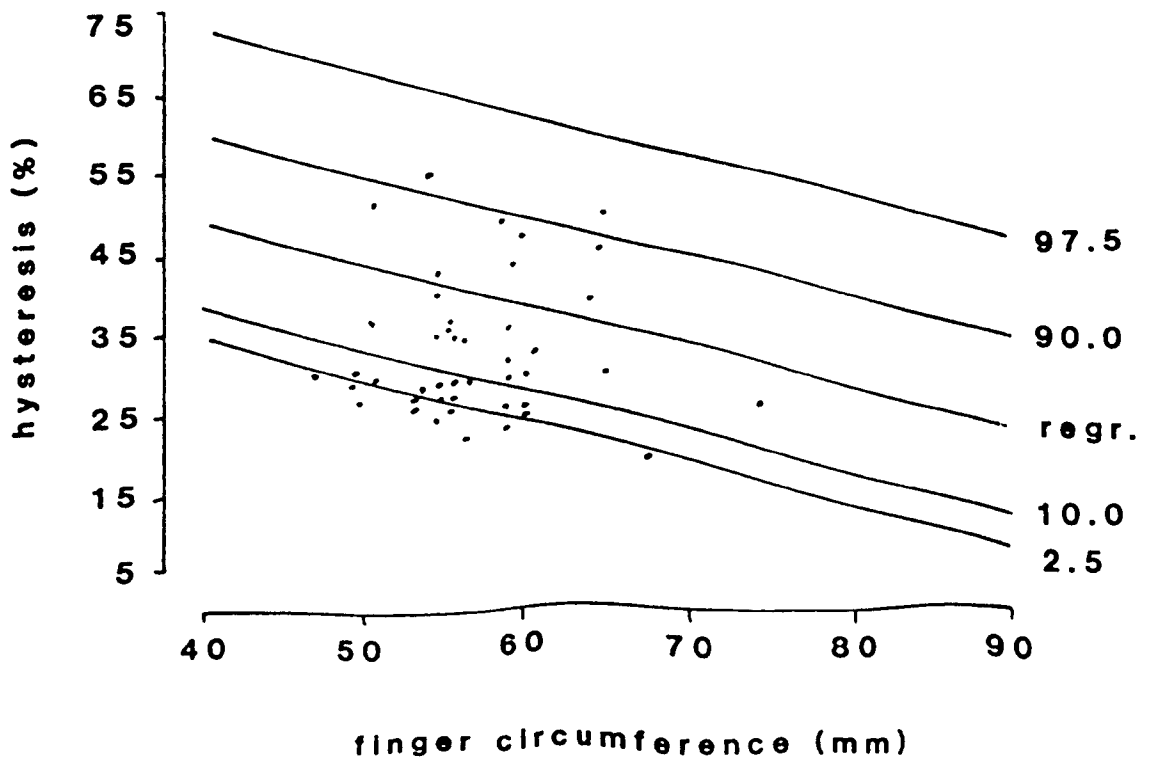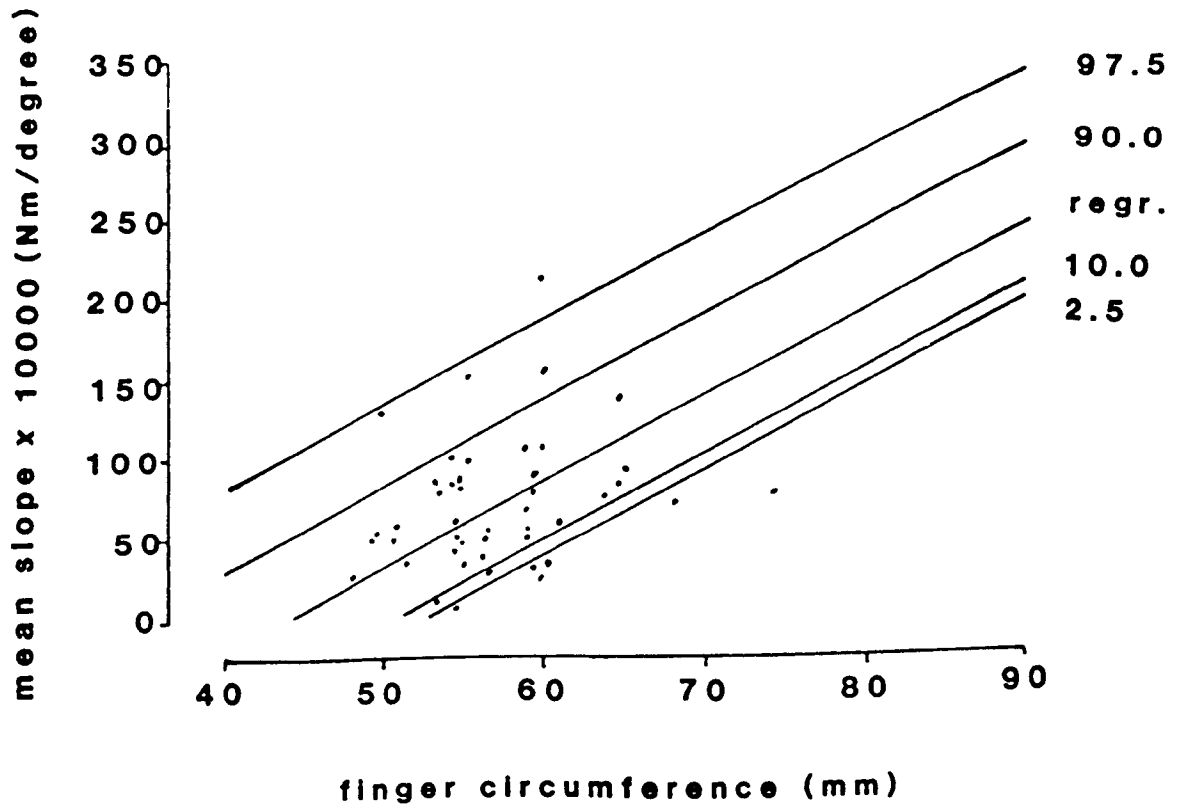
Figure 2.4

Figure 2.5

Average values for mean slope in different groups, superimposed on normal regression line and 2.5 percentile.

A = normal female.

B = active rheumatoid arthritis.

C = inactive rheumatoid arthritis.

D = subluxed MCP joint.

N = average for all normal subjects (male and female).
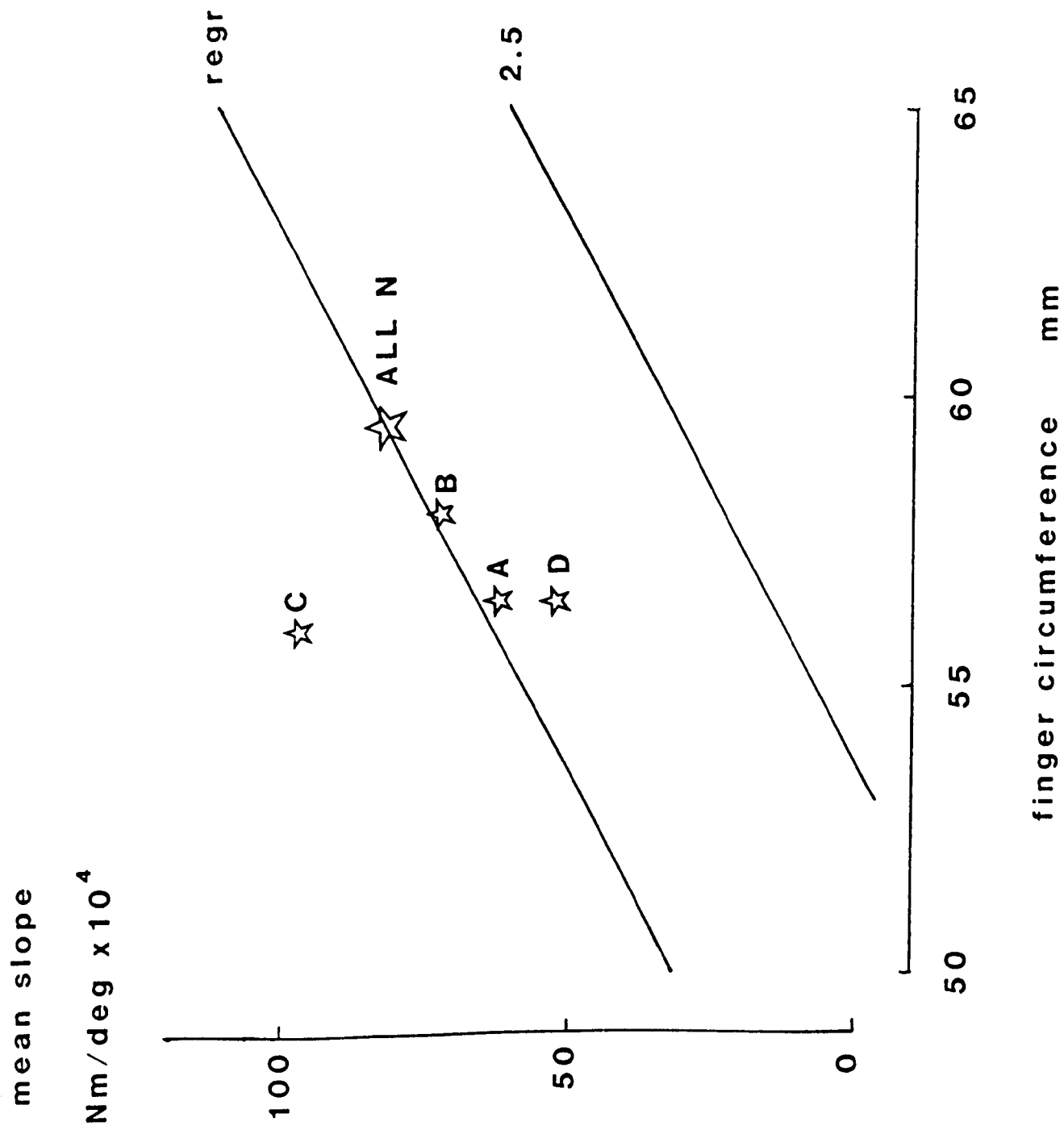
Figure 2.5

with active rheumatoid arthritis are stiffer than normals but this is masked by virtue of their increase in finger circumference due to inflammatory changes. This is illustrated in Figure 2.5. Point A represents the mean value for normal females for both finger circumference and elastic stiffness. Point B represents the mean value for finger circumference and elastic stiffness of patients with active rheumatoid arthritis: it can be seen that even though these patients lie below the regression line for stiffness they are perhaps stiffer in absolute terms by virtue of their increase in finger circumference and it may be this that the patients are experiencing. To test the validity of this hypothesis a group of patients with active rheumatoid arthritis were studied at times when their subjective stiffness was changing rapidly. The results of these studies will be detailed in the following pages.

Circadian variation

Stiffness was measured in 14 subjects with rheumatoid arthritis every 3 hours for 24 hours. Grip strength and dynamic grip strength variables (Helliwell et al, 1988b) were also measured. Univariate statistical analysis was not performed on these results: to allow for different stiffness in different individuals a statistic based on the difference between the mean and the actual stiffness variable at each time point for each individual was obtained. Using this method 95% confidence intervals can be generated although with the small number of subjects measured these were rather wide and circadian variation in stiffness was not demonstrated. For grip strength there was a trend towards maximum grip strength at 6pm. in the afternoon and minimum grip strength at 3am in the morning although these results did not achieve

significance.

An attempt was made to associate symptomatic stiffness with objective stiffness: in only 3 out of 14 cases did the time of maximum symptomatic stiffness correlate precisely with the time of maximum elastic stiffness. Patients were rather better at identifying maximum viscous stiffness, correct associations occurring in 7 of 14 patients. Of more interest was the change in equilibrium position which occurred: 8 of the 14 patients reached a minimum value, that is maximum ulnar deviation, between 3am and 9am and 9 of the 14 patients reached a maximum value, that is maximum radial deviation, between 3pm and 6pm. This finding supports the use of full hand resting splints to prevent increasing deformity in rheumatoid arthritis and may explain some of the subjective early morning stiffness experienced in rheumatoid arthritis (reference to Figure 2.2 is recommended to illustrate this point).

Response to a single oral dose of Ibuprofen

The aim of this study was to correlate the clinical and arthrographic response to a single oral dose of ibuprofen with the pharmacokinetic profile of the drug. Eight patients were included in the study. All non-steroidal anti-inflammatory drugs were stopped before the start of the study. On day 1 baseline data were obtained and on day 2 data were obtained at the same time intervals following a single oral dose of 800mg of ibuprofen. The pharmacokinetic profile revealed a peak serum concentration of ibuprofen at one hour with a time to half peak of about 3 hours. It was unfortunate that objective deterioration in stiffness occurred in the patients on the first (control) day: this was in contrast to the second day when decreases in elastic and viscous stiffness were seen. Again a poor relationship between

subjective and objective scores was found although a good correlation between subjective scores of pain and stiffness occurred.

Closer inspection of the results shows that 4 of the 8 patients improved markedly on both subjective and objective scores for both stiffness and strength whereas the other 4 patients did not show any objective improvement, although they improved subjectively. Interestingly it has been previously noted that only certain patients are capable of response in conventional trials of NSAIDs, certainly on objective criteria such as proximal interphalangeal joint circumference (Huskisson, 1976). The results suggest there is sufficient evidence to extend this study and to perform dose/response experiments in order to validate the effect.

Effect of intra-articular steroids

In all, 19 joints were injected with a single dose of triamcinolone acetonide (Lederspan 5-10mg). All the injections were done using the dorsal approach and a 23 gauge needle and measurements were made before injection, at 24 hours and 1 week following injection. The results revealed that at 24 hours there was an increase in both elastic and viscous stiffness which was not detected symptomatically; at 7 days there was a significant decrease in elastic stiffness but an insignificant decrease in viscous stiffness. At the same time parallel increases in range of movement and decreases in basal finger circumference were found. Again only a moderate association between symptomatic stiffness and objective stiffness occurred with agreement in directional change of stiffness in 16 out of 26 occasions for elastic stiffness and 15 out of 26 for viscous stiffness.

Effect of high dose intravenous methylprednisolone

Nineteen patients with active rheumatoid arthritis were given 1g of intravenous methylprednisolone on 3 alternate days. Stiffness measurements were made before the first infusion, before the second infusion, before the third infusion and at 1 week. There was an insignificant decrease in mean slope after the first infusion but this remained unchanged on the other measurements. Similar changes occurred for viscous stiffness but marked improvements were seen in grip strength during the week. For both elastic and viscous stiffness there was a suggestion of increased stiffness a week after the first infusion of methylprednisolone, but patients seemed unaware of this. It was felt that this was a clear indication of the discordance between subjective experience and objective measurement and that possibly the reduction in pain and general euphoria experienced by the patient as a result of high dose steroid therapy masked any local changes and suggested that patients predominantly used pain as the criterion by which they described the severity of their symptomatology.

Effects of physiotherapy

Ten patients with active rheumatoid arthritis and 10 patients with inactive rheumatoid arthritis were treated by physiotherapy. For the active group wax, megapulse and exercises were prescribed and for the inactive group ice, faradism and exercises. The effect of these quite different modalities was measured using the arthrograph, the design being such that patients were treated with a passive and an active modality on successive days followed by a control day when no treatment was administered. Significant improvements in elastic stiffness were seen following the application of wax to the inactive group and following exercises in the active

group. Large symptomatic changes occurred following ice but these were not detected arthrographically.

The effects of arthroplasty

Unfortunately this aspect of the study was limited by inadequate numbers of patients. Some interesting observations were made on one particular patient for 7 months following arthroplasty. The changes occurring illustrate some of the problems with arthrographs as an objective measure of joint stiffness. The patient had a subluxed, destroyed MCP joint and an elastic stiffness pre-operatively of 3.3 x 10^{-3} Nm/deg, the area of the curve being 41.7 x 10^{-3}. Grip strength was 17 N and pinch strength 15 N. Three months after successful arthroplasty the elastic stiffness was 5.2 x 10^{-3} Nm/deg, the area 48.3 x 10^{-3}, and grip was 20 N, pinch 12N. Seven months after operation the elastic stiffness was 7.7 x 10^{-3} Nm/deg and the area 60.9 x 10^{-3} Nm/deg and grip had risen to 39 N, pinch to 18 N. Undoubtedly in this case part of the increase in stiffness following operation was a result of restoration of normal joint mechanics and post-operative scarring. However, further increases in stiffness which parallel the increases in grip strength are likely to have followed an increase in forearm muscle size as a result of the continuing rehabilitation process. Similar results were found with the knee following a period of immobilisation by Heerkens et al, (1988).

Conclusions

What can be said of this study of objective stiffness using the new Leeds Microprocessor controlled arthrograph? Firstly, the system on the whole was acceptable to both patient and doctor and enabled rapid acquisition of data. The

results were shown to be reproducible, reliable and not subject to inter/intra observer error, a major advantage if the measure was to be of use in, for example, clinical trials. However, an essential requirement of any objective measure is that it should be relevant to the disease in question and it was felt that, overall, the results suggested that stiffness as measured by the arthrograph has little relevance to stiffness experienced by the patient. On reflection, this judgement may have been unduly hard and it would seem useful to summarise the main findings.

1. Patients with active rheumatoid arthritis who complained of joint stiffness were not objectively stiff when measured by this arthrograph.

2. Rheumatoid arthritis is not an homogenous disease and when patients are subdivided according to the stage of their disease significant differences appear, in terms of stiffness, between patient groups. These can be explained on a pathological basis.

3. In certain situations where symptomatic stiffness is changing rapidly the arthrograph is capable of recording this change but the quantity of objective change does not correspond closely with the quality and direction of symptomatic change. Although this was a disappointing feature of the study and, although the patient's experience is of importance in clinical studies, the findings suggest that objective stiffness at the joint may be of equal relevance and importance to, for example the plasma viscosity, in assessing change to therapeutic interventions.

When the clear discrepancy between objective stiffness and subjective stiffness was found in active rheumatoid arthritis a number of alternative explanations were

suggested and some were briefly explored during the course of the thesis. Again, for clarity, these will be enumerated.

1. Mention has already been made of the hypothesis that an increase in finger circumference has masked an increase in absolute stiffness for the patient with arthritis (see Figure 2.5). It was suggested that if objective changes in stiffness could be recorded at a time when subjective stiffness was changing rapidly then this hypothesis would have some support. It was felt that the studies detailing the response to a single oral dose of ibuprofen and to an intra-articular injection of steroid offered cautious preliminary support for this hypothesis.

2. It was also conjectured that the patient may really be complaining of a limitation of movement at the joint rather than an increased resistance to movement. An attempt was made to measure the joint range of movement; the linear part was the static torque displacement curve illustrated in Figure 2.2. The results offered some support for this idea: results for normal subjects showed a mid-range of 26° and for 4 subjects with rheumatoid arthritis 20°, 22°, 26° and 20° respectively. Two hypermobile subjects had mid-ranges of 32° and 34° respectively. However, a major problem with determining joint ranges in patients with rheumatoid arthritis is the pain elicited in the joint when it is moved to the extreme range of movement. Because of this it was felt that a larger study of joint range in patients with rheumatoid arthritis was precluded, although a recent and innovative technique for treating inflamed arthritic joints which involves the application of a Bier's regional block may provide the opportunity to extend these observations.

3.   It was felt that patients may be confusing pain with stiffness. In each of the individual studies rarely did subjective pain and stiffness change independently. Further support was provided by a paper which showed that early morning stiffness could be successfully relieved by the administration of a pure analgesic (Emery and Gibson, 1986). Alternatively patients may use the word "stiffness" as the best available word to describe what they are feeling or even when they are prompted to using it by the physician. When questioned more closely different descriptive terms are produced, such as limited range of movement, inflexible, rigid and stuck. It was felt that if the symptomatology of arthritis could be approached in a similar way to that which had been made for pain by Melzack (Melzack, 1975) with the McGill Pain Questionnaire, then more meaningful information on the quality of stiffness, as well as the quantity (ie. duration) could be obtained.

4.   An alternative explanation is based on neurophysiological evidence from animals. Unmyelinated C fibre stimulation in rats can alter receptor field size for contiguous mechano-receptors (served by A delta myelinated fibres). In a similar way it has been suggested (Helliwell et al, 1988) that chronic pain in arthritic joints can alter mechano-receptor thresholds from the joint in such a way as to provide erroneous information on joint stiffness.

5.   Could the muscle wasting associated with rheumatoid arthritis contribute to the subjective experience of stiffness? This argument has been proposed previously (Wright and Plunkett, 1966, Yung et al, 1986). In the first case it was suggested that the increased effort necessary to move a joint by a

Table 2.5

Wrist and arm circumferences (cm) - from Yung (1981). Forearm 1, 2, 3 measured at ¼, ½, ¾ of the distance between the ulna styloid process and the medial epicondyle of the humerus.

Dimension	NORMALS (n = 47)		RHEUMATOID ARTHRITIS (n = 37)	
	Mean	sd	Mean	sd
Wrist	15.65	0.948	17.27	1.579
Forearm 1	17.21	1.45	18.04	1.94
Forearm 2	22.29	2.02	22.61	2.56
Forearm 3	24.75	1.87	24.74	4.39

weakened muscle would contribute to the feeling of joint and muscle stiffness. However, Wright and Plunkett pointed out that patients with myopathy or other primary muscle diseases do not complain of stiffness in their joints. The reason for this is that the forces capable of being generated by muscles far exceed the necessary force to move the joint even where severe weakness has occurred. Yung et al (1986) suggested that since muscles contribute up to 40% of total torque measured at the joint then any muscle wasting occurring as a certain consequence of inflamed joints will mask any increases in stiffness occurring in the joints themselves. Yung (1981) measured the forearm circumference in 3 places in a normal control group and in a group of patients with rheumatoid arthritis and found no difference between the two groups. Indeed, the results suggested an increase in forearm circumference in patients with rheumatoid arthritis (see Table 2.5). However, it may also be that there is a qualitative difference in muscles in rheumatoid arthritis since it has been reported that up to 85% of patients have subclinical polymyositis on EMG testing (Steinberg and Wynn-Parry, 1961).

If qualitative and quantitative changes in muscle were prominent in rheumatoid arthritis and if these changes could be allowed for when measuring joint stiffness by the arthrograph then a true reflection of joint stiffness could be obtained answering many of the questions raised in the above discussion.

Summary

Joint stiffness in normal subjects is age, sex and joint dependent although these

differences are probably explained in terms of anthropometric variation. Joint stiffness in rheumatoid arthritis, when measured by arthrographs using the equilibrium position as a datum, does not differ from normal. Expected changes in joint stiffness are seen in response to anti-inflammatory drugs and to intra-articular steroids.

The discrepancy between objective/subjective stiffness in rheumatoid arthritis may occur for a number of reasons including an increase in relative finger girth, semeiological confusion, limited range of movement, altered mechanoreceptor thresholds, and associated muscle wasting.

CHAPTER 3

THE SEMEIOLOGY OF STIFFNESS

Introduction

Literature review: the language of arthritis

Development of stiffness questionnaire

Results

Discussion

Summary

Introduction

The word <u>stiff</u> derives from Old English stif, Middle English <u>stijf</u>, Swedish <u>styf</u>, and Middle German <u>stif</u>. According to the Complete Oxford English Dictionary (1933) the word means rigid, not flexible or pliant. The first references to the word in literature pertained to objects: "Horror gan the virgin's hart to perse, and her faire locks up stared stiffe on end" (Spencer, 1590). Only later was the word used in relation to joints and muscles: "You and I, ma'am, I think are too stiff to dance" (Barber Cox, Thackeray, 1840) and " I am like a stiff Irish post-horse which, after it has stood still for an hour or two in the stable, can hardly move a limb" (Pennyfather, 1865). Reference to the modern literature illustrates the trans-continental and trans-cultural use of the word: "She got up unsteadily and stretched, groaning against the stiffness" (The Bone People, Keri Hulme, 1985).

According to the shorter Oxford English dictionary (1973) the following definitions pertain:

Semeiology (Greek: sign, signal)

1.   Sign language

2.   The branch of medical science which is concerned with symptoms.

Semeiotic:

(Relating to symptoms).

This chapter will review the literature relating to symptoms, particularly stiffness in arthritis. A new questionnaire for evaluating the symptom of stiffness will be described. The questionnaire was administered to patients with both inflammatory and non-inflammatory rheumatic disease and to health professionals in order to contrast

beliefs about the meaning of stiffness and to make qualitative comparisons, based on symptomatology, between patient groups.

Review of literature: the language of arthritis

Although stiffness has headed the list of diagnostic criteria for rheumatoid arthritis for over 30 years (Ropes et al, 1959, Arnett et al, 1988) and has remained a major outcome variable in many studies of the efficacy of antirheumatic drugs and physical therapy, this pre-eminence has been challenged. Abramson (1967) felt that the symptom of stiffness was difficult to elicit because patients variously described stiffness as numbness, weakness, aching and other discomforts. He found, in a household survey, that 26% of the non-arthritic respondents said that they woke up with some morning stiffness and as a diagnostic test for arthritis he found a sensitivity of only 64%. A similar result was obtained in Leeds some years ago (Wright, personal communication) in which patients with rheumatoid arthritis were asked to explain exactly what they meant by morning stiffness. Of 31 patients interviewed, 21 redefined their stiffness as immobility, 4 as pain and immobility, and 6 were undecided. Steinberg (1978) in a thoughtful editorial attempted to separate the symptom of pain from stiffness. He reiterated that normal subjects experience morning stiffness and he felt that in rheumatoid arthritis, if the disease is active, pain supersedes stiffness. Steinberg imagined a spectrum of symptoms with increasing severity from no symptoms, slight stiffness/no pain, stiffness/pain, to severe pain only. He said that of 68 patients with rheumatoid arthritis, 67 indicated that pain on motion of the joint was the major feature of their morning stiffness.

The suggestion that patients confuse pain with stiffness has recently been supported in

a study of the effect of pure analgesics on early morning stiffness in rheumatoid arthritis (Emery and Gibson, 1986). These authors found that nefopam, a pure analgesic, was more effective than placebo in relieving early morning stiffness in 27 patients with rheumatoid arthritis who were also taking anti-inflammatory drugs. Rhind et al (1987) also emphasised the importance of pain in the symptom complex of arthritis. On questioning a group of 97 patients with rheumatoid arthritis the majority of this group described their joints as painful and stiff, but on further prompting stiffness was mainly defined as limited range of movement. Forty-three out of 100 patients re-described their stiffness as pain.

Symptom interpretation has been discussed by philosophers. Burge (1979) pointed out that we attribute beliefs and thoughts to people even though they incompletely understand the contents of those beliefs and thoughts. People may, having regard to communal conventions governing, for example, figures of speech, wrongly describe sensations attributable to arthritis. Words interpreted in conventionally established ways are familiar, but they may yield a bias towards taking others at their word. Doctors, rather than reinterpret the subject's word 'arthritis' in a mechanistic or linguistic sense, may simply accept the description.

Of interest is the way that children report the sensations from their joints. The language of childhood arthritis has been explored by the Manchester group (Beales et al, 1983a, Beales et al, 1983b). This group spent some time talking to children with arthritis and asking them to describe how their joints felt and to draw what they felt was happening to their joints. One child described her bones as being glued together. Younger children (less than 11 years of age) tended to interpret sensations 'in a

vacuum' with no reference to internal pathology. Many younger children denied that they had pain at all, although when prompted, described aching. One child insisted that the sensations were quite pleasant.

In clinical medicine there is a well established routine for taking a full history concerning pain. The following characteristics of the pain are elicited: site, character, timing, severity, radiation, precipitating factors and relieving factors. A complete history of the pain is necessary to obtain the necessary diagnostic clues. Renal pain, for instance, is typically a deep aching pain situated in the loin, radiating to the groin, occurring in 'waves' and associated with vomiting. In the same way, arthritic diseases may be separated by their arthritic symptomatology, although the range and variety of descriptors seems more limited. Nevertheless, it is felt by rheumatologists that osteoarthritis and non-articular rheumatism characteristically do not produce more than 30 minutes early morning stiffness, whereas rheumatoid arthritis and other inflammatory diseases may cause severe and prolonged morning stiffness (McCarty 1985). However, recently this notion has been challenged (Hazes et al, 1993). Ninety-three patients with rheumatoid arthritis (both active and inactive) and 46 patients with non-inflammatory arthritis were studied. This group found a poor discrimination between active and inactive rheumatoid arthritis and between inflammatory and non-inflammatory arthritis based on the severity and duration of early morning stiffness. Furthermore, they found that descriptions used by the patients were no different between the two groups (see Table 3.1).

An alternative approach to the semeiological confusion that exists with arthritic symptomatology is to approach the problem in a similar way to that which has been

Table 3.1

Descriptions, n(%) used by patients with rheumatoid arthritis or non-inflammatory conditions (n = 35 Osteoarthritis, 9, localised soft-tissue rheumatism, 2, non-articular rheumatism).

From Hazes et al (1993)

Descriptor	Rheumatoid Arthritis n = 86	Non-inflammatory n = 41

STIFFNESS:
  overall
  localised
  tightness
  need to stretch
	35 (41)
	14 (16)
	4 (5)
	16 (19)
	1 (1)
		22 (54)
		6 (15)
		4 (10)
		11 (27)
		1 (2)

PAIN:
  overall
  localised
	37 (43)
	32 (37)
	5 (6)
		17 (42)
		13 (32)
		5 (10)

LIMITATION OF MOVEMENT	13 (15)	5 (12)
NEED TO MOVE OR EXERCISE	6 (7)	2 (5)
FUNCTIONAL PROBLEM	27 (31)	11 (27)

made by Melzack for pain (Melzack and Torgerson, 1971, Melzack, 1975). These authors, in the McGill Pain Questionnaire, have constructed a table of 3 major classes of word descriptors relating to pain: sensory, affective and evaluative words which are used by the patient to specify their subjective pain experience. The words were drawn from the literature and from preliminary discussion with pain sufferers. They were then presented to 20 university graduates and these subjects were asked to arrange the words into different categories directed by the experimenters. If over 65% agreement was obtained for a particular word then this was accepted as a valid and agreed descriptor and used in the questionnaire. Within groups the words were also graded by severity so that a patient filling in the questionnaire can be assessed in several ways: by the number of words chosen, by the type of word chosen and by the point which the patient selects on the arbitrary within-group scale. Further dimensions are added by using a whole body image on which the site of the pain can be indicated and a visual analogue scale for pain severity. Undoubtedly this questionnaire offers a greater range of responses and a greater depth to the pain description that patients can offer. Despite the fact that there is a high inter-relationship between the 3 scales (sensory, affective, and evaluative), Melzack feels that this does not invalidate what he calls the unique information from each scale (Melzack, 1985).

The considerable number of studies evaluating the McGill pain questionnaire have recently been reviewed (Jamieson, 1988). Jamieson felt that the concept of assessing the multi-dimensional aspects of pain experience have been confirmed but, on the basis of principle component analysis, suggested that the original categories could be refined. Some doubt also exists on the scaling within sub-groups.

Helliwell (1987) felt that a similar table of descriptive words could be constructed for

the symptom of stiffness. The initial approach would be to obtain as many possible descriptive terms of stiffness from patients with arthritis and then to construct the table using these words in a ranking order according to group and severity. In this way, it was thought it may be possible to define sub-groups of arthritic subjects on the basis of their symptoms, so providing a more useful classification with which to compare objective scores of stiffness using devices such as the arthrograph.

Development of the stiffness questionnaire

A list of 56 words, descriptors used to describe the sensations arising from joints, was compiled as follows: 29 words from patient descriptions:

- puffy, heavy, jammed, locked, solid, fixed, rigid, stuck, set, wooden, tight, taut, limited, creaking, cramped, squashed, compressed, un-coordinated, grinding, sore, squeezed, restricted, grating, clumsy, jerky, seized, stiff, weak, won't go.

An additional 5 words from the literature; the paper by Rhind et al (1987):

aches, hurts, tense, inflexible, painful. (The patients interviewed by Rhind et al also used the descriptors: limited, solid, fixed, sore, rigid, set, tight, immobile).

18 words as synonyms: these were derived from a thesaurus of synonyms (Roget's Thesaurus 1962). These are reproduced for interest. Within this list the words extracted and used are underlined.

STIFF

Unyielding (adjective strength): staunch, resolute, stubborn, unstretchable, inelastic, rigid, solid.

Crippled: (adjective weakness) lame, limping, hobbled, stiff in the joints, arthritic.

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STIFF

Unyielding (adjective strength): staunch, resolute, stubborn, unstretchable, inelastic, rigid, solid.

Crippled: (adjective weakness) lame, limping, hobbled, stiff in the joints, arthritic.

Still (adjective quiescence): unmoving, unstirring, unbudging, fixed, immovable, unable to move, stuck, frozen, stiff.

Rigid (adjective hardness): stubborn, firm, inflexible, unbending, <u>unyielding</u>, resistant, inelastic, without spring, clumsy, tense, taught, tight, stiff, stark, stiff as a poker, stiff as a board, stiff as a buckram.

Dead (adjective death): corpse, cadaverous, stiff.

Insensible (adjective physical insensibility): <u>inert</u>, stony, stiff, <u>cold</u>, <u>dead</u>, <u>numb</u>, <u>paralysed</u>.

Narrow minded (adjective misjudgment): fastidious, stiff, unbending.

Obstinate (adjective obstinacy): stubborn, unyielding, firm, stiff, rigid, inelastic, wooden, hard, inflexible, unbending, <u>immovable</u>.

Inactive (adjective inactivity): <u>sluggish</u>, stiff, <u>rusty</u>, <u>languid</u>, heavy, <u>leaden</u>, <u>lethargic</u>.

Clumsy (adjective unskilfulness): unhandy, <u>all thumbs</u>, butterfingered, thick fingered, ungainly, lumbering, hulking, stumbling, gangling, stiff, rusty, graceless, inelegant, top-heavy, <u>cumbersome</u>, ponderous, <u>awkward</u>.

Restraining (adjective restraint): limiting, limited, unbending, unyielding, restricted, cramped.

Two words were extracted from the McGill Pain Questionnaire:

throbbing, pulling. (10 other words, already identified above, were also common to the McGill Pain Questionnaire:- cramp(ing), cold, numb, tight, taut, squeez(ing), heavy, ach(ing), hurt(ing), sore).

One word was also added to expand the dimension, of 'weakness':

limp

The 55 words were then presented to a group of health professionals. A copy of the

questionnaire is given in appendix 2. Subjects were invited to categorise each of the words under one of nine headings: weakness, friction, limited range of movement, pain, swelling, resistance to movement, no feeling, lack of movement, and disability. These headings were selected on a priori grounds by the author.

100 questionnaires were sent to health professionals. 54 replies were obtained and 50 were analyzed. Those replying comprised medical staff (16), physiotherapists (11), bioengineers (8), nursing staff (7), occupational therapists (4), secretarial staff (2), a pharmacist (1), and a social worker (1). Subjects were asked to sort the list of words into different categories; more than one category could be used if necessary. The author sought 60% agreement between respondents as the cut-off point for agreed representation of a particular word in a particular class. The final result is given in Table 3.2.

It can be seen from Table 3.2 that health professionals 'agree' that the word stiff refers to resistance to movement, although quite a number of respondents placed the word stiff under the headings Limited Range of Movement (36%) and Lack of Movement (24%).

Having obtained some measure of agreement between health professionals on the meaning of the descriptors it was intended to administer a similar questionnaire to patient groups. However it was felt that the questionnaire was too cumbersome. A number of comments were received from the health professionals, the commonest being that there was often difficulty in discerning between the three movement groups (limited range, resistance to and lack of). Some respondents, even the very well qualified, felt that it was far too hard. As a result the number of descriptors was

Table 3.2

Health Professional Questionnaire (see Appendix 2): Results

CATEGORY HEADING	Words achieving ≥60% agreement between respondents
Weakness	Languid, lethargic, limp, weak
Friction	Creaking, grating, grinding
Limited ranges of movement	Limited, restricted
Pain	Aches, hurts, painful, sore, throbbing
Swelling	Puffy
Resistance to movement	Inelastic, stiff, stubborn, unstretchable, unyielding
No feeling	Cold, dead, numb, wooden
Lack of movement	Fixed, inert, immovable, jammed, locked paralysed, seized, set, solid, stuck
Disability	

reduced and the final patient questionnaire (given in appendix 3) consisted of eight categories and 28 words (see table 3.3). The final list was chosen on the following basis: of the words agreed upon, and presented in table 3.2, all those identified either by patients or in the rheumatological literature, were retained. In addition 'tight', 'tense', 'rigid', 'inflexible' and 'heavy' were added since these words were part of the original patient list, although they did not achieve 60% concordance by the health professionals.

This final version of the questionnaire was presented to both in and out-patients at the Royal Bath Hospital, Harrogate, and Leeds General Infirmary. Patients were asked to do two things. Firstly, the patients were asked to define each of the words by writing each word under what they thought was the most appropriate of the given categories. They were asked not to use the word more than once (in contra-distinction to the health professionals). Secondly, patients were asked to underline the words that best described their joint symptoms and they were permitted to underline as many words as they felt appropriate.

The questionnaire was administered to 100 patients with rheumatoid arthritis, 50 patients with osteoarthritis, 50 patients with ankylosing spondylitis, and 50 patients with non-articular rheumatism. Patients with rheumatoid arthritis had an inflammatory polyarthritis with radiological erosions and many, but not all, were sero positive for rheumatoid factor. Active rheumatoid arthritis was diagnosed if two of the following three criteria were found:- (i) more than five joints swollen and painful, (ii) ESR greater than 28mm 1st hour, (iii) more than 45 minutes early morning stiffness. Patients with osteoarthritis were diagnosed on clinical and radiological grounds. Patients with

Table 3.3

Patient Questionnaire (see Appendix 3). Final list of descriptors and their 'agreed' categories.

CATEGORY HEADING	Words
Weakness	Lethargic, weak
Friction	Creaking, grating, grinding
Limited range of movement	Limited, restricted
Pain	Aches, hurts, painful, sore
Swelling	Puffy, tight, tense
Resistance to movement	Stiff, stubborn
No feeling	Cold, numb, wooden, heavy
Lack of movement	Fixed, jammed, locked, rigid, set, solid, stuck, inflexible

Table 3.4

Summary of Patient Groups

Group	n	age (y) mean (range)	sex F	M
Rheumatoid arthritis	100	58.6 (27-80)	67	33
Active disease	29	55.8 (47-65)	23	6
Osteoarthritis	50	66.3 (34-87)	40	10
Ankylosing spondylitis	50	40.6 (20-76)	6	44
Non-articular rheumatism	50	46.4 (22-71)	41	9

ankylosing spondylitis were diagnosed on the basis of a history of pain, spinal stiffness and radiological sacroiliitis and spondylitis. Patients with non-articular rheumatism were diagnosed on the basis of chronic non-articular pain at multiple sites with normal x-rays, normal serology and normal ESR. A summary of their demographic characteristics is given in Table 3.4.

Results

Table 3.5 presents a summary of the number words chosen, the adequacy of completion, and the words most commonly ignored (that is not sorted). There was a poor overall completion rate varying from 46% for osteoarthritis to 72% for active rheumatoid arthritis. The poor completion rate was due mainly to patients failing to sort each of the 28 words under an appropriate heading and this omission was commonest in the osteoarthritis group. Some words were often unsorted: cold, stuck, jammed, stubborn, wooden, tense and heavy, by at least two groups of patients. Alternatively, most patients were able to underline words which they felt adequately described the sensations arising from their joints, the median number of words chosen varying from nine to 12 with ranges from 0 to 26.

Patient definitions of individual descriptors

The headings under which individual descriptors were placed served to provide a definition of each word. Table 3.6 compares the headings used by the patient groups compared to the headings used by the health professionals for the word stiff. It is apparent that the heading commonest to all five groups was Resistance to Movement, but two other headings were commonly used, although less frequently: Limited Range of Movement and Lack of Movement. Other headings were used infrequently. For

Table 3.5

Number of words chosen, completion rate, and completion quality by disease group.

DISEASE	Number of words chosen median (range)	% Correctly Completed	% Failing to underline words	% Not sorting every word	Words commonly not sorted (% not sorting)
RHEUMATOID ARTHRITIS - All	9 (0-26)	57	6	37	Solid (34), cold (32), stuck (30), stubborn (30), wooden (30), heavy (32)
ACTIVE RHEUMATOID ARTHRITIS	10 (4-26)	72	0	28	Cold (32)
ANKYLOSING SPONDYLITIS	9 (2-21)	66	0	34	
OSTEOARTHRITIS	10 (0-21)	46	6	48	Lethargic (34), solid (36), cold (38), weak (30), stuck (36), hurts (32), stubborn (30), jammed (40), grinding (30), sore (32), wooden (36), rigid (42), set (44), tight (34), tense (40), heavy (36), inflexible (36)
NON-ARTICULAR RHEUMATISM	12 (0-22)	58	6	36	Cold (34), stuck (30), jammed (32), tense (30)

Table 3.6

Definition of "stiff" by health professionals (HP) and patient groups. Patients were asked to define <u>stiff</u> by choosing one of eight headings (definitions). Health professionals were allowed to choose more that one definition, if necessary.

Figures are percentages. (* indicates % of respondents choosing "stiff" as a descriptor for their joint symptoms).

RA = rheumatoid arthritis, OA = osteoarthritis, AS = ankylosing spondylitis, NAR = non-articular rheumatism.

HEADING	RA (72%)*	OA (74%)*	AS (92%)*	NAR (66%)*	HP
Weakness	0	0	0	2	0
Friction	4	2	0	2	12
Limited range of movement	26	20	24	20	36
Pain	5	0	2	0	14
Swelling	2	4	0	0	2
Resistance to movement	38	32	38	50	64
No feeling	0	2	0	0	0
Lack of movement	17	18	34	12	24

Table 3.7

Definition of "restricted" by health professionals (HP) and patient groups. Patients were asked to define "restricted" by choosing one of eight headings. Health professionals were allowed to choose more than one heading, if necessary.

Figures are percentages. (* indicates percentage of respondents choosing "restricted" as a descriptor for their joint symptoms).

RA = rheumatoid arthritis, OA = osteoarthritis, AS = ankylosing spondylitis, NAR = non-articular rheumatism.

HEADING	RA (61%)*	OA (56%)*	AS (64%)*	NAR (54%)*	HP
Weakness	0	0	0	0	0
Friction	1	2	0	2	0
Limited range of movement	57	56	66	66	78
Pain	0	0	4	0	0
Swelling	2	0	0	0	2
Resistance to movement	18	8	20	18	20
No feeling	0	0	0	0	0
Lack of movement	10	12	8	4	14

Table 3.8

Definition of "limited" by health professionals (HP) and patient groups. Patients were asked to define "limited" by choosing one of eight headings. Health professionals were allowed to choose more than one heading, if necessary.

Figures are percentages. (* indicates percentage of respondents choosing "limited" as a descriptor for their joint symptoms).

RA = rheumatoid arthritis, OA = osteoarthritis, AS = ankylosing spondylitis, NAR = non-articular rheumatism.

HEADING	RA (58%)*	OA (58%)*	AS (48%)*	NAR (48%)*	HP
Weakness	2	0	0	4	4
Friction	0	0	2	0	0
Limited range of movement	73	48	72	62	90
Pain	2	0	2	0	0
Swelling	0	0	0	2	0
Resistance to movement	6	8	6	8	8
No feeling	0	0	0	0	0
Lack of movement	5	20	10	2	12

comparison, two of the other descriptors have been analyzed in detail and are presented in Tables 3.7 and 3.8. Again, for 'restricted', Resistance to Movement, Limited Range of Movement and Lack of Movement were the three commonest headings used; Limited Range of Movement was the most frequently used heading. For 'limited' similar results were found.

Descriptors chosen by patient groups

It is clear from table 3.5 that a wide range of descriptors were chosen by all four patient groups. Some words, such as 'painful', were chosen by most patients in all four groups. Others, as was pointed out in table 3.5, were less commonly chosen, eg: stuck, and wooden. The percentages of patients according to this disease group underlining each of the 28 descriptors are given in table 3.9. For many words no differences between groups were found, eg: painful, limited, and hurts. Other words appear to discriminate between patient groups: these include stiff, numb and heavy.

Table 3.10 shows the disease category to which each of the words chosen most frequently belongs. A similar presentation is given in Table 3.11 where, for each disease group, the words chosen by more than 50% of the patients in that group are given. Using this criterion, significantly more words were chosen by non-articular rheumatism patients, as compared to osteoarthritis and rheumatoid arthritis.

To examine the ability of the descriptors to discriminate between the disease categories, logistic regression was performed using the disease category as the dependent variable and the descriptors as independent variables. Rheumatoid arthritis was compared to non-articular rheumatism, osteoarthritis and ankylosing spondylitis. In each case

Table 3.9

Percentage of respondents underlining each of 28 words presented, by disease group.

RA = rheumatoid arthritis, OA = osteoarthritis, AS = ankylosing spondylitis, NAR = non-articular rheumatism. RA-a = active rheumatoid arthritis.

WORD	RA	RA-a	AS	OA	NAR
Aches	64	66	70	64	74
Cold	15	10	8	26	36
Creaking	41	38	28	50	52
Fixed	16	21	18	26	8
Grating	49	48	44	48	34
Grinding	41	28	32	38	58
Heavy	23	31	18	32	54
Hurts	43	52	42	46	54
Inflexible	33	38	44	26	24
Jammed	13	14	10	20	10
Lethargic	29	31	42	24	56
Limited	58	55	48	58	48
Locked	28	34	14	36	30
Numb	16	21	22	30	40
Painful	86	97	78	78	86
Puffy	51	55	16	54	50
Restricted	61	69	64	56	54
Rigid	20	21	20	20	10
Set	16	21	12	6	8
Solid	12	14	10	10	6
Sore	38	45	34	34	56
Stiff	72	83	92	74	66
Stubborn	12	17	10	12	10
Stuck	10	14	6	12	12
Tense	27	31	48	26	40
Tight	25	28	42	36	52
Weak	50	48	36	48	58
Wooden	10	7	4	10	8

Table 3.10

Disease category in which words were chosen (underlined) by highest percentage of respondents.

DISEASE	Words chosen most frequently among whole sample (% choosing)
Rheumatoid Arthritis - all	Limited (58), weak (50), grating (49), wooden (10)
Rheumatoid Arthritis - active	Painful (97), stuck (14), stubborn (17), restricted (69), rigid (21), set (21), puffy (55)
Ankylosing Spondylitis	Stiff (92), tense (48), inflexible (44)
Osteoarthritis	Fixed (26), jammed (20), locked (36), wooden (10), limited (58)
Non-articular Rheumatism	Lethargic, (56), creaking (52), aches (74), cold (36), hurts (54), numb (40), grinding (58), sore (56), tight (52), heavy (54)

Table 3.11

Words underlined by more than 50% of patients by disease category.

* vs. Non articular rheumatism $x^2 = 1.94$ NS

+ vs. Non articular rheumatism $x^2 = 5.41$ $p < 0.025$

DISEASE	Number of words chosen by more than 50%	Words chosen (% choosing)
RHEUMATOID ARTHRITIS	7 *	Painful (86), limited (58), aches (64), puffy (51), stiff (72), weak (50). restricted (61)
ACTIVE RHEUMATOID ARTHRITIS	7	Painful (97), limited (55), aches (66), puffy (55). stiff (83)
ANKYLOSING SPONDYLITIS	7	Painful (78), creaking (50) limited (58), aches (64), puffy (54), stiff (74), restricted (56)
OSTEOARTHRITIS	4 +	Painful (78), aches (70), stiff (92), restricted (64)
NON-ARTICULAR RHEUMATISM	13	Painful (86), lethargic (56) creaking (52), aches (74), puffy (50), stiff (66), weak (58), restricted (54), hurts (54), grinding (58), sore (56), tight (52), heavy (54)

rheumatoid arthritis was given a score of 0 and the comparator disease a score of 1. This means that in table 3.12 to 3.14, where the significant coefficients and their odds ratios are presented, if the odds ratio is greater than 1 there is an increased likelihood (by the magnitude of the odds ratio) of having the comparator disease, and if the odds ratio is less than 1 an increased magnitude of having rheumatoid arthritis (by the reciprocal of the odds ratio). For example, in table 3.12, if a patient underlined the word 'lethargic' on the questionnaire, then she is 3.9 times more likely to have non-articular rheumatism. If the word 'stiff' is underlined then she is 5 times more likely to have rheumatoid arthritis.

For each patient, the following statistic was calculated:-

$$L = \ln (p/1\text{-}p) = b_0 + b_1 x_1 + b_2 x_2 + ...b_i x_i$$

where p = probability of having disease, (range 0 - 1)
b_0 = constant
b_i = coefficient of ith descriptor
x_i = response to ith descriptor (0 or 1)

In figure 3.1 a histogram of the values of L for rheumatoid arthritis compared to non-articular rheumatism is given. Good separation between the scores is demonstrated. The mean score of L for rheumatoid arthritis = -2.493 $\pm$ 2.162 and for non-articular rheumatism = 0.775 $\pm$ 1.754 (t = -9.27 p = 0.0000).

L was also calculated by using only the descriptors with significant coefficients, but discrimination was not as good (t = -5.35 p = 0.0000). Similar analyses were carried out for rheumatoid arthritis compared to osteoarthritis (see table 3.13 and figure 3.2) and rheumatoid arthritis compared to ankylosing spondylitis (see table 3.14 and figure 3.3). Discrimination between rheumatoid arthritis and osteoarthritis is not as good as

Table 3.12   Rheumatoid arthritis/Non-articular rheumatism

Significant coefficients and their odds ratios. Results of logistic regression with disease as dependent variable (rheumatoid arthritis = 0, non-articular rheumatism = 1), descriptors as independent variables (if underlined by patient = 1, not underlined = 0).

WORD	Coefficient	Std. error	Sig.	Odds ratio
Lethargic	1.3658	0.5783	0.0182	3.9187
Stiff	-1.6435	0.7248	0.0234	0.1933
Solid	-3.1996	1.4073	0.0230	0.0408
Cold	1.8075	0.7457	0.0154	6.0952
Grating	-2.3254	0.7652	0.0024	0.0977
Numb	1.7961	0.7535	0.0171	6.0258
Grinding	2.1319	0.8126	0.0087	8.4312
Heavy	2.4132	0.7420	0.0011	11.1697

Table 3.13   Rheumatoid arthritis/osteoarthritis

Significant coefficients and their odds ratios. Results of logistic regression with disease as dependent variable (rheumatoid arthritis = 0, osteoarthritis = 1), descriptors as independent variables (not underlined - 0, underlined = 1).

WORD	Coefficient	Std. error	Sig.	Odds ratio
Numb	1.3047	0.6360	0.0402	3.6866
Set	-2.7286	1.1276	0.0155	0.0653

Table 3.14 Rheumatoid arthritis/ankylosing spondylitis

Significant coefficients and their odds ratios. Results of logistic regression with disease as dependent variable (rheumatoid arthritis = 0, ankylosing spondylitis = 1), descriptors as independent variables (not underlined - 0, underlined = 1).

WORD	Coefficient	Std. error	Sig.	Odds ratio
Painful	-2.4062	0.9646	0.0126	0.0902
Limited	-1.7132	0.6496	0.0084	0.1803
Aches	1.8395	0.7623	0.0158	6.2932
Puffy	-3.0600	0.7327	0.0000	0.0469
Stiff	2.5147	0.8701	0.0039	12.3627
Cold	-2.0673	1.0370	0.0462	0.1265
Restricted	1.4154	0.6451	0.0282	4.1181
Numb	2.2167	0.7930	0.0052	9.1768
Tight	1.6251	0.6294	0.0098	5.0787
Tense	2.3413	0.6956	0.0008	10.3947

Figure 3.1

Split histogram of scores for L statistic: rheumatoid arthritis compared to non-articular rheumatism.

Details of computation of L statistic are given in text.

Figure 3.1

Figure 3.2

Split histogram of scores for L statistic: rheumatoid arthritis compared to osteoarthritis.

Details of computation of L statistic are given in text.

L score

number of patients
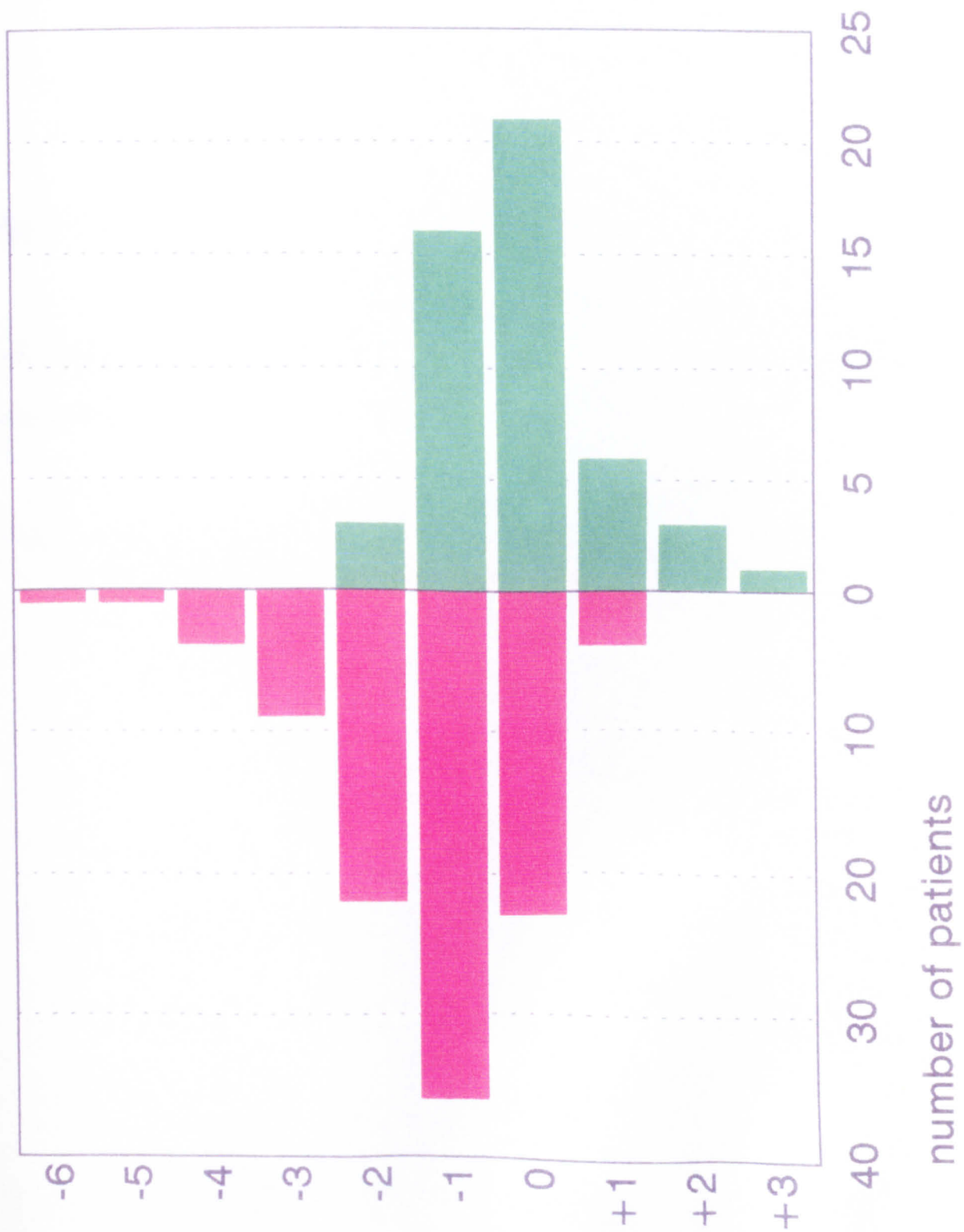
Figure 3.2

Figure 3.3

Split histogram of scores for L statistic: rheumatoid arthritis compared to ankylosing spondylitis.

Details of computation of L statistic are given in text.
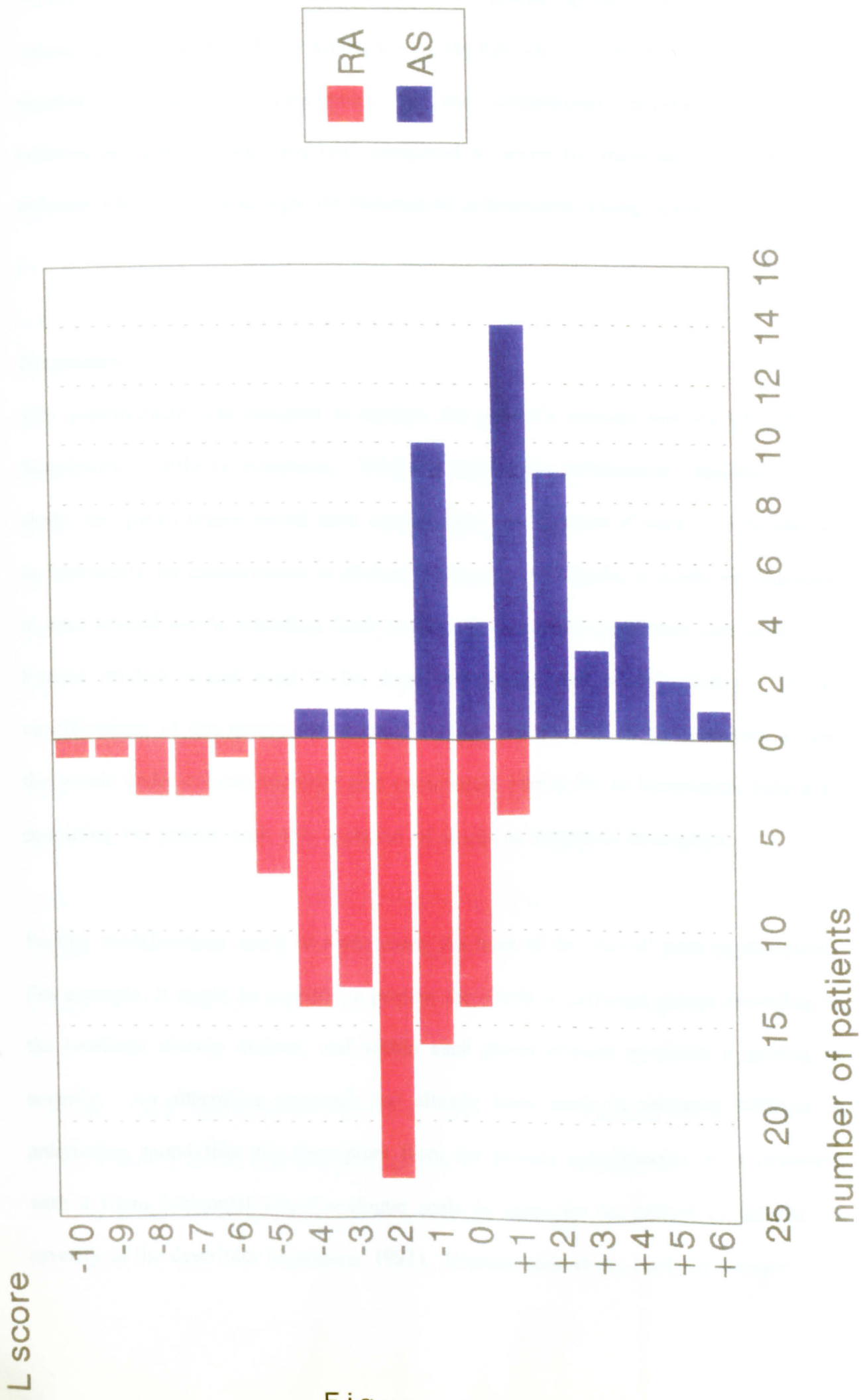
Figure 3.3

between rheumatoid arthritis and the other two disease groups, as indicated by the values of the t statistic. (For RA/OA, t = -5.38; RA/AS, t = -9.49). Furthermore the number of significant descriptors in the comparison between rheumatoid arthritis/osteoarthritis was only two, compared to seven for rheumatoid arthritis/non-articular rheumatism and eight for rheumatoid arthritis/ankylosing spondylitis.

Discussion

The questionnaire was designed to explore the patient's concept and use of different descriptors of arthritic symptoms. Whilst providing the information required for this study, the questionnaire would need considerable modification if were it to be used as an instrument for measurement in clinical practice. For example, it would be necessary to omit several words, including those commonly not sorted by patients (see table 3.5). Further studies would need to be done on validity and reproducibility. Useful modifications of this questionnaire could include the removal of the necessity to sort the words under column headings (the commonest reason for an incomplete response) providing the patient with only a choice of words as symptom descriptors.

Further modifications could be made along the lines of the McGill pain questionnaire. For example, it might be possible to present the words in different groups according to the headings already defined, and within each group attempt to obtain a grading of severity. An alternative approach has already been made in assessing stiffness in ankylosing spondylitis: the descriptors from the present questionnaire were presented with a 10cm horizontal visual analogue scale in order for the patient to indicate the severity of the descriptor (Jamieson, 1993). Interestingly, in the study by Jamieson, the

patients with ankylosing spondylitis chose a slightly different spectrum of words to describe their joints: restricted, 82%; painful, 73%; aches, 73%; stiff, 73%; hurts, 64%; rigid, 55%; tight, 55%; sore, 55%; inflexible, 55% (compare to Table 3.9).

The poor completion rate indicated in table 3.5 casts some doubt on the reliability of the results using this questionnaire. The main problem was patients either not understanding the instructions, or not wishing to sort out each word under the column headings. The percentage of patients not sorting all the words was highest in the group with osteoarthritis who, perhaps significantly, were older than the other patients. The author frequently found that elderly patients in particular had difficulty in understanding what was required of them. Other problems included patients ascribing the descriptors to the column headings, eg: 'I feel friction in my joints and this is painful so I will write friction under the painful heading', descriptors sorted into more than one column, answering 'yes' or 'no' under column headings, indicating that the descriptors apply to how they feel generally (eg: 'cold') and creation of new descriptors. These latter problems were rarely encountered but give an indication of some of the ways in which the questionnaires were not always satisfactorily completed. Nevertheless the questionnaire has provided useful information on the words patients use to describe the symptoms from their joints, how these words are used differently between patient groups, and the concepts that patients have of the meaning of these words.

The word 'stiff' was invariably sorted by patients independent of disease group and table 3.6 clearly shows that both patients and health professionals understand the word 'stiff' to mean increased resistance to movement principally, and secondarily limited range of movement (equating lack of movement more with limited range of movement

than resistance to movement). The concordance between patient groups and health professionals on two other words, 'restricted' and 'limited' is also indicated in the results section. This exercise would not have been valid if any of these words had been infrequently sorted by the patient groups.

Rhind et al (1987) felt that patients were using the word stiff as a euphemism for pain and limited range of movement. In fact, the frequency with which the descriptors were chosen, in this study and in that of Rhind, were similar: (this study in brackets and see Table 3.9).

Limited movement	57 (58)	painful	44 (86)
Rigid	17 (20)	aches	35 (64)
Stuck	14 (10)	hurts	29 (43)
Inflexible	14 (33)	sore	18 (38)
Solid	5 (12)	tight	35 (25)
Fixed	3 (16)	tense	29 (27)

In accordance with the design of their study, Rhind did not present the word 'stiff' as a pure descriptor. The obvious discrepancy between the two studies in the use of pain descriptors is difficult to explain - her subjects were prompted at interview to select words which described their joint stiffness and the subjects may have been discouraged from selecting pain descriptors only.

This questionnaire has also allowed patients to provide a more complete description of how their (arthritic) joints feel. Patients with non-articular rheumatism chose significantly more words to describe their joints that any of the other patient groups. A similar result was obtained by Leavitt et al (1986) comparing 50 patients with non-articular rheumatism and 50 patients with rheumatoid arthritis using a modified McGill

pain questionnaire. Leavitt found that patients with non-articular rheumatism used words with greater spatial diffusion and words less localised to the joints, with more constrictive qualities (words such as radiating, steady, spreading, spasms, gnawing, unlocalised, pricking, crushing, shooting, pressing, splitting, cramping, nagging and pins and needles). The evaluative words of the McGill pain questionnaire were used more commonly by patients with non-articular rheumatism. In the current study patients with non-articular rheumatism more commonly used words referring to energy (lethargic, weak, heavy, cold), pain (painful, aches, hurts, sore) and frictional symptoms (creaking and grinding).

The use of these different words enabled a clear discrimination to be made between non-articular rheumatism and rheumatoid arthritis using logistic regression analysis. It should be realised, however, that the good discrimination obtained is partly contrived: a true test of the discriminatory power of this questionnaire would be to apply the calculated coefficients to the replies of a new group of mixed patients suffering from rheumatoid arthritis and non-articular rheumatism. Nevertheless, the ability of this questionnaire to show a clear distinction between patient groups on the basis of descriptors used, is of considerable interest in understanding the patient's language of arthritis. Discrimination between rheumatoid arthritis and ankylosing spondylitis was equally good, the significant descriptors being more numerous - 'aches', 'stiff', 'restricted', 'numb', 'tight' and 'tense' having the largest effect. On the other hand, it was quite clear that patients with ankylosing spondylitis do not regard their joints as swollen or particularly painful when compared to rheumatoid arthritis.

The similarity of words chosen by patients with rheumatoid arthritis and osteoarthritis

reduced the significance of the difference between the scores for the discrimination statistic, only two coefficients achieving significance ('numb' with an odds ration of 3.69 and 'set' with an odds ratio of 0.07). Of course, only 29 patients with rheumatoid arthritis had 'active' disease according to the definition described in the introduction and it is possible to speculate that patients with inactive rheumatoid arthritis, possibly burnt-out disease with secondary osteoarthritis, may use the same descriptors as patients with osteoarthritis (for rheumatoid arthritis as a whole this was certainly true for the descriptors creaking, grating and grinding).

The nature of arthritis pain in rheumatoid and osteoarthritis has also been described using the McGill pain questionnaire by Charter et al (1985). This group found, a similar word choice for both patient groups with frequent use of inflammatory words such as throbbing and burning and an overall increase in pain intensity with duration of disease. It is also worth remembering that Hazes et al (1993) could find no difference between osteoarthritis and rheumatoid arthritis in terms of duration or severity of early morning stiffness. Published studies would seem to show, therefore, that patients with rheumatoid arthritis and osteoarthritis are hard to separate on a symptomatic basis, a surprising finding to a practising rheumatologist.

Using an algometer Gerecz-Simon et al (1989) demonstrated that the pain threshold for patients with ankylosing spondylitis was higher than that for patients with osteoarthritis and in turn the threshold for osteoarthritis was higher than that for rheumatoid arthritis. The word 'painful' was chosen by 86% of patients with rheumatoid arthritis (97% of those with active disease), 78% of patients with ankylosing spondylitis and 78% of patients with osteoarthritis, adding another dimension to this observation.

Summary

A stiffness questionnaire has been developed. Using this stiffness questionnaire patient groups and health professionals agreed that when using the word 'stiff' they mean, firstly, increased resistance to movement and secondly, limited range of movement.

When offered a list of 28 symptom 'descriptors' and invited to choose the words which best describe the symptoms from their joints, patients with non-articular rheumatism chose a greater number of words than patients with rheumatoid arthritis, osteoarthritis and ankylosing spondylitis.

Using the profile of word selection for each patient group it is possible to discriminate clearly between rheumatoid arthritis, ankylosing spondylitis and non-articular rheumatism, but there is little distinction between rheumatoid arthritis and osteoarthritis.

CHAPTER 4

PROPRIOCEPTION IN NORMAL AND ARTHRITIC JOINTS

Introduction

Literature Review

    Neuro-anatomy, Neuro-physiology of articular and cutaneous mechano-receptors

    Measuring proprioception in humans

Methodology and Results

    Movement perception threshold

    Vibration perception threshold

Discussion

Summary

Introduction

Kinaesthesis is defined by the Oxford English dictionary as 'the sense of muscular effort that accompanies a voluntary motion of the body'. Articular neuro-physiologists (Ferrell, 1992) would simplify this into 'awareness of limb movement' and would further describe awareness of the static or steady state position of the limb as stataesthesis. Normally these two sensations cannot be separated since a change in position involves movement and movement produces a change in position. For some time contrasting opinions on the neural origin of these sensations have been expressed. Some authors (including Ferrell, 1992) have stressed the importance of articular mechano-receptors in conveying these sensations while the Matthews' group (Goodwin et al, 1972) have provided evidence to suggest the involvement of muscle spindle sensory endings in providing proprioceptive sensation. In fact, both opinions are now thought to be correct with further proprioceptive information coming from periarticular cutaneous mechano-receptors.

This chapter will review the neuro-anatomy and neuro-physiology of proprioception as background to a study of proprioceptive thresholds in patients with rheumatoid arthritis.

Neuro-anatomy and neuro-physiology of articular and cutaneous mechano-receptors

Based on the classification of Freeman and Wyke (1971) four classes of articular receptors are recognised. All four types are found in synovial joints of humans, although the proportions of each may differ from joint to joint. Wyke (1981) clearly stated that no receptors were to be found in articular cartilage, intra-articular menisci

or synovial tissue. However, more recent articles (Johansson and Sjolander, 1993) have suggested that all types of mechano-receptors are seen in menisci, particularly those of the knee, and in the outer sub-membranous layers of synovium.

Type 1. "Ruffini".

Clusters of thinly encapsulated corpuscles each associated with a single nerve 5-9 microns in diameter (Aß fibres) particularly found in capsule, but also found in other articular tissues such as menisci and ligaments. Slowly adapting, low threshold receptors some of which are tonically active. Respond preferentially to longitudinal tension in joint capsule. Signal static position, intra-articular pressure, amplitude and velocity of movement.

Type 2. "Pacinian"

Multi-lamina corpuscles with single nerve fibre 8-12 microns diameter (Aß). Smaller than equivalent corpuscles in glabrous skin (see below), widely distributed throughout capsule and ligaments. Rapidly adapting, low threshold receptors activated on acceleration, deceleration and vibration.

Type 3. "Golgi"

Corpusculated spray ending morphologically similar to type 1 associated with single nerve fibre 13 -17 micron diameter (Aδ). Mainly found in ligaments. Slowly adapting, high threshold receptors normally silent in immobile joints. Respond at extremes of movement when periarticular ligaments under tension.

Type 4a. Free nerve endings associated with small myelinated nerve fibres 0.5-5

micron diameter (Aδ). Form a diffuse lattice throughout joint capsule and have close anatomical relationship to type 1 and 2 receptors. Normally silent at rest these receptors respond to extremes of mechanical deformation, chemicals or inflammatory mediators.

Type 4b. Free nerve endings associated with unmyelinated nerve fibres (type C). Widely distributed especially in intrinsic and extrinsic joint ligaments with similar response characteristics to type 4a. Very high threshold, slowly adapting, slow velocity conduction.

Impulses from these articular afferents are transmitted via primary articular and accessory articular nerves polysegmentally to the spinal cord and centrally where they exert primary perceptual and reflexogenic effects. Impulses are transmitted centrally via dorsal column and spinocerebellar tracts. Dorsal column neurones relay via the thalamus to post-central and parietal cortex.

Reflex effects from articular mechano-receptors can be divided into arthrostatic and arthrokinetic reflexes (Wyke, 1981). Type 1 receptors are responsible for tonic discharge, presumably signalling joint position, and exert reflex effects on tonic fusimotor neurones so that resting (and presumably postural) tone is partly dependent on discharge from these afferents. Arthrokinetic reflexes provide a coordinated facilitatory and inhibitory cascade on motor units, again via phasic fusimotor neurones. Type 1 and 2 receptors are responsible for this activity which may be apparent in the contralateral limb. At extremes of joint range type 3 receptors have direct reflex inhibitory effect on ipsilateral alpha motor neurones. Abnormal mechanical stresses and

chemicals may also have inhibitory effects on alpha motor neurones via type 4 receptors. Johansson and Sjolander (1993) have stressed the importance of low threshold joint afferents in providing functional joint stability via their reflexogenic effects on the fusimotor system and, therefore, muscular stiffness. As a cororally, they have extrapolated this role to the genesis of pain in musculoskeletal pain syndromes.

Which receptors are responsible for signalling stiffness and limited range of movement? For the latter it seems clear from the preceding discussion that type 3 and type 4 receptors would be responsible for signalling as the joint approached the limit of anatomical range. Information on joint stiffness may, however, be derived from several receptors. To determine stiffness, information is required on force and movement. Skoglund (1973) has suggested the type 1 receptors, lying preferentially along the longitudinal axis of the joint capsule, are influenced by muscle tension and are therefore able to signal resistance to movement. Acute distension of a joint in normal human volunteers provides a sensation of 'tightness' (Jayson and Dixon, 1970), presumably due to increased activity in Ruffini receptors. Burgess and Clark (1969) have shown, in the cat, receptors tuned to both directional movement (flexion or extension) and static position. It seems likely that, rather than having a specific 'stiffness' receptor, information on joint stiffness is derived from articular position/movement receptors, from muscle (including Golgi tendon receptors and muscle spindle afferents) and perceived effort (α motor neurone discharge).

Kinaesthetic information is therefore derived from articular mechano-receptors, muscle

spindle afferents and cutaneous mechano-receptors (Wyke, 1981, Ferrell, 1992). For some time the role of articular mechano-receptors in kinaesthesis and stataesthesis was disputed. Goodwin et al (1972) were able to show that anaesthesia of joint afferents had only a minimal effect on kinaesthesia; at the same time they demonstrated that vibratory stimuli applied to muscles could induce an illusion of movement. This work was supported by Eklund (1972) who also demonstrated that actively contracting muscle provided better position sense than passive muscle. Clark et al (1979) demonstrated that stataesthesis was preserved following intra-articular anaesthesia (to anaesthetize capsular receptors) and skin anaesthesia (to anaesthetize cutaneous mechano-receptors). Burgess (1976) also felt that skin mechano-receptors were not important in kinaesthesis. On the other hand Gandevia and McClosky (1976) and more recently, Ferrell and Craske (1992) have demonstrated the importance of articular mechano-receptors in stataesthesis and kinaesthesis, particularly in finger joints. Gandevia and McClosky used the anatomical quirk first described by Barnett and Cobbold to demonstrate that disengagement of long flexor tendons inhibited detection of movement in the finger; anaesthesia of the digit also inhibited detection of movement. Ferrell and Craske confirmed this result using an experimental arrangement which masked the position of the finger from the subject and allowed them to use a matching finger silhouette to indicate stataesthesis. Ferrell (1992) has suggested that these discrepant results may have occurred because the contribution of different mechano-receptor information to kinaesthesis and stataesthesis varies from joint to joint throughout the body. Therefore, in the finger joint articular mechano-receptors have a more important role than muscle receptors: the opposite occurring for large joints such as the knee. That both muscle spindle afferents and cutaneous mechano-receptors project to the sensory cortex is not in doubt and it seems likely that position and

movement sense be derived from these modalities. This would explain the preservation of proprioception following capsulectomy or total joint replacement.

Cutaneous mechano-receptors

Cutaneous mechano-receptors have similar neuro-anatomical and neuro-physiological characteristics to those seen in the joint (Burgess and Perl, 1973).

Encapsulated Pacinian corpuscles are low threshold, rapidly adapting receptors served by Aα fibres showing no linear directionality. These receptors respond to acceleration and are sensitive to vibration. They are difficult to excite at frequencies less than 30Hz and appear to show tuning maximally responding between 150 and 400Hz to minimal displacements of 1 micron. Meissner corpuscles are also low threshold, rapidly adapting mechano-receptors served by Aα fibres demonstrating a velocity-dependent stream of impulses when the skin is displaced mechanically at a constant velocity. These receptors are also sensitive to vibration, tuned to respond to frequencies between 10 and 70 Hz.

Ruffini spray corpuscular endings signal mainly static displacement but are also responsive to movement; they are slowly adapting low threshold receptors which may provide tonic output and are served by Aβ fibres.

Merkel corpuscles served by Aα fibres signal position and velocity and are slowly adapting. Iggo (1976) has termed the Merkel receptor 'the touch spot' receptor and suggests that the afferent discharge persists for several minutes under constant displacement of the skin.

The neuro-physiological characteristics of cutaneous mechano-receptors are of particular interest in relation to response to vibratory stimuli. Talbot et al (1968) describe the threshold to vibratory stimuli at frequencies varying from 0 - 400Hz. There was an abrupt and rapid fall in the threshold at 40 Hz; below this subjects described the sensation as flutter and above this as vibration. In the monkey glabrous skin he was able to describe two populations of receptors: high sensitivity, low threshold, wide receptive field receptors tuned to approximately 300Hz, probably represented by Pacinian corpuscles and a higher threshold smaller receptive field receptor tuned to about 30 Hz, probably represented by Meissner corpuscles. The tuning, high sensitivity and wide receptor field of Pacinian corpuscles was confirmed in the monkey by Lindblom and Lund (1966), who also made the interesting observation that single Pacinian corpuscles could respond to distant vibratory stimuli (for example, a fan in the ceiling of the laboratory), but did not respond to intrinsic cardiac or respiratory rhythm. Knibestol (1975), studying Merkel and Ruffini receptors in intact human glabrous skin, demonstrated directional responses in Ruffini receptors, for example stretching of the skin over a distal interphalangeal joint, and non-directional pressure responses of the Merkel receptors. Both receptors were slowly adapting and showed similar thresholds to Pacinian and Meissner corpuscles. Again of interest, the Ruffini receptors showed spontaneous resting activity.

Measurement of kinaesthesis and stataesthesis in vivo

Three measures have been employed.

(i)   Static position sense.

The distal portion of a joint is held and moved, unseen to the subject, to a new position. The subject has to match that position either in the contralateral joint, a manikin or at

a later time in the ipsilateral joint. In order to minimise cutaneous afferents at the point of contact with the apparatus constant firm pressure has been applied. Skinner et al (1984) found good reproduction for static position sense of the knee with a small error of 1-2°. They found that the matching error increased with age. The magnitude of error was confirmed by Corrigan et al (1992), but Barrett et al (1990) found a mean matching inaccuracy of about 5°. In the proximal interphalangeal joint of the finger Ferrell and Craske (1992) demonstrated good position matching with errors of about 3° at 140° flexion, 4° at 160° flexion and 6° at 120° flexion.

(ii)   Movement perception

Perception of movement expressed as the smallest change in angle detectable, is velocity dependant (Browne et al, 1954, Kokmen et al, 1978, Ferrell and Craske, 1992). The latter authors showed that in the proximal interphalangeal joint(PIP) of the finger 1° of movement was detectable at a velocity of 200°/min but only 10° at 20°/min. Change in amplitudes of 0.1 and 0.01° were not detectable at any velocity. Skinner et al (1984) found the threshold for movement at the knee at an angular speed of 24°/min was 3°, and again this increased with age. There was, however, large inter individual variation. Corrigan et al (1992) using speeds of less than 0.5°/min, found knee thresholds to be as low as 1°, an astounding degree of perceptual sensitivity which suggests information may have been derived from cutaneous receptors. In the finger Kokmen et al (1978) demonstrated that the threshold for movement detection varied from 0.66° at 0.5 Hz to 0.26° at 8 Hz. They found the threshold for movement detection in the MCP joint was lower than the MTP joint and was higher in older than younger people. Browne et al (1954), on the other hand, showed that the threshold to detection in the great toe was 4.5°, but there was wide variability and the distribution was skewed, some subjects having detection angles of up to 20°. Browne et al found no difference in movement perception threshold between the two speeds 1°/sec and

2°/sec.

Barrett et al (1990) have repeated the observation that stataesthetic perception is a function of age. These authors also showed that perception was decreased in osteoarthritis and after total knee replacement but in both these cases perception was facilitated by the use of a knee bandage, presumably enhancing cutaneous receptor information.

Measurement of vibration perception in vivo

The similarities between the waveform characteristics of cutaneous vibratory and auditory signals, and the considerable experience of testing auditory perception thresholds have led to some translation from methods used in audiometry to those used in vibration perception. Furthermore, the units used to describe auditory thresholds (decibels) can also be used to express tactile vibration perception thresholds although, on the whole, researchers have preferred to use absolute amplitude as the unit of measurement. The subject of vibration perception has also received considerable interest as a measure of early neuropathic change particularly in subjects with diabetes mellitus and in industry as a measure of vibration white finger. For this reason, extensive normative data has been gathered using standardised devices.

Laidlaw and Hamilton (1937) found age-related decreases in vibration perception, but no difference in perception threshold between the tips of the digits and thumb (average for all 5, 10.6μ). Gregg (1951) found vibration perception to be independent of contact area and pressure and, using a fixed frequency of 120Hz, found the lowest digital threshold to be 0.37μ at the thumb. In 1984 Bloom et al described the use of a

commercially available device to measure vibration perception threshold. This device (the Biomedical Biothesiometer) produced a vibratory stimulus to a $1cm^2$ diameter plastic probe at a fixed frequency of 100Hz. In a large series of normal subjects he was able to show a logarithmic increase in threshold with age, the threshold at age 20 approximately 0.25μ, at age 70, 0.7μ. Wiles et al (1991) using a similar device, found lower thresholds but the same relationship to age. Vibration perception threshold increased from 0.1μ at age 20 to 0.45μ at age 70.The discrepancy between these two groups is probably due to different contact pressure: Bloom et al held the tactor in firm contact but with minimal pressure, whereas Wiles et al used the weight of the Biothesiometer which, since this is about 500g, would represent considerably increased contact pressure.

Strictly speaking, because of the neuro-physiology of the receptor types responsible for vibration perception, the threshold of detection should be tested at 2 frequencies according to the tuning of the Meissner and Pacinian receptors. Hayward and Griffin (1986) used two frequencies, 63 and 125Hz with a 6mm diameter tip and a contact pressure of 1 Newton. They found the 63Hz threshold to be less than the 125Hz threshold. They also investigated factors affecting vibration perception threshold and found this to be elevated in vibration white finger, advancing age and with decreasing finger temperature below 20°C. There was no change in threshold with smoking habit. Talbot et al (1968) also defined factors affecting vibration perception threshold and included contact area and shape, contact pressure, axis of movement, skin temperature, age and sex. Wiles et al (1991), in their large study of a normal population, included sex as an independent variable in their multiple regression equation; the effect was very small compared to that of age.

Could persistent articular nociceptive discharge influence articular mechano-receptor responsiveness?

A number of neuro-physiological pointers from the experimental literature indicate that chronic painful articular conditions may 'deceive' the sufferer by facilitating aberrant information from articular mechano-receptors. Cook et al (1987) have shown that persistent C fibre stimulation increased the receptor field size for cutaneous mechano-receptors. The 'responsiveness' also changed in that the number of action potentials at a given stimulus increased. It was suggested that the effect was mediated via interneurons in the dorsal horn of the spinal cord. Guilbaud (1985) has demonstrated similar changes in thalamic receptors indicating plasticity of neuronal connections both at cord and mid-brain level. This inter-relationship between the nociceptive and non-nociceptive systems has been recognised for some time and it was upon this that the gate control theory of pain was based (Melzack and Wall, 1965). The importance of descending pathways was also stressed by the latter authors who pointed out that nociceptive input from peripheral structures could not only be modulated at spinal cord level by afferent input in large myelinated fibres but also by descending pathways in the dorso-lateral funiculus. Lindblom and Mayerson (1976) have also demonstrated this effect in patients who had implanted dorsal column electrodes for chronic pain syndromes: stimulation of dorsal columns proximally produced profound analgesia in distal structures and, incidentally, an increase in vibration perception thresholds.

The preceding discussion would suggest that patients with chronic nociceptive activation due to inflammation and distortion of joint structures may have altered mechano-receptor thresholds mediated by interneurons in the dorsal horn of the spinal cord. The work of Cook et al (1987) suggests that such a persistent discharge would

cause a decrease in mechano-receptor thresholds and this might explain why patients perceive increased articular stiffness: for a given muscular effort receptors signalling tension in the joint capsule would provide proportionally more response without a parallel change in position which might be perceived at cortical level as an increase in joint stiffness.

What information is available on mechano-receptor thresholds in patients with chronic inflammatory arthritis? In osteoarthritis stataesthesis is aberrant (Barrett et al, 1990) and in anterior cruciate deficient knees both stataesthesis and kinaesthesis are fallible (Corrigan et al, 1992). Recently Ferrell et al (1992) have shown that stataesthesis in the PIP joint of the hand is distorted in patients with rheumatoid arthritis but no information on movement perception threshold is, as yet, available in this disease.

Measurement of movement perception threshold

a. Preliminary tests

The Leeds microprocessor controlled finger arthrograph (Howe et al, 1985) was modified for use as a movement perception device. For the measurement of stiffness the patient sits comfortably with the forearm pronated and resting on the arthrograph device. The arthrograph motor is mounted such that the shaft of the motor emerges vertically from the body of the arthrograph and is attached, horizontally, to a short aluminium arm measuring 5cm in length. A split plastic cylinder is attached to the arm and the third finger of the hand is secured within this plastic sleeve by a velcro strap; the MCP joint of the third finger is positioned such that the axis of the joint is in line with the axis of rotation of the shaft of the arthrograph motor. (see plate 4.1)

Plate 4.1

The Leeds Microprocessor Controlled Arthrograph.
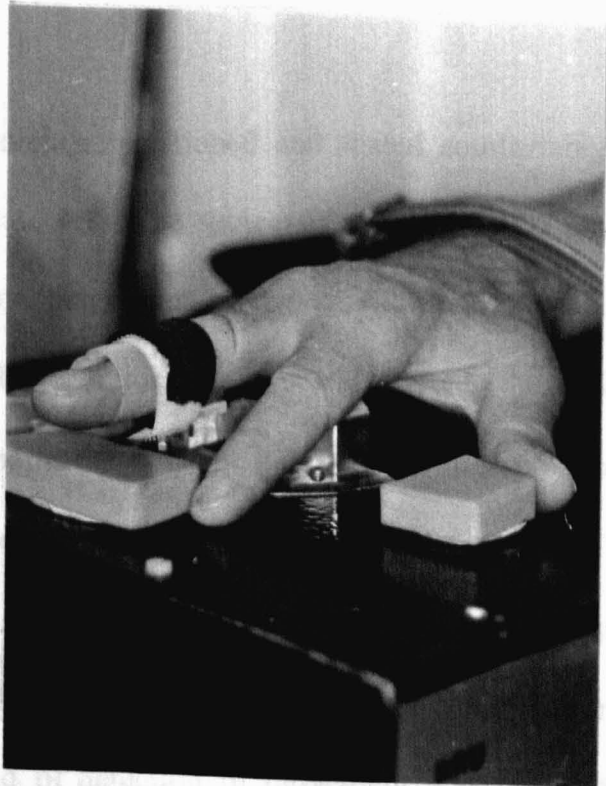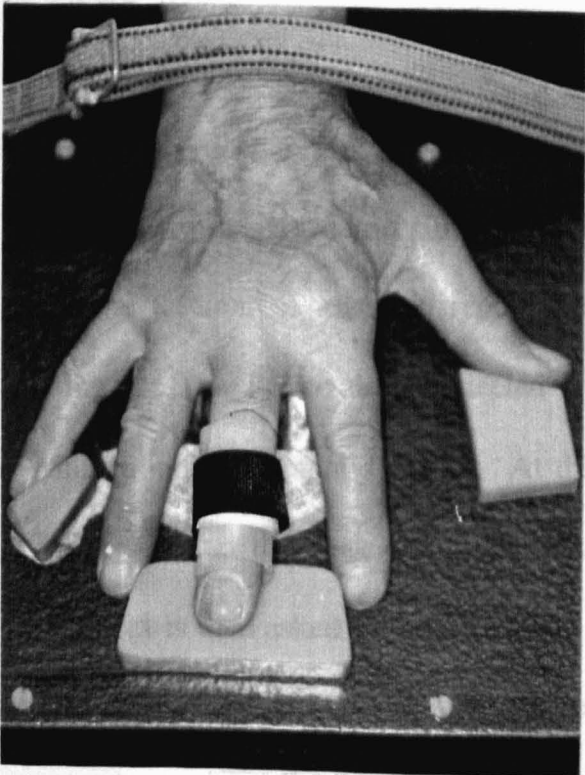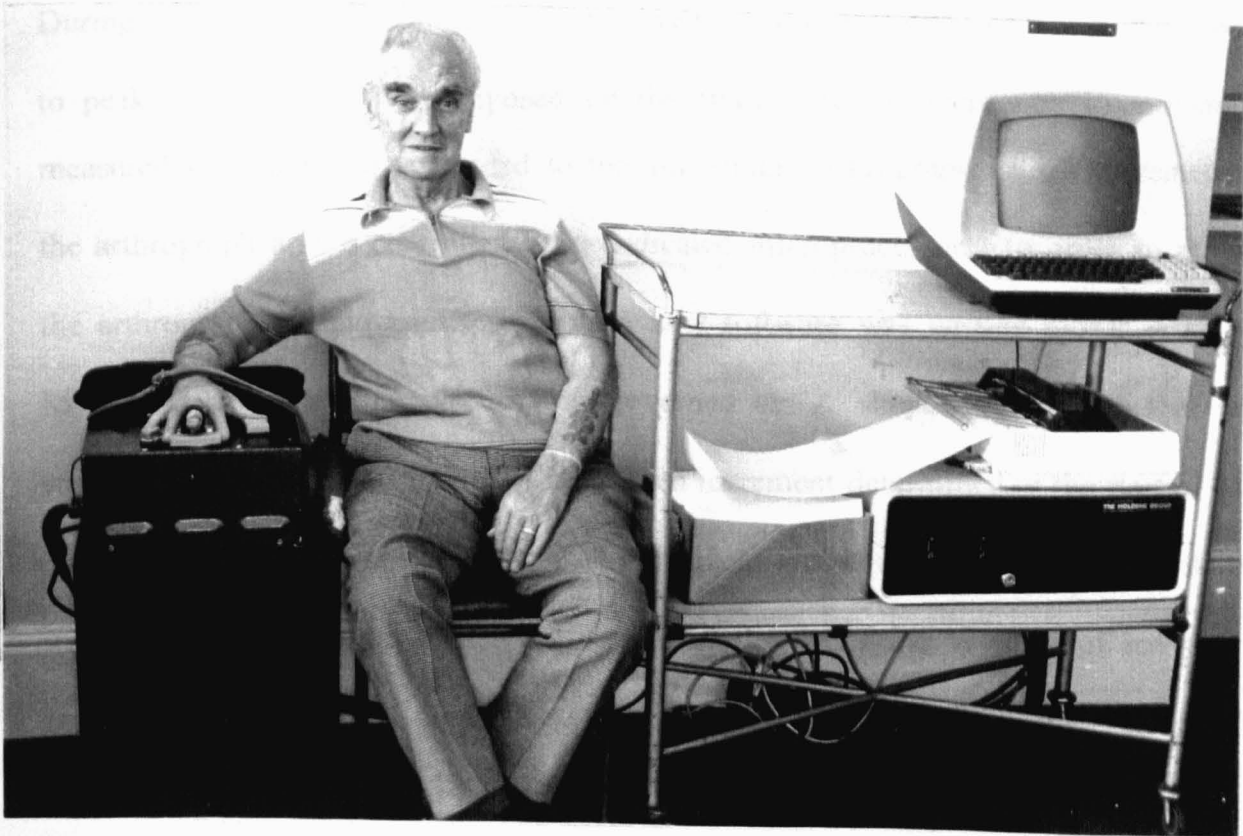
Plate 4.1

During stiffness measurements, cyclical movement at a frequency of 0.5Hz and a peak to peak amplitude of 8° is imposed on the finger and the resistance to movement measured by strain gauges bonded to the aluminium arthrograph arm. Movement of the arthrograph arm is controlled by a dedicated microprocessor. In order to modify the arthrograph for movement perception new software was written by Dr A Howe. Movement at the arthrograph arm was governed by 'Z' shaped signal such that each successive deflection was increased by a fixed increment determined at the start of each test. For each increment the velocity of movement was constant, but differed between increments such that the higher the increment the faster the velocity of movement. Increments were selected on the base unit of 'bits', one 'bit' representing 0.04°. The first three displacement cycles, using increments of 10 and 20 'bits', are illustrated in Figure 4.1.

The test procedure is as follows. The patient is positioned and seated comfortably as previously described and illustrated in Plate 4.1. The subject is advised on the nature of the test and is asked to report the first perception of movement in the examined finger. The increment is selected by the operator, and the test started, the patient indicating movement verbally. At this point the movement of the arthrograph arm is reversed and the peak amplitude achieved is recorded on the computer screen. The subject is then asked to indicate when all perception of movement disappears and again the movement of the arthrograph is reversed, the amplitude at reversal again appearing on the screen. In this way the threshold of detection of movement and the point at which movement is no longer perceptible are measured, usually by averaging three consistent results. As is common with studies of this kind the threshold of detection of movement is higher than that for the disappearance of movement. As expected, the

Figure 4.1

Diagrammatic representation of wave-form used in movement perception threshold tests.

Two tests are illustrated: in black, a test using an increment of 10 bits: first three cycles shown. In red, a test with increment of 20 bits: first three cycles shown.

Note time scale: the time to complete a cycle increases with the displacement. Approximately 10 cycles are completed in the first 10 seconds with each increment.

amplitude (bits)

1 sec.
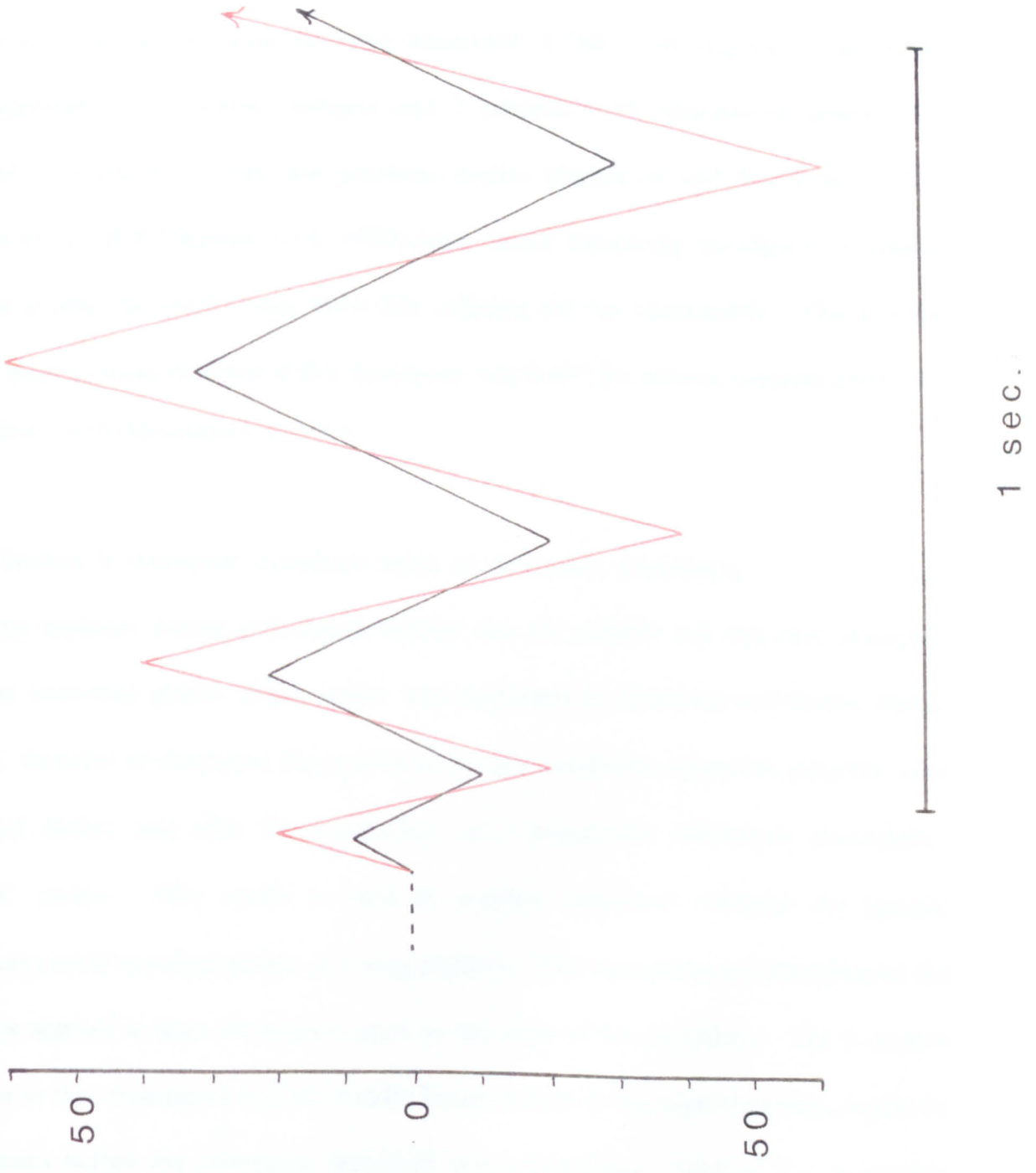
Figure 4.1

threshold was different for differing angular velocities (increments) as indicated in two normal subjects in Table 4.1.

b.   Measurements of movement perception in normal subjects and in patients with rheumatoid arthritis

All tests were performed using the same increment: 1 'bit', 0.46 deg/sec. The results of measurements in 6 normal subjects and 3 subjects with rheumatoid arthritis are presented in Table 4.2. Note that previous studies (Gandevia and McClosky, 1976, Kokmen et al, 1978, Skinner et al, 1984) have found increasing perception threshold with age so that the results from these few subjects are not comparable. The average angular displacement detected at this increment was 0.69° for normal subjects and 0.96° for subjects with rheumatoid arthritis.

c.   Studies to determine cutaneous input to movement perception.

It became apparent during preliminary studies that all subjects felt that skin sensation from the enclosing plastic finger holder was important in detecting movement during the test. In order to determine the magnitude of this cutaneous input two subjects were measured before and after the application of a proprietary cutaneous anaesthetic, 'EMLA' cream. This cream is used to prepare cutaneous surfaces for painful procedures such as venepuncture in young children. The manufacturers recommend the cream is applied at least 60 minutes prior to the start of the procedure. The 2 normal subjects in this experiment had the middle finger coated in the anaesthetizing cream for 60 minutes before the perception threshold was remeasured. Despite this precaution subject B felt that the anaesthetizing cream had not been effective and that perception of movement was still possible by the pressure of the finger holder on the skin of the

Table 4.1

Movement perception threshold and angular velocity. Figures are in 'bits' and represent the average of three tests.

Increment	Angular Velocity (deg/sec)	Threshold (deg)			
		Subject 1		Subject 2	
		Increasing	Decreasing	Increasing	Decreasing
1	0.46	13.3	10.3	13.7	8.3
2	0.92	16.3	11.0	17.5	8.0
3	1.41	20.0	11.0	19.0	11.0
4	1.89	26.0	13.0	22.3	12.0
5	2.35	-	-	24.0	13.0

Table 4.2

Movement perception threshold (MPT) in normals (N) and in rheumatoid arthritis (RA). Figures represent the average of three or four tests. Angular velocity = 0.46 deg/sec.

Subject	Age	Sex	Diagnosis	MPT ('bits')		MPT (deg) appearance (increase) only
				Increasing	Decreasing	
1	45	M	N	13.6	8.3	0.60
2	35	M	N	14.3	10.5	0.63
3	33	F	N	13.3	10.3	0.58
4	36	F	N	14.5	8.8	0.64
5	42	M	N	17.0	13.5	0.75
6	50	F	N	21.7	18.7	0.95
Mean	40.2		N	15.73	11.68	0.69
1	46	F	RA	15.7	10.0	0.69
2	50	F	RA	30.5	28.0	1.34
3	70	F	RA	21.6	19.3	0.85
Mean	55.3		RA	22.60	19.1	0.96

finger. The results for subject A were as follows: before local anaesthetic, threshold up, 13.6 'bits', down 8.3 'bits'; after local anaesthetic threshold up 15 'bits', down 13.3 'bits'. For subject B the corresponding figures were: before local anaesthetic threshold up 13.3 'bits', down 10.3 'bits'; after local anaesthetic threshold up 9.3 'bits', down 8.7 'bits'.

Further experiments were conducted with a modified finger attachment as illustrated in plate 4.2. In this case the finger was secured at the nail, by means of a small (7x7mm) double-sided adhesive patch, to a short strip of copper plate, the position of which was adjustable in order to accommodate fingers of different lengths. With this method of attachment the subject retains some cutaneous information from the nail bed but it was found that this could be largely removed by the application of a rubber tourniquet just proximal to the nail bed (see Plate 4.3). The function of this tourniquet was to serve partly as a distraction (it was uncomfortable) and partly to cause congestion in the distal finger tip which again provided distracting cutaneous information. In spite of this precaution, it was felt necessary to exclude any remaining cutaneous information by performing digital nerve block using 1% local anaesthetic to the digital branches of the palmar nerve at both sides of the base of the finger. Using an identical test procedure, at an increment of 1 'bit', the results for these three different conditions in 6 subjects are given in Table 4.3. Attachment at the end of the digit did not result in a change of movement perception threshold and the results with the rubber tourniquet in place are substantially the same. After digital nerve block there is a significant rise in perception threshold confirming that cutaneous information at the point of attachment of the finger contributes to movement detection.

Plate 4.2

Modified finger attachment for the arthrograph arm.

Plate 4.2

Plate 4.3

The use of a rubber tourniquet to remove touch sensation from the nail bed.

Plate 4.3

Table 4.3

Effect of digital nerve block on MPT (detection threshold) using both circumferential and terminal finger fixation. Angular velocity 0.46 deg/sec. Figures are in 'bits' and represent the average of three tests.
CFH = circumferential fixation.
AFH = fixation at finger nail.
AFH/RB = use of rubber tourniquet proximal to nail bed.

Subject Number	Before local anaesthetic			After local anaesthetic	
	CFH	AFH	AFH/RB	CFH	AFH
1	6.0	8.3	8.7	10.0	9.3
2	9.6	7.0	10.0	10.7	18.0
3	15.3	10.7	16.0	20.3	26.0
4	10.3	16.7	10.0	13.0	20.3
5	13.3	7.0	9.5	-	7.3
6	13.6	7.0	9.0	-	8.7
Mean	11.35	9.45	10.53		14.9
s.d	3.38	3.83	2.72		7.6

Measurement of vibration perception threshold

Vibration perception was measured using a commercially available device, the Biothesiometer (Biomedical Instrument Co, Newbury, Ohio). This is a hand-held device which provides a vibratory stimulus through a polyethylene stylus with a contact area of $1cm^2$ at a fixed frequency of 100Hz. The amplitude of vibration can be varied using a simple rheostat provided with the device and the voltage is displayed on a linear scale. A calibration table, with which to convert displayed voltage to microns of displacement at the stylus tip, is provided with the device. Both contact area and contact pressure have been shown to be important in measuring vibration perception (Hayward and Griffin, 1986) and for this reason the manufacturers recommend using the weight of the device to produce a standard contact pressure. The device weighs 500 grams and when hand held resting on the subject weighs approximately 350 grams, providing a contact force of approximately $3N/cm^2$.

The calibration of the Biothesiometer was checked using a piezo-electric accelerometer (4292 Bruel and Kjaer) attached with beeswax to the tip to the vibration probe. The accelerometer was attached via a screened cable to a pre-amplifier and then via a low pass filter with a corner frequency of 240 Hz to a frequency analyzer (type 2570/P, NE Technology Ltd). Signals were sampled at a frequency of 30 kHz for 10 cycles and the signal analyzed to provide acceleration (root mean square) recorded for each setting of the linear scale. The Biothesiometer was calibrated both unloaded, with the device supported, and loaded as in the normal test procedure with the accelerometer interposed between the biothesiometer stylus and the finger (see Plates 4.4 and 4.5). Since the geometry of this arrangement may have altered the displacement of the stylus a small plastic cap was manufactured to fit over the accelerometer and provide the same contact

Plate 4.4

Calibrating the biothesiometer with the tip unloaded.
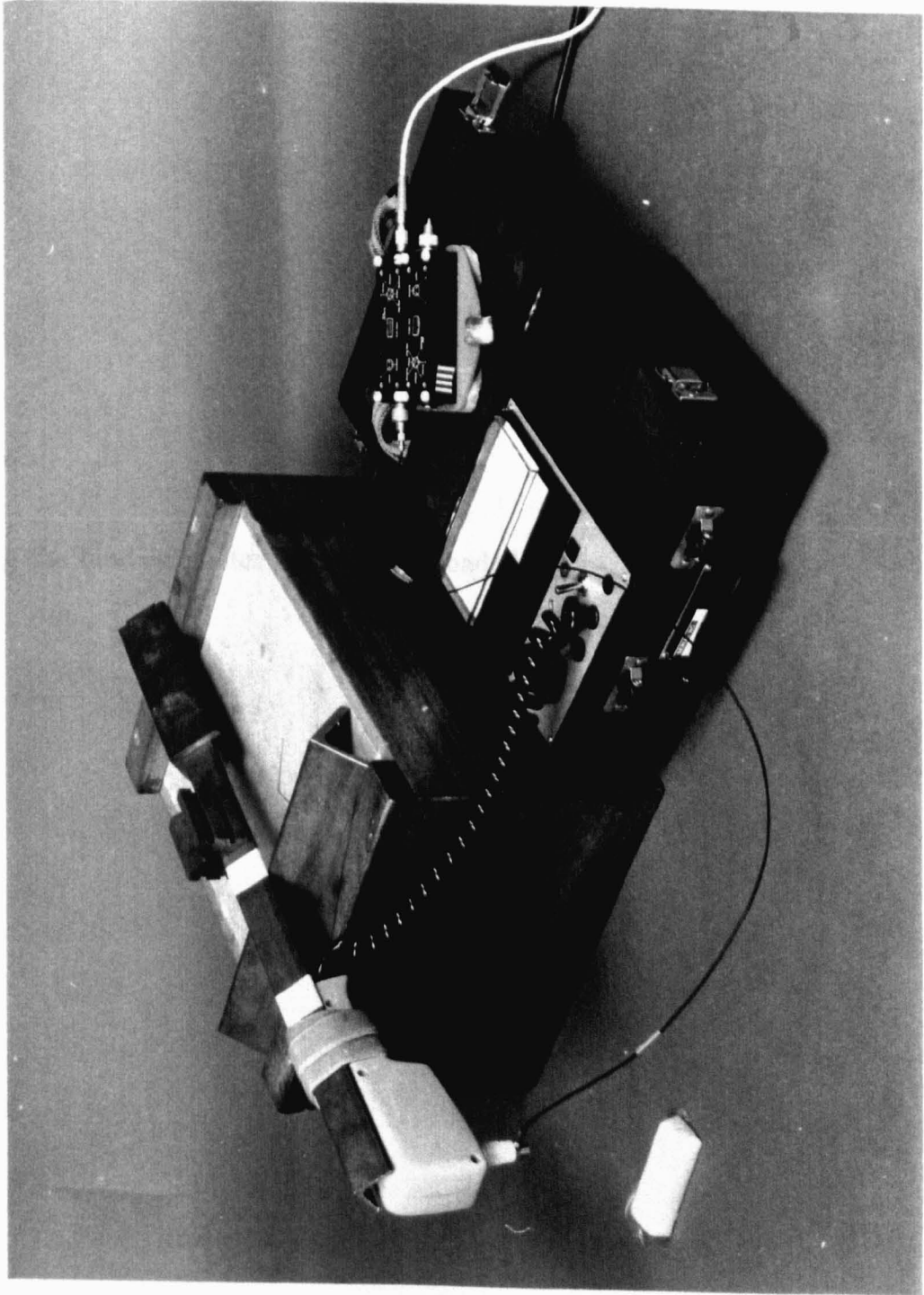
Plate 4.4

Plate 4.5

Calibrating the biothesiometer with the tip loaded.
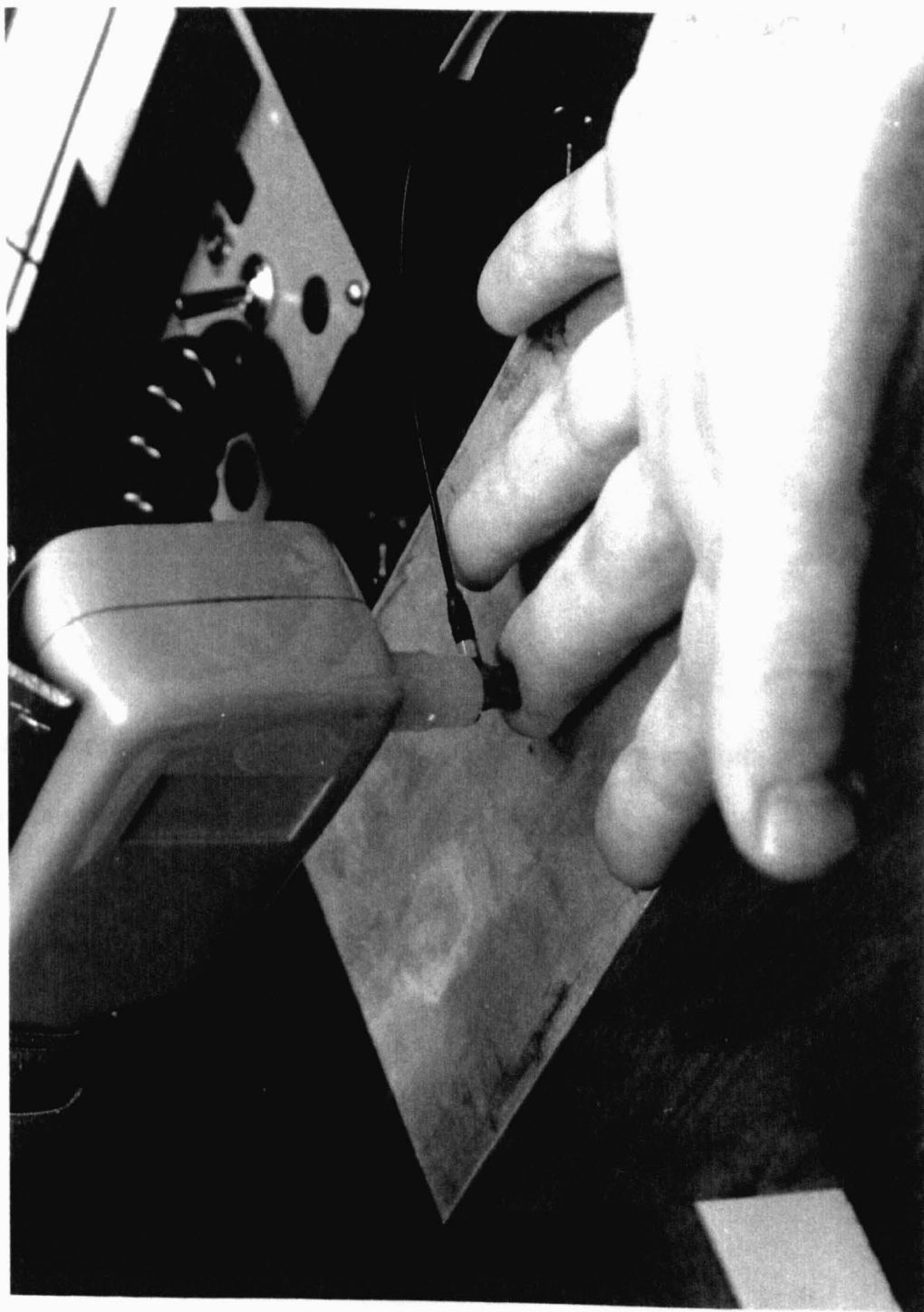
Plate 4.5

Figure 4.2

Diagrammatic representation of the plastic cap attached to the biothesiometer stylus in order to maintain contact geometry during calibration.
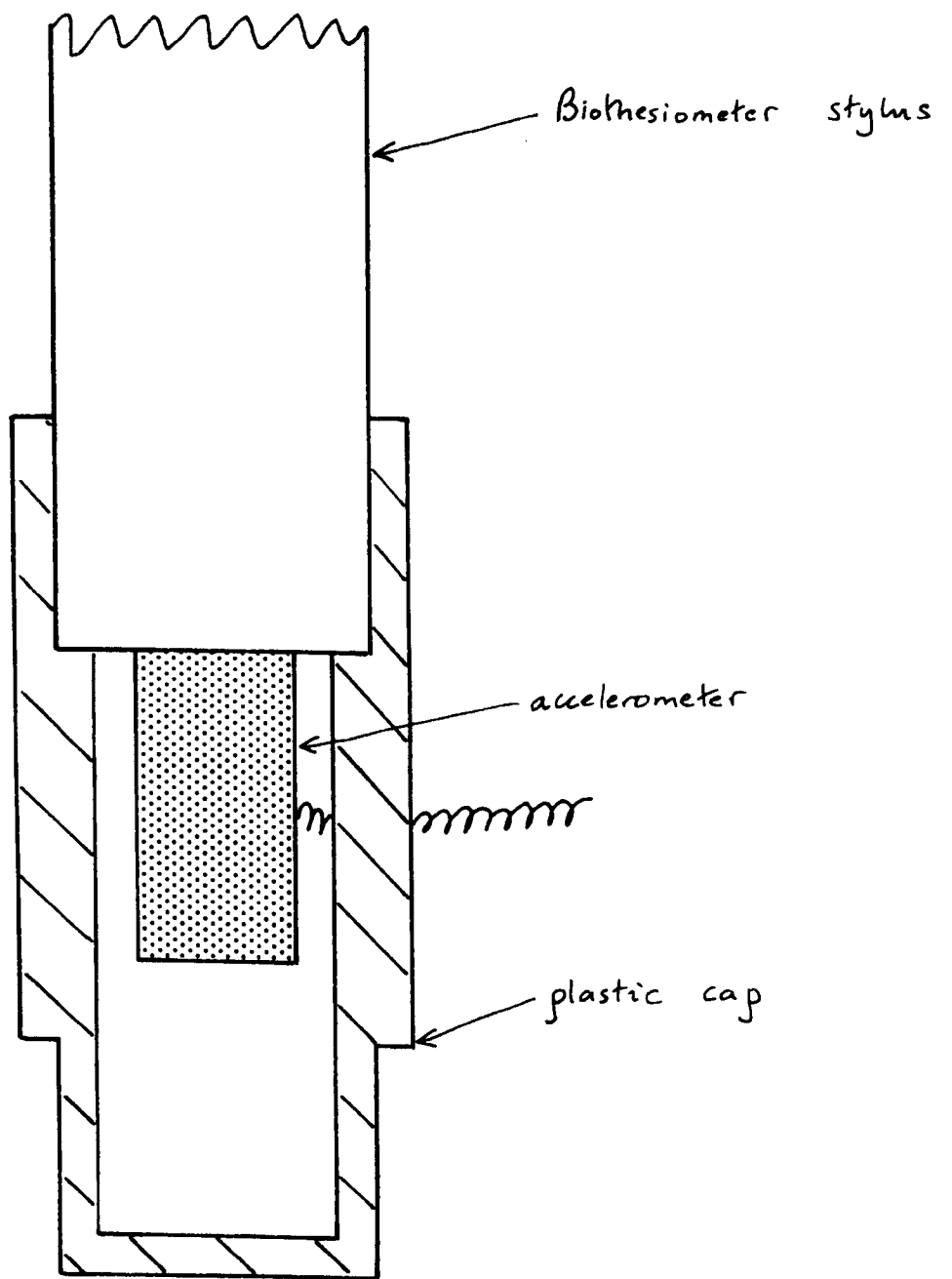
Figure 4.2

area at the finger, as illustrated in Figure 4.2. The results of these experiments are presented in Table 4.4 and illustrated graphically in Figure 4.3. It can be seen that the manufacturer's figures differ substantially from those measured during the experiments described above, particularly at the lower end of the scale. Furthermore, the measured calibration curves were particularly 'flat' between voltage points 2 and 10, within which 50% of all normal perception thresholds are found. The calibration curve in the unloaded condition displays resonance at the higher amplitudes, possibly as a result of the experimental geometry.

b. Measurement of vibration perception threshold in normal and rheumatoid arthritis

The subject group comprised 50 patients hospitalised with rheumatoid arthritis (16 males, 34 females). Patients were excluded if there was a history of vibration exposure, Raynaud's phenomenon, median nerve compression, cervical myelopathy, overt clinical peripheral neuropathy, or concurrent illness with a disease likely to cause a change in sensory threshold (eg: diabetes mellitus). The patients were divided into active or inactive disease according the state of the involved finger joints using previously established criteria (Helliwell et al 1988a). If soft tissue swelling and pain were present in the MCP3 joint, patients were considered to have active disease in this joint. The finger pulp of the middle finger of the dominant hand was tested in all cases; this finger was selected because the proximal interphalangeal and the metacarpophalangeal joints are commonly involved by the rheumatoid process and because the previous studies of joint stiffness were carried out on this digit (Helliwell et al, 1988a). In 21 cases, for comparison, the vibration perception threshold of the thumb pulp on the same hand was

Table 4.4

Calibration of Biothesiometer

Biothesiometer Scale reading (volts)	Peak amplitude (microns)			Manufacturers calibration amplitude (microns)
	Unloaded	Loaded	Loaded with cap	
0	1.23	-0.42	1.91	0.00
2	1.34	0.95	1.93	0.04
4	1.89	0.89	1.95	0.16
5	2.26	1.27	1.94	0.25
6	2.71	1.20	1.91	0.36
8	4.62	1.28	2.09	0.66
10	6.61	1.72	2.32	1.00
20	24.50	4.37	5.15	4.00
30	50.97	9.28	12.49	9.20
40	94.16	17.27	23.22	16.40
50	152.30	28.18	*	25.50

* not measured because resonance occurred when the system, including the cap, was tested unloaded (max. amplitude = 0.4mm).

Figure 4.3

Calibration curves for biothesiometer.

Three conditions are illustrated:

Manufacturers calibration figures (M).

Calibration figures with tip loaded (L).

Calibration figures with tip loaded with plastic cap to maintain contact geometry (C).

(a)   over full biothesiometer scale.

(b)   over lower end of scale.

The curves for calibration with the stylus tip unloaded are not presented because of the resonance in this condition (see Table 4.4).
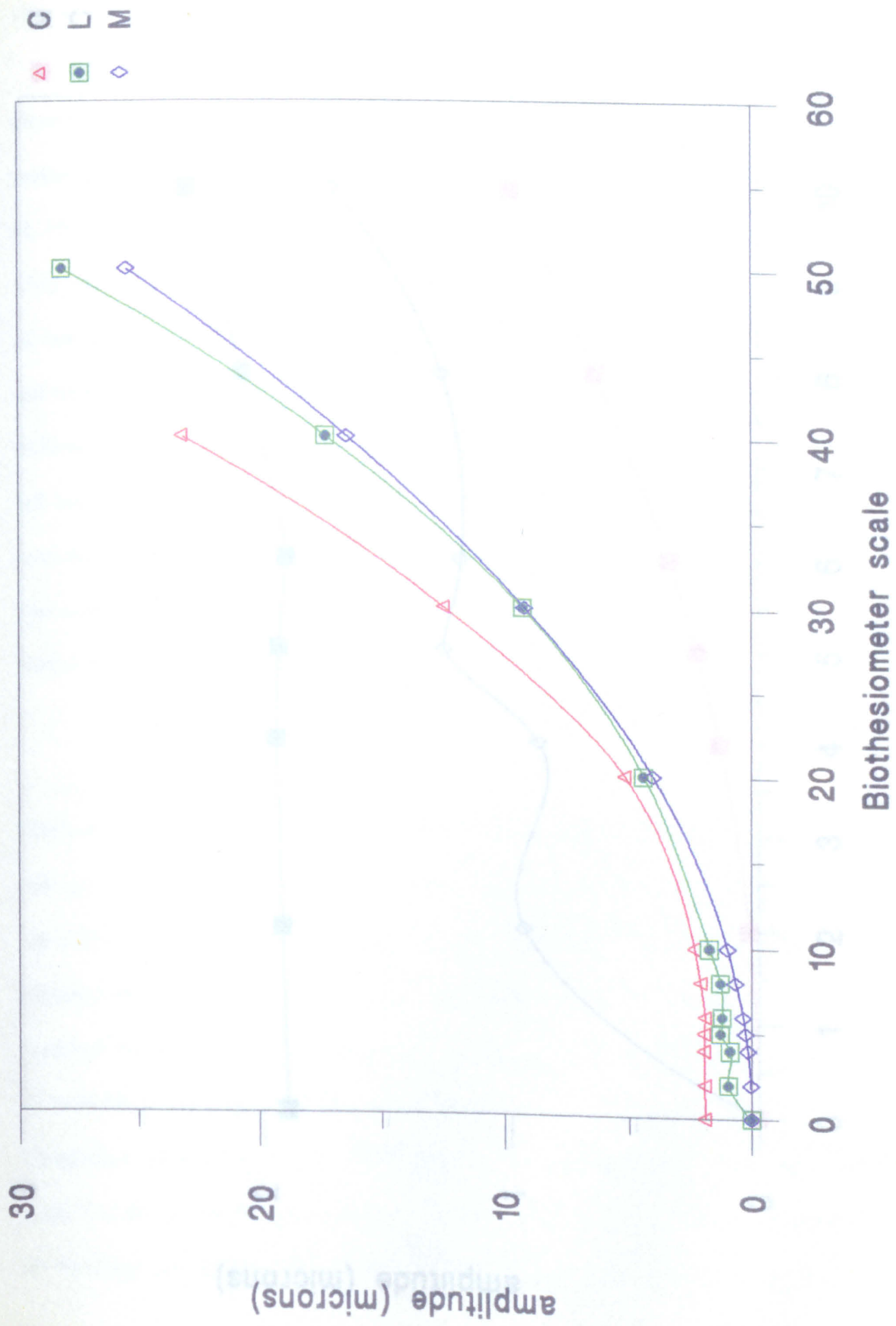
Figure 4.3 a
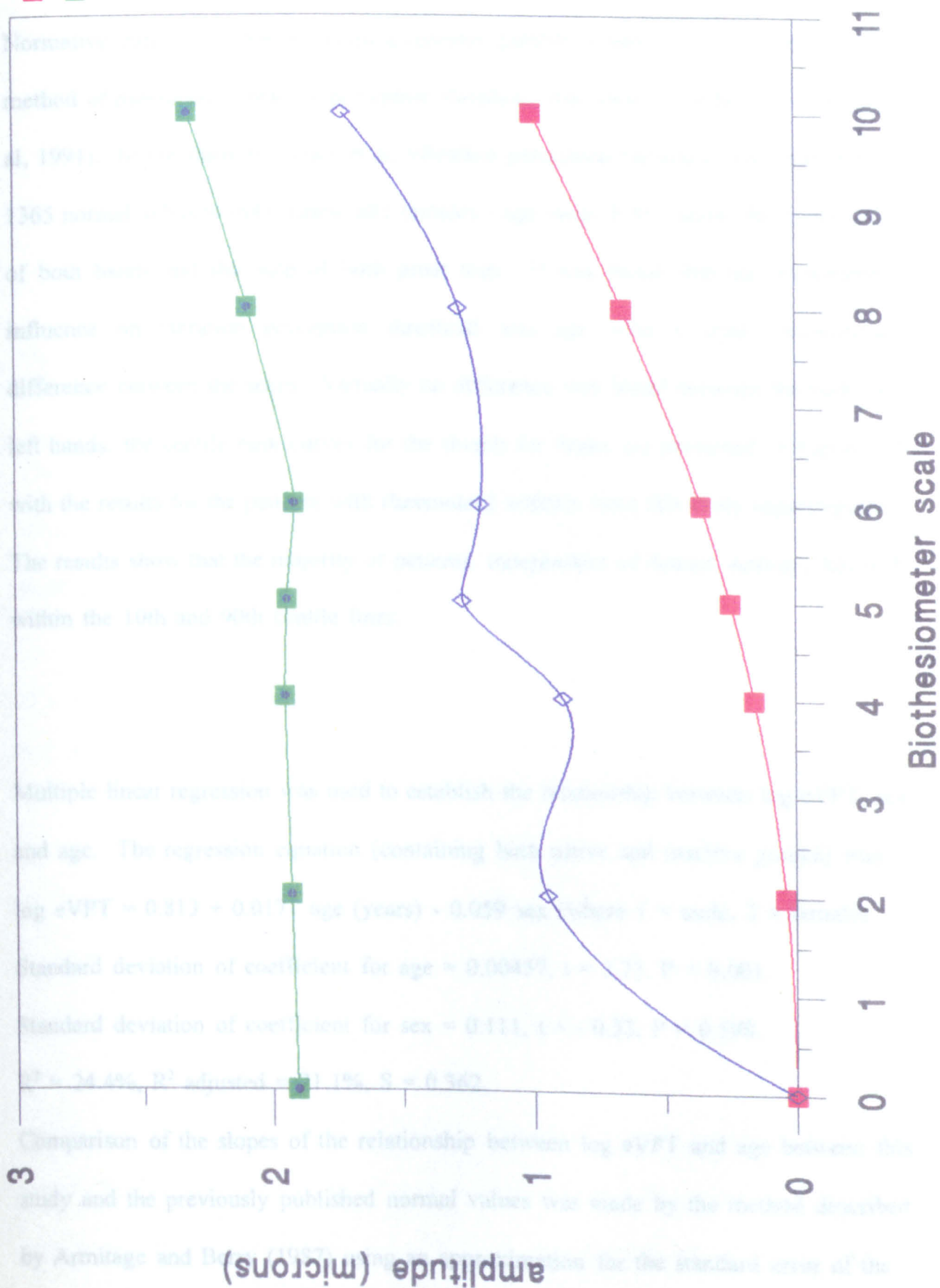
Figure 4.3b

also measured.

Normative data were obtained from a recently published series in which an identical method of measuring vibration perception threshold was used at our hospital (Wiles et al, 1991). In the study by Wiles et al, vibration perception threshold was measured in 1365 normal subjects (684 males, 681 females - age range 8-91), using the thumb pulp of both hands and the pulp of both great toes. It was found that the predominant influence on vibration perception threshold was age, with a small insignificant difference between the sexes. Virtually no difference was found between the right and left hands; the centile rank curves for the thumb for males are presented in Figure 4.4 with the results for the patients with rheumatoid arthritis from this study superimposed. The results show that the majority of patients, independent of disease activity, fall well within the 10th and 90th centile lines.

Multiple linear regression was used to establish the relationship between log eVPT, sex and age. The regression equation (containing both active and inactive groups) was:

log eVPT = 0.813 + 0.0171 age (years) - 0.059 sex (where 1 = male, 2 = female).

Standard deviation of coefficient for age = 0.00457, t = 3.73, P = 0.001.

Standard deviation of coefficient for sex = 0.111, t = - 0.53, P = 0.598.

R^2 = 24.4%, R^2 adjusted = 21.1%, S = 0.362.

Comparison of the slopes of the relationship between log eVPT and age between this study and the previously published normal values was made by the method described by Armitage and Berry (1987) using an approximation for the standard error of the

Figure 4.4

The 10th, 50th and 90th centile lines for vibration perception threshold in normal subjects as a function of age (Wiles et al 1991). Superimposed are the results for 50 patients with rheumatoid arthritis.

□ = active rheumatoid arthritis.

◊ = inactive rheumatoid arthritis.

Vibration threshold

active
inactive

90
50
10

20

10

0

10 20 30 40 50 60 70 80 90

Age (years)
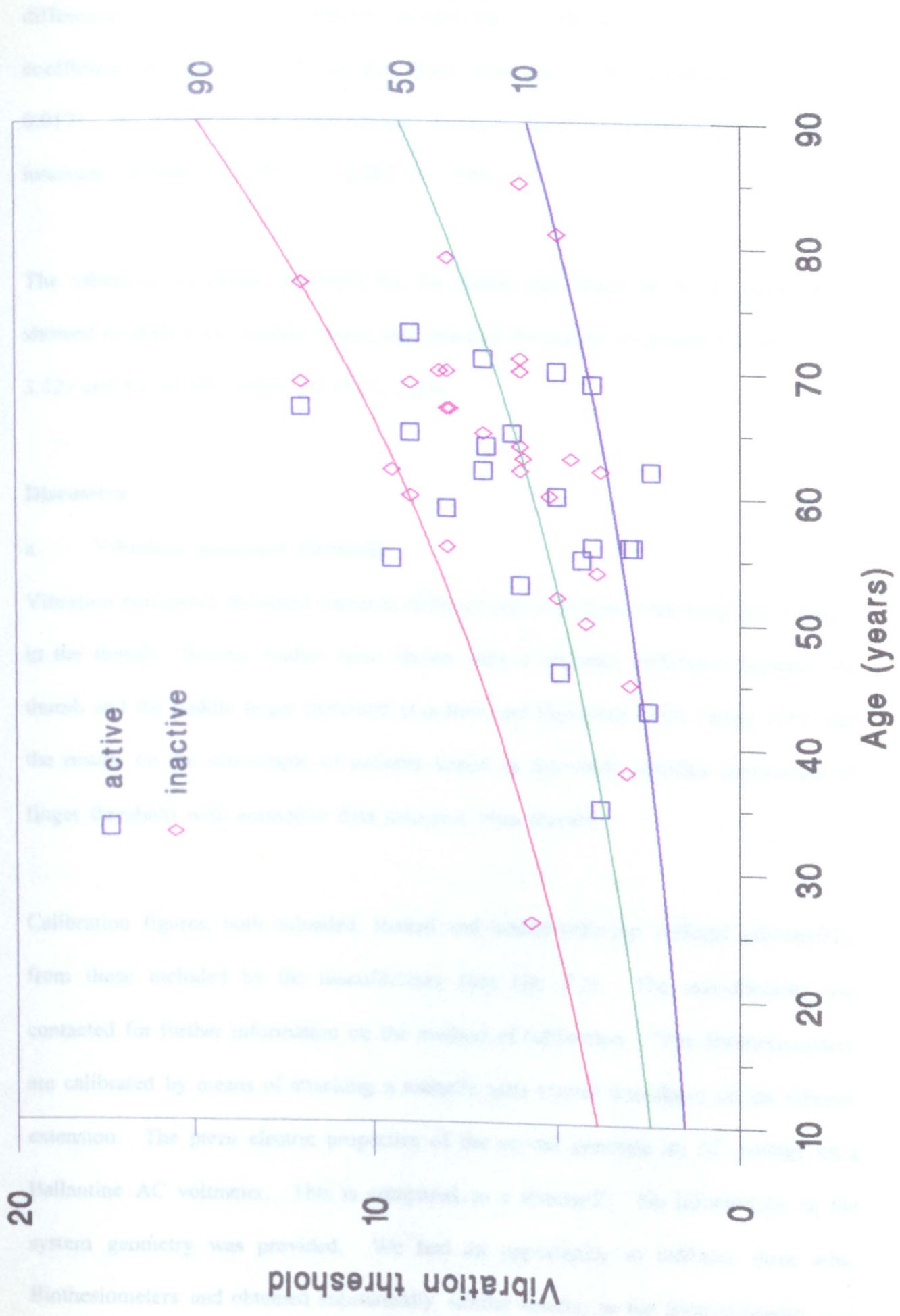
Figure 4.4

difference between slopes. Results showed that for Wiles et al, intercept = 0.68, coefficient for age = 0.0167, for this study intercept = 0.81, coefficient for age = 0.0171. No difference was demonstrated between these coefficients (95% confidence intervals, -0.0094 + 0.0086, $t = -0.087$, P = NS).

The vibration perception threshold for the thumb and finger in the 21 cases tested showed no difference: median (mean and standard deviation) for thumb 5.2 units (5.92, 3.52) and for middle finger 5.2 (5.67, 2.43).

Discussion

a.   Vibration perception threshold.

Vibration perception threshold varies at different sites throughout the body but is lowest in the thumb. Several studies have shown only a minimal difference between the thumb and the middle finger threshold (Laidlaw and Hamilton 1937, Gregg 1951) and the results on the sub-sample of patients tested in this study justifies comparison of finger threshold with normative data obtained from thumbs.

Calibration figures, both unloaded, loaded and loaded-with-cap differed substantially from those included by the manufacturer (see Fig. 4.3). The manufacturer was contacted for further information on the method of calibration - "The Biothesiometers are calibrated by means of attaching a rochelle salts crystal transducer on the vibrator extension. The piezo electric properties of the crystal generate an AC voltage on a Ballantine AC voltmeter. This is compared to a standard". No information on the system geometry was provided. We had an opportunity to calibrate three other Biothesiometers and obtained substantially similar results, so the Biothesiometer used

in these experiments was unlikely to be faulty. The 'flat' initial part of the measured (loaded) calibration curve is of concern since, according to Wiles et al (1991), 50% of normal subjects up to the age of 70 have thresholds less than 8 (see Fig. 4.4). Perhaps a more relevant way of quoting vibration threshold using this technique is to express the result as a range: threshold A, up to 10, threshold B, 11 to 15, threshold C, 16 to 20, and so on. However, recording the results in this way would only rationalise the detection of an increased threshold - this device is insensitive to threshold reductions.

Although formal comparison of the intercept could not be made, the superimposed data and the regression equations suggest that this sample is equivalent to the previously tested normal group in respect of vibration perception threshold. With this result in mind, what conclusions can be made with reference to the hypothesis suggested in the introduction? It is likely that the Biothesiometer tests dynamic vibration perception in Pacinian corpuscles of the glabrous skin, yet the hypothesis suggests that chronic articular nociceptive stimulation alters articular mechano-receptor thresholds. Ideally, therefore, vibration thresholds should have been measured directly adjacent to the involved joint, but unfortunately normative data are not available for sites proximal to the finger tip. Even so it could be argued that an inappropriate mechanical stimulus was employed: it is likely that slowly adapting Ruffini type articular receptors as well as rapidly adapting Pacinian receptors are involved in signalling stiffness. Nevertheless, because experimental studies in animals have shown widespread receptor field changes in rapidly adapting mechano-receptors as a result of chronic nociceptor stimulation, the author believes that the stimulus used was appropriate, but accepts that the site may be inappropriately distant from the source of inflammation.

b.   Movement perception threshold.

Although the magnitude of angular displacement for movement perception was found to be similar to that previously recorded, the technique was felt to be unsatisfactory for a number of reasons.

1.   Contrary to expectations an increase in perception threshold was found with increasing angular velocity (see Table 4.1). Ferrell has previously shown that increasing angular velocity is associated with decreasing threshold for perception of movement. This discrepancy may have resulted from the different methods used to measure movement perception. When the patient signals perception of movement the software records the maximum amplitude recorded at this point. Because of the relatively poor resolution of the system it is likely that a higher threshold will result when using a larger increment. This is illustrated in Figure 4.5.

2.   Although the results for movement perception in the normal subjects tested compare favourably to those previously recorded by Kokmen (1978) in the MCP joint (0.69° for this study, 0.658° in a group of subjects aged 19-34, by Kokmen et al), it is clear that the perception of movement in this study is dependent on cutaneous information at the point of attachment of the digit.

3.   Even with modification of the method of finger attachment, information from receptors other than those in the joint are important in perception of movement. (See Table 4.3).

Figure 4.5

An explanation of the apparent increase in movement perception threshold with increasing angular velocity.

Black line: tests at an increment of 10 bits.

Red line: tests at an increment of 20 bits.

If the movement perception threshold of this subject is 25 bits detection of movement would be signalled at point A at an increment of 20 bits, and point B at an increment of 10 bits. The computer will 'register' a threshold of 40 bits at the higher increment and 30 bits at the lower increment.

MPT = movement perception threshold.

MPT

MPT

B

A

1 sec.

60 40 20 0 20 40 60

amplitude (bits)
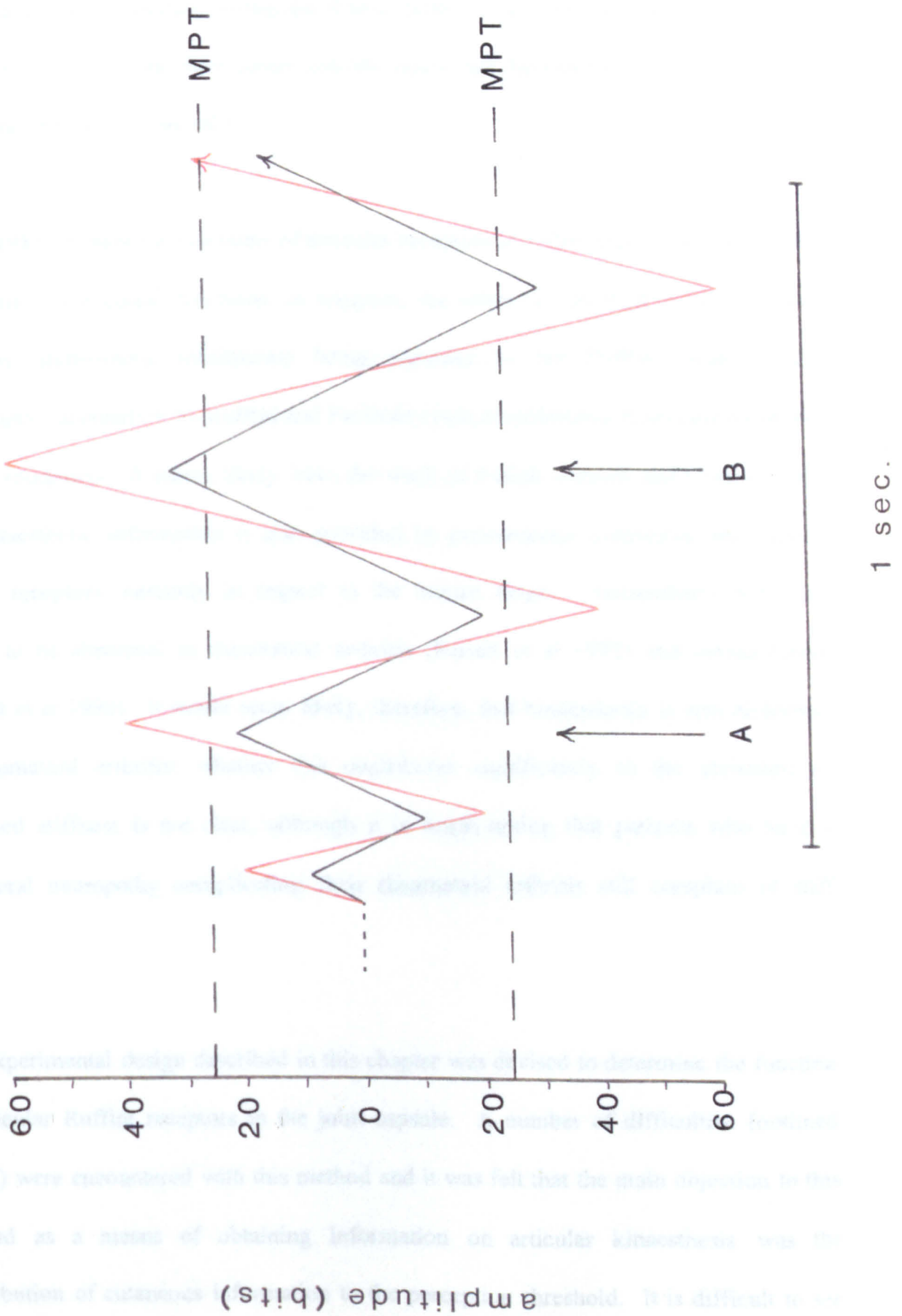
Figure 4.5

4. Most subjects complained of difficulty in making precise assessments of the appearance of movement in their fingers. This was mostly because of background vibration within the device, largely due to mains electricity (50 Hz). One subject with rheumatoid arthritis could not distinguish the appearance of movement because of this.

Wyke (1981) defines the functions of articular receptors as reflexogenic, perceptual and nociceptive. Perceptual functions, he suggests, are subserved by Ruffini and Pacinian receptors, stataesthetic information being provided by the Ruffini receptors and kinaesthetic information by Ruffini and Pacinian (with contributions from cutaneous and muscle receptors). It seems likely from the work of Ferrell (Ferrell and Craske 1992) that stataesthetic information is also provided by peri-articular cutaneous and muscle spindle receptors, certainly in respect to the human finger. Stataesthesis has been shown to be abnormal in rheumatoid arthritis (Ferrell et al 1992) and osteoarthritis (Barrett et al 1990). It would seem likely, therefore, that kinaesthesis is also abnormal in rheumatoid arthritis: whether this contributes significantly to the sensation of increased stiffness is not clear, although it is worth noting that patients who have a peripheral neuropathy complicating their rheumatoid arthritis still complain of stiff joints.

The experimental design described in this chapter was devised to determine the function of articular Ruffini receptors in the joint capsule. A number of difficulties (outlined above) were encountered with this method and it was felt that the main objection to this method as a means of obtaining information on articular kinaesthesis was the contribution of cutaneous information to the perception threshold. It is difficult to see

how these problems can be overcome. Clearly, it is unethical and impractical to perform digital nerve blocks for all test procedures. Possibly the use of a tight fitting finger stall which provides a uniform pressure over the whole area of the finger might distract the subject from other cutaneous stimuli during the test; it would be possible to provide this by using a pneumatic bag like the plastic inflatable fracture splints, but such a system would present difficulties in attaching the finger to the arthrograph arm.

Summary

Vibration perception thresholds have been measured in a group of subjects with rheumatoid arthritis and have been found to be equivalent to a group of normal subjects. This result does not support the hypothesis that altered mechano-receptors thresholds, due to chronic nociceptive stimulation, are important in the experience of joint stiffness in rheumatoid arthritis.

Articular mechano-receptors may be responding both appropriately, to capsular distension and distortion, and inappropriately, as a result of synovial inflammation. Further data on articular mechanoreceptor thresholds signalling kinaesthesis are required, but many practical difficulties remain to be overcome.

CHAPTER 5

FACTORS AFFECTING GRIP STRENGTH MEASUREMENT AND RELATIONSHIP TO MUSCLE MORPHOLOGY IN NORMALS AND IN PATIENTS WITH RHEUMATOID ARTHRITIS

Introduction

Literature Survey

> Techniques for measuring strength

> Factors affecting strength measurements

> Strength measurement in rheumatoid arthritis

> Relationship between muscle morphology and strength measurements

Methods

> Grip strength measurement

> Muscle morphology measurement

Results

> Isometric grip strength and dynamic qualities in rheumatoid arthritis and in normals

> Cross-sectional area of forearm muscles in normals and rheumatoid arthritis

> Relationship between grip strength, cross-sectional area, pain and deformity in rheumatoid arthritis.

Discussion

Summary

Introduction

It seems clear that muscles and their associated tendons provide a significant contribution to passive joint stiffness as measured by the arthrograph. The contribution varies from joint to joint, possibly being as high as 70% at the knee and 50% at the finger in flexion/extension. In rheumatoid arthritis there is a marked reduction in isometric strength and, if this were reflected by a concomitant decrease in muscle bulk, this would have a noticeable effect on stiffness measurements. However, forearm circumferences, measured in rheumatoid arthritis, were found to be no different from normals by Yung et al in 1986 (see Table 2.5). It is possible that there are qualitative deficiencies in muscle in rheumatoid arthritis to account for this paradox, but other factors which may affect grip strength could account for this result, including joint pain, joint deformity and abnormalities of tendons. In this chapter, following the literature survey, a study of isometric muscle strength in normal subjects and in patients with rheumatoid arthritis is described. The relationship between muscle cross-sectional area and grip strength is determined in both patient and normal groups, and other factors such as pain and deformity are taken into consideration. In Chapter 6, these experiments are continued with measurements of qualitative differences in muscles in patients and normal controls.

Literature Survey

a)   Techniques for measuring strength.

Most of the data available on isometric strength have been made using rigid spring-loaded devices or cable tensiometers (Bechtol 1954, Hunsicker and Donnelly 1955).

As far as grip strength is concerned, the devices are often adjustable for different hand sizes (Montoye and Faulkner 1964). The instruments devised for use in community and industrial surveys have been found unsuitable for rheumatic hands, in which strength may be only a small percentage of normal and in which pain may be a limiting factor. Following the introduction of the pneumatic dynamometer by Geckler (1939), this system was found suitable for arthritic hands and was successfully adapted by Wright (1959a) to measure strength in a series of patients with rheumatoid arthritis.

Although the pneumodynamometer is cheap, portable and acceptable to most patients with rheumatoid arthritis, the device has certain limitations. Intra-observer variation is low only with experienced observers, suggesting that they unconsciously smooth the results obtained. This is to be expected in a test where the peak value is only seen for a brief period: during an isometric squeeze marked fluctuation of the maximum value occurs. This problem can be overcome by the use of peak hold facilities as suggested by Fernando and Robertson (1982). Grindulus and Calverley (1983) have shown that patients with rheumatoid arthritis do not like sustaining maximal isometric grip for longer than 5 seconds, their patients preferring a briefly attained maximum grip strength.

Other practical and theoretical problems occur with pneumodynamometers. The standard pneumodynamometer design consists of an air-filled rubber bag which is manipulated by the patient. The pressure within the closed system is a function of the force exerted and the area over which it is applied; this means that the same pressure can be achieved by the use of a small force over a large area as with a large force over a small area. In other words the result would depend on the type of grip the patient

applies to the bag or bulb. A further limitation is the non-linearity of the system: air is compressible. Finally, many grip strength assessments are now made using an air-filled bag attached to an aneroid manometer, the latter having a tendency to become inaccurate with time.

In a move away from air-filled devices Dickson et al (1972) described a well-designed cantilevered spring-loaded device for measuring pinch grip strength and the force of flexion of the individual extended fingers. An improvement on this design was described by Carus et al (1985) who described the use of a strain-gauge device in which the position of the hand-held transducer could be altered according to hand size and in order to measure different grips such as pinch grip, key grip. Further modification of this idea and extension into the practical sphere was provided by Jones et al (1985) who designed an apparatus capable of measuring grip strength, individual finger force, key twist and lateral pinch and also pan and kettle lifting grip and forces.

Strain gauged devices are much more precise measures of force and have enabled an assessment of the relevant contribution of different movements to total hand strength. For example, of the three pinch grips available, (i) the prehensile pinch thumb pulp to finger pulp; (ii) the tripod pinch thumb pulp to two finger tips; (iii) the lateral or key pinch, thumb pulp to side of index finger, key pinch has been shown to exert the greatest force partly because the index finger can be supported by the other fingers providing a buttress against which the thumb can act (Walker et al, 1978, Evans and Lawton, 1984).

Electronic strain gauges also provide an analogue output from which peak hold and on-

line analysis facilities can be obtained. This approach was originally made by the Dunedin group (Laws et al, 1979 and Myers et al, 1979) who connected a standard sphygmomanometer bag via a pressure transducer to a microprocessor which sampled pressure readings every 20 milli-seconds during grip assessment. They were therefore able to calculate the rate of development of grip and the time taken to reach maximum grip in addition to the maximum grip strength itself. They related rate of development of grip to power (dP/dT(max) x 0.0385 watts where P = pressure recorded within system, T = time and dP/dT(max) = maximum rate of increase in grip). Further evaluation of the dynamic qualities of grip strength was provided by Helliwell et al (1988), who felt that the only independent variables from the grip/time curve were maximum grip, time to maximum grip and fatigue rate, all three providing adequate discrimination between rheumatoid arthritis and normals.

Factors affecting strength

Community and industrial surveys have shown:

1.   For each decade, males are stronger than females.

2.   The dominant hand is about 10% stronger than the non-dominant hand.

3.   Strength increases to a maximum about the age of 35 for males (40 for females) and thereafter declines with age (Bechtol, 1954; Montoye and Faulkner, 1964; Anderson and Cowan, 1966; Schmitt and Toews, 1970; Kellor et al, 1971; Montoye and Lamphiear, 1977; Fernando and Robertson, 1982; Grimby et al, 1982; Viitasalo et al, 1985; Mathiowetz et al, 1985; Mathiowetz et al, 1986).

Strength appears to be related to anthropometric measurements, showing a positive linear correlation with weight and height (Anderson and Cowan, 1966; Lamphiear and Montoye, 1976; Balogun et al, 1991). Circadian variation may be of importance when

assessing strength (Wright, 1959a and b), although using a number of isometric assessments Tornvall (1963) was unable to show circadian variation in normal subjects. The psychological state is important in measuring strength. Lee et al (1974) have shown a significant physician/patient interaction when measuring grip strength: intra-observer error was acceptable but inter-observer error showed marked differences in results obtained with each patient, the maximum difference being about 15%. Ikai and Steinhaus (1961) demonstrated large differences in isometric elbow force precipitated by gun shot, patient vocalisation, hypnotic suggestion, alcohol ingestion and amphetamine ingestion, clearly a study with more experimental latitude than would be permitted now. Other factors such as malnutrition and sepsis, which influence muscle cross-sectional area, decrease isometric strength but no significant effect has been recorded for trauma, surgery or steroid administration (Brough et al, 1986).

On the whole it appears that voluntary strength closely matches strength measured by tetanic stimulation, certainly in the experiments described by Merton (1954) using the adductor pollicis muscle. However, it may have been that Merton was unable to isolate the physiological effect of adductor pollicis: Edwards et al (1977) have suggested that the long thumb flexors may contribute to this movement, therefore producing an artificially large force.

Strength measurement in rheumatoid arthritis

Pain and stiffness in the joints are the main symptoms of rheumatoid arthritis. They are closely followed by weakness, particularly of grip strength. This has been recorded objectively by a number of authors (Lee et al, 1974; Walker et al, 1978, Sheehan et al, 1983; Helliwell et al, 1987a) in addition to a host of clinical trials where grip strength

is used as a measure of outcome. Objective reports of weakness have also been made in the elbow and shoulder joints (Al-Kassar, 1986) and knee (Nordesjo et al, 1983; Wigren et al, 1983).

Not surprisingly loss of (grip) strength has been found to correlate with loss of hand function, particularly manual dexterity (Lee et al, 1974; Sheehan et al, 1983). However, in a situation where grip strength is improving this may not be the case (Jones et al, 1991), presumably the improvement of function coming later - unless irreversible joint deformity has occurred. In normal elderly (78-81y) subjects function, measured as walking time and step tests, surprisingly is poorly related to isometric and isokinetic strength at the knee (Danneskiold-Sansoe et al, 1984) although grip strength correlates well with the OPCS Scale of dexterity (Turner and Ebrahim, 1992).

Helliwell et al (1987a) showed loss of grip strength to 25% of values obtained in normal age-matched subjects. What are the reasons for this profound weakness? Patients often complain that their limbs seem to have lost bulk; yet Yung et al (1986) could show no evidence of reduction in forearm circumference in patients with long-standing rheumatoid arthritis. No doubt the pain elicited on gripping and the deformity in the joints of the hand contribute to the reduction in grip strength. There is some evidence that intrinsic abnormalities of the muscle may contribute to weakness in rheumatoid arthritis. Steinberg and Wynn-Parry (1961) found electromyographic evidence of polymyositis in 85% of a group of 93 subjects with rheumatoid arthritis. A similar result was obtained by Lenman and Potter (1966) who performed surface EMGs and obtained voltage/tension curves in 23 patients with rheumatoid arthritis, 10 normal and 21 with a myopathy. They found abnormalities of EMG/tension curves in

65% of the patients with rheumatoid arthritis, these mainly occurring after several seconds maximal grip. Lenman and Potter felt that, because the early phase of the curve was similar in rheumatoid arthritis compared to normals, the main cause of abnormality of the EMG/tension curve in rheumatoid arthritis was stiffness and pain elicited in the joints and not primary neuromuscular disease. Haslock et al (1970) performed a pathological study on 34 subjects with rheumatoid arthritis, all undergoing a motor end point muscle biopsy under general anaesthetic. The group all had clinical indications for biopsy, such as weakness, wasting or a sensory abnormality, so the results are likely be skewed, but they found myositis in 24%, peripheral neuropathy in 26%, steroid myopathy in 12% and muscle cachexia (defined as a decrease in muscle fibre calibre with an increase in nuclei, changes seen in diseases such as carcinomatosis) in 38%. Cantrell (1976) also felt that weakness was a primary problem in rheumatoid arthritis, being present in the early stages of the disease without deformity and not necessarily associated with pain.

Relationship between muscle morphology and strength measurements

A short review of muscle anatomy is presented to clarify the ensuing discussion. Each muscle is covered by a fascia of fibrous connective tissue (epimysium). Within each muscle are bundles separately wrapped in connective tissue (perimysium). Within each bundle are thousands of muscle fibres, again embedded in connective tissue (endomysium). This connective tissue, and any tissue present within the inter-muscular septa constitutes, along with the tendons and muscle aponeuroses, the non-contractile portion of muscle. The functional unit within a muscle is the group of muscle fibres innervated by a single motor neurone fibre, the motor unit. In humans the number of muscle fibres in a particular muscle group is determined genetically and is manifest at

the time the embryo has reached the age of 4-5 months: subsequently it is the thickness of the fibres that vary (Astrand and Rodahl, 1986). Some muscles have parallel muscle fibres, but, generally, muscles have fibres which do not extend the entire length of the muscle and insert on to a common tendon at an angle (called the angle of pennation): some muscles are unipennate and others are multipennate.

Other elements of the muscle cell are the sarcolemma, myofibrils and sarcoplasm. The sarcolemma is a thin membrane enveloping the muscle fibre and serves an active transport function facilitating depolarisation of the muscle cell. Within the muscle cell are myofibrils arranged parallel to one another and aligned with the sarcolemma so that points with the same density lie at the same level, each repeating cycle being called a sarcomere. The filaments of myosin and actin, the active contractile elements of the myofibril, are responsible for this pattern.

At a more macroscopic level, functionally and histochemically muscles are composed of two different fibre types: slow twitch (type 1) fibres and fast-twitch (type 2) fibres. They can be differentiated histochemically using a myofibrillar ATPase stain which differentiates the fibres on the basis of the amount of ATPase bound to myosin (Astrand and Rodahl, 1986). Under normal conditions the proportions of type 1 and type 2 fibres seem to be under genetic control, identical twins having a very similar proportion of fibre types in a given muscle, in contrast to non-identical twins (Komi et al, 1977). Neural influences determine the fundamental dynamic properties of the contractile material: motor neurons contacting type 1 fibres are relatively small with low firing rates compared to those innervating type 2 fibres. It may be possible to change the fibre characteristic by the stimulation pattern of the innervating motor nerve

(Astrand and Rohahl, 1986).

The force a muscle can produce is independent of fibre type and is related to the physiological cross-sectional area given by:

$$m/pl \qquad \text{where m is mass of muscle}$$

$$p \text{ is density of muscle}$$

$$l = \text{mean fascicle length.}$$

For a unipennate muscle an allowance must be made for pennation angle (Cutts et al, 1991) and so physiological cross-section area becomes:

$$(m/pl) \cos \alpha \quad \text{where} \quad \alpha = \text{angle of pennation,}$$

Physiological cross-sectional area is not the same as anatomical cross-sectional area, the ratio being of the order of 1.31 in the human calf (Davies et al, 1986).

Factors affecting grip strength have been discussed earlier, but it is worth reiterating that grip strength should be measured in relation to age and sex. It would seem that these age-related and sex differences can be explained on the basis of muscle fibre size (Ikai ad Fukanaga, 1969; Segal and Wolf, 1990). Adult females have smaller muscle fibres but no differences in fibre type. It is interesting to note that in early childhood there are no differences in fibre size between males and females and acquired differences are probably a result of hormonal influences as well as life style. In the elderly there is a gradual loss of motor neurones (Campbell et al, 1973) which results in a progressive decline in fibre numbers and size without a change in fibre composition (Grimby et al, 1982).

Predicting strength, particularly grip strength, on the basis of anthropometric variables

has resulted in a plethora of regression equations often including weight, height, external dimensions (such as bi-acromial diameter and limb girth), estimates of lean body weight and body mass index. Viitasalo et al (1985) emphasised that age-related decline in strength should also be related to body mass index. It would appear to be weight that is the significant factor in most studies, particularly when the other dimensions have been controlled for by appropriate statistical techniques (Rasch and Pierson, 1963; Laubach and McConville, 1969; Lamphiear and Montoye, 1976). Balogun et al (1991) recommend that grip strength normative data be based on both body weight and age rather than age alone, as is current practice.

Some authors have attempted to refine this dimension by relating strength to limb or muscle cross-sectional area. Ikai and Fukanaga (1969) measured CSA of the upper arm by an ultrasonic technique and were able to show that differences between the sexes and different ages were eliminated when strength was expressed per unit of muscle cross-sectional area. Frisancho (1981), using a huge population base of over 19,000, measured upper arm circumference and triceps skin fold thickness to calculate upper arm muscle CSA: assumptions employed were that the upper arm is cylindrical, that the humeral diameter was the same for all subjects and that the fat in the subcutaneous layer was of uniform compressibility. Frisancho's equations were refined by Heymsfield et al (1982) who, comparing estimated upper arm CSA with actual CSA (as measured by computed tomography), derived a correction factor for humeral area and non-circularity; his corrected equations gave an average error of 7.7%. Frisancho (1984) employed these revised equations on his original sample and found an inverse relationship between age and CSA for males, but not females.

It would appear that anatomical cross-sectional area provides a good correlation with strength despite the obvious limitations of estimation and the poor relationship to physiological cross-sectional area. Davies et al (1986) found correlations between strength and CSA of 0.86 for young subjects and 0.67 for old subjects. This relationship was confirmed in the human adductor pollicis by Bruce et al (1989a and b), who found that the correlation between strength and CSA was 0.91. They found that their method for estimating adductor pollicis CSA underestimates the actual cross-sectional area by about 40%. Although the anatomical CSA is sufficient for comparative work, and seems to explain adequately much of the variation in strength between subjects, if the functional properties of individual muscles are predicted from anatomical CSA's then grossly misleading results might be obtained (Brand et al, 1981; Fukunaga et al, 1992).

Strength is independent of muscle fibre type but only in <u>untrained</u> subjects (Maughan and Nimmo, 1984). Maughan (1984) mentioned that the maximal voluntary contraction per unit of cross-sectional area is higher for sprinters than marathon runners, possibly as a result of type 2 fibres in the sprinters exerting a greater force per unit cross-sectional area. The independence of the relationship between force and fibre type is also in doubt when measuring isokinetic torques, particularly at speeds greater than 180° per second where type 2 fibres may produce a torque greater than type 1 (Maughan, 1984). Schantz et al (1983), studying 21 untrained students and 5 body-builders and using muscle biopsy and CT estimation of CSA, found a good relationship between maximum knee extension, maximum elbow extension, maximum elbow flexion and CSA. A graph of maximum knee extension torque against knee extensor muscle CSA was a straight line with body-builders appearing at the upper end of the line and

untrained students at the lower end. Force per unit of cross-sectional area was therefore constant between these groups. Dividing CSA by mean fibre area provided the same figure for both males and females showing there were the same number of fibres per muscle independent of sex and size of individual.

The effect of training on muscle strength and size is of interest. Initial gains in strength are not reflected in increases in muscle CSA (Astrand and Rodahl, 1986) and it is postulated that initial gains in strength are a result of enhanced neuro-muscular efficiency. Differences in neuro-muscular efficiency may also explain some of the variation in grip strength seen after allowance is made for muscle CSA. Moreover, differences between athletes (who are, theoretically, all fully trained) may be accounted for by neurophysiological differences, as well as psychological factors.

In view of the above considerations it is worth listing why patients with rheumatoid arthritis might be so much weaker than normals.

1.   Malnutrition and disuse are likely to lead to a reduction in fibre diameter and hence muscle CSA (Heymsfield et al, 1982; Brough et al, 1986, Bruce et al, 1989a).

2.   Disuse and aberrant muscle mechanics are likely to lead to a decrease in muscular efficiency.

3.   A decrease in fibre quality due to subclinical inflammation may also be important.

4.   Direct inhibitory effects from nociceptors onto alpha motorneurons.

5.   Abnormal articular geometry and muscle mechanics as a result of deformity.

6.   Attrition and inflammation in muscle tendons and disruption of tendon insertion.

Methods

Ethical Committee approval for this study was obtained. Normal subjects were recruited from rheumatology outpatients if they did not have a systemic disease and if they did not complain of symptoms referable to their arms: these subjects had low back pain or osteoarthritis of the lower limbs. Normal subjects were also recruited from social centres catering for elderly people, eg. Help the Aged, National Back Pain Association meetings and a ladies' crown green bowling club. Patients with rheumatoid arthritis all had disease diagnosed according to criteria of Arnett et al (1988). The patients were recruited either from inpatient beds, where they had been admitted for rehabilitation, (as with the majority), or from routine rheumatology clinics.

Grip and pinch strength were measured with the MIE (MIE Medical Research Ltd Leeds) digital pinch grip analyzer linked to a microprocessor (Helliwell et al, 1987a; Helliwell et al, 1988b). The device consists of two cushioned aluminium bars approximately 6 inches long incorporating strain-gauges into one of the bars so that, no matter where or how the subject grips the device, a true reading is obtained. The separation of the handles is adjustable to suit any hand size or deformity. A digital readout facility in Newtons force is provided with peak hold facilities and the output is interfaced with a BBC model B microprocessor which provides instantaneous analysis of the grip time curve from which maximum grip (or pinch) strength, time to 95% of maximum grip and fatigue can be obtained. Total grip time is 4.4 seconds. After an initial practice the grip strength is recorded with verbal and visual encouragement; the patient sits comfortably with the forearm resting on the arm of the chair or on an adjacent table. Pinch strength was measured between thumb pulp and the radial side of the buttressed index finger. The dominant hand was measured in all

Plate 5.1

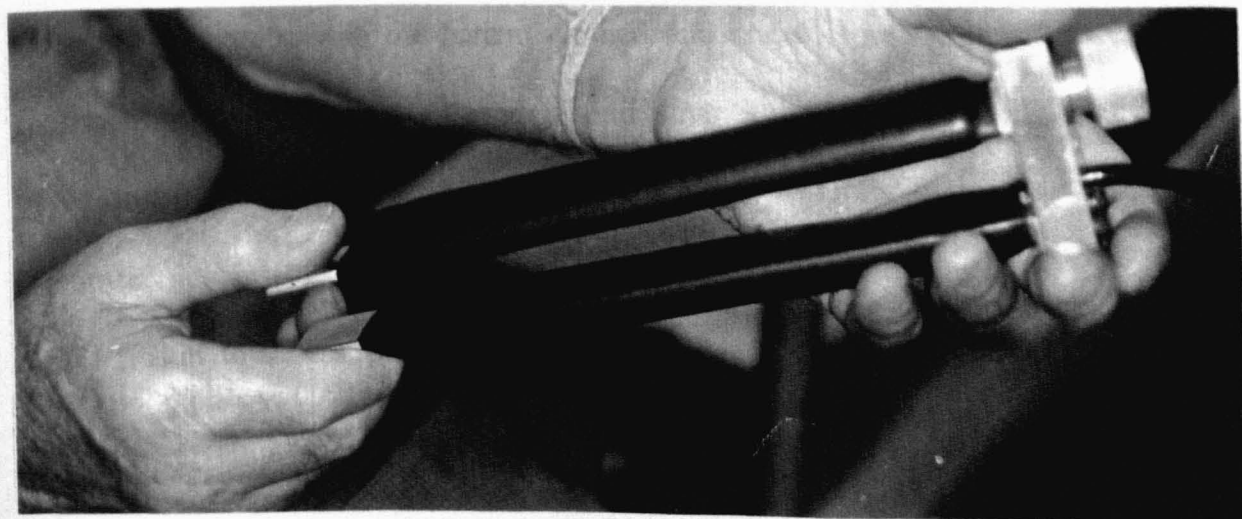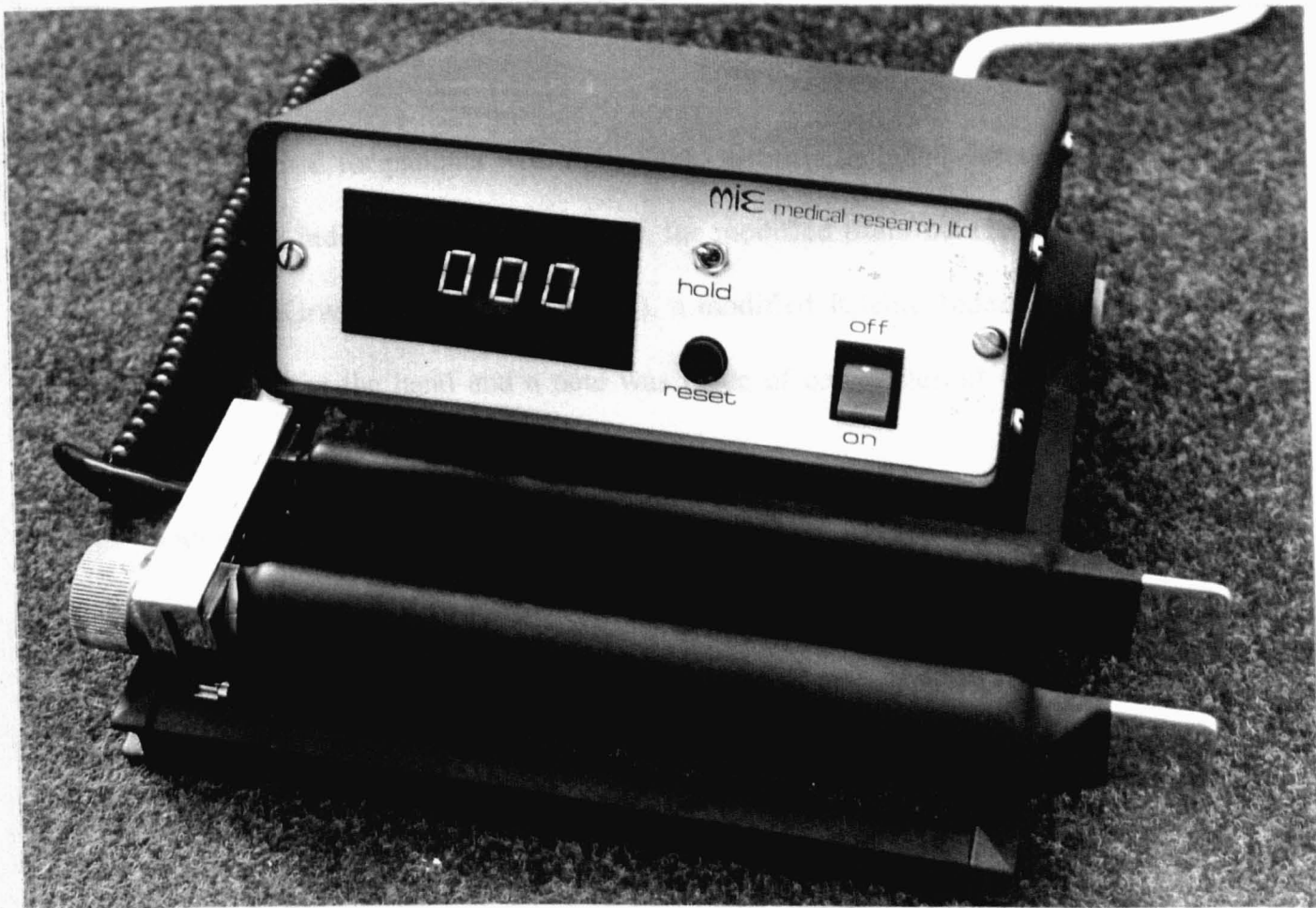The MIE Medical Electronics Ltd Pinch Grip Meter.

Plate 5.1

cases. The device is illustrated in Plate 5.1.

Other data collected for patients with rheumatoid arthritis included duration of disease, Ritchie Articular index (Ritchie et al, 1973), the modified Stanford Health Assessment Questionnaire (Kirwan and Reeback, 1986), a modified Ritchie Index for the hand, a deformity index for the hand and a note was made of corticosteroid consumption.

The modified Ritchie index for the hand consisted of squeezing, as in the Ritchie Articular index, the wrist complex, the MCP joints 2-5, and the PIP joints 2-5. The response to each squeeze was scored as follows: 0 = no response, 1 = complain of pain, 2 = complained of pain and winced, 3 = complained of pain, winced and withdrew hand. The maximum score was, therfore, 9.

The deformity index had a maximum score of 15 and was weighted in favour of the wrist. Patients with volar subluxation or other deformity at the wrist scored 5; a score of 1 was recorded for each of the MCP joints that was subluxed; a score of 1 was recorded for each of the PIP joints that showed deformity (either z deformity at the thumb, swan-neck deformity or boutonniere deformity).

Anthropometric data recorded were: height in centimetres using a wall-mounted scale, weight in kilograms with the patient clothed and seated, forearm length measured in centimetres between lateral epicondyle and ulnar styloid process using a cloth tape, mid-forearm circumference in centimetres using a cloth tape and third finger circumference just distal to the finger web using a graduated plastic loop (Helliwell, 1987). Skin thickness was measured by a standard caliper ('John Bull' Harpendon

Skinfold Caliper, British Indicators, Ltd) on the dorsal surface of the forearm midway between the lateral epicondyle and the ulnar styloid process and at the same distance on the ventral aspect of the forearm; readings were taken immediately, ignoring any creep that subsequently occurred.

Estimation of forearm muscle cross-sectional area

The mid-portion of the forearm was chosen because, at this point, the majority of flexor and extensor muscles involved in maximal isometric grip are found. Usually the part of the forearm with the maximum diameter occurs at the junction of the upper third and lower two thirds of the forearm due to the inclusion of muscles pronator teres and brachioradialis. A diagrammatic representation of the cross-section through the middle of the forearm taken from a standard atlas of anatomy (Grant, 1962) is shown in Figure 5.1.

An estimation of limb volume using measurements of limb diameter, assuming each to be a truncated cone, has been made by Jones and Pearson (1969) and Katch and Weltman (1975). Both these groups found that the calculated volumes tended to be under-estimates, but found good correlations and regressions for the whole limb based on anthropometric data. In this study cross-sectional area rather than volume was chosen because of the extensive literature relating cross-sectional area to grip strength and other anthropometric variables.

Figure 5.1

Diagram of cross-section of human forearm at the level of insertion of the pronator teres (from Grant 1962).

A - diagram of muscles in cross-section:-

U = ulna.

R = radius.

PL = palmaris longus.

FCR = flexor carpi radialis.

FDS = flexor digitorum superficialis.

FCU = flexor carpi ulnaris.

FP = flexor profundus.

FPL = flexor pollicis longus.

PT = pronator teres.

BR = brachioradialis

ECRL = extensor carpi radialis longus

ECRB = extensor carpi radialis brevis

ED = extensor digitorum

EDM = extensor digitorum minimus

ECU = extensor carpi ulnaris

EPL = extensor pollicis longus

APL = abductor pollicis longus

S = supinator

B - shaded area represents flexor muscles at this point.

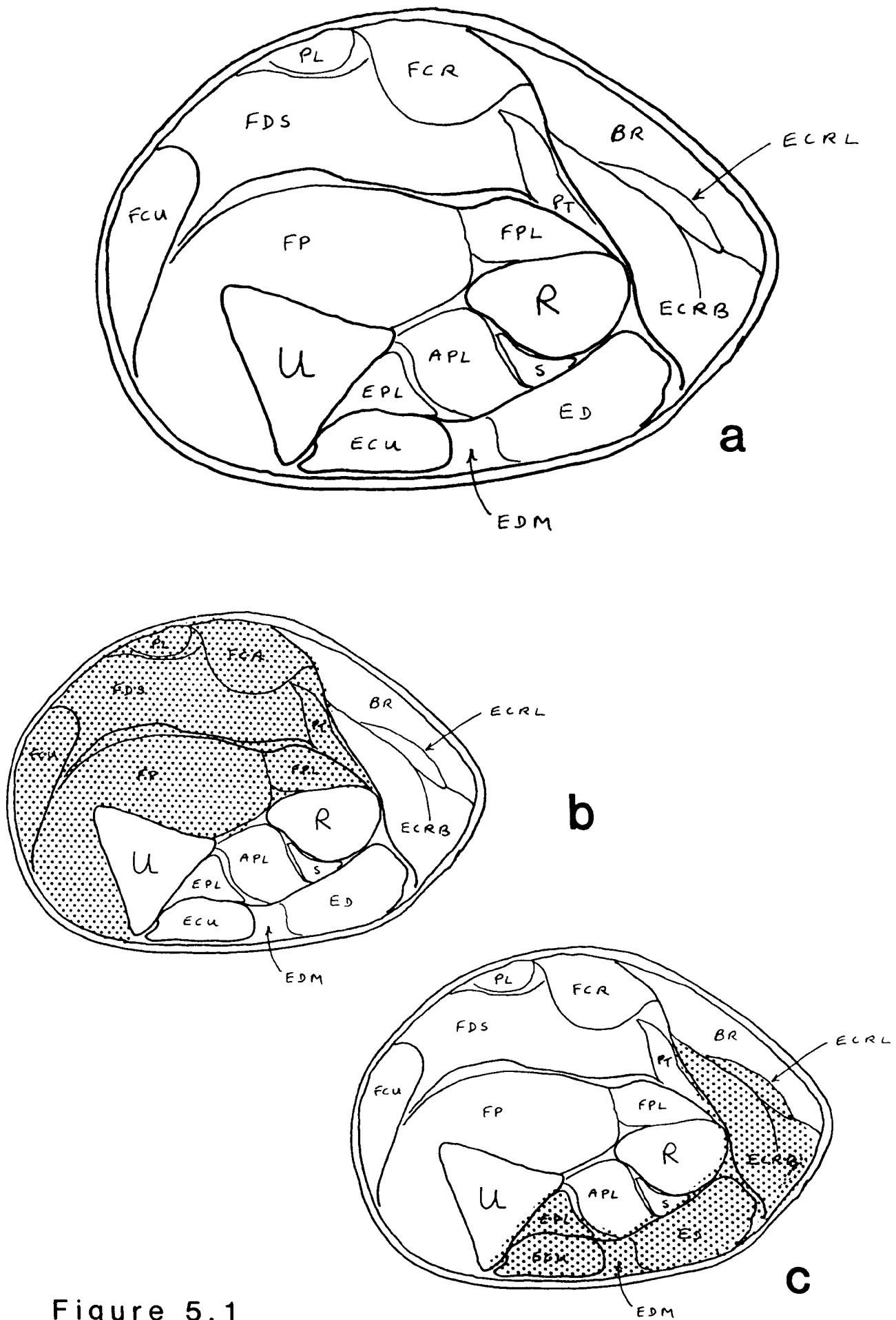C - shaded area represents extensor muscles at this point.

Figure 5.1

The formula for calculating muscle cross-sectional area in this study is given by:

$$\text{CSA(cm}^2) = \pi \left(\frac{FOC}{2\pi} - \frac{ST_d + ST_v}{40} \right)^2$$

where FOC = forearm circumference in centimetres

ST_d = dorsal skin thickness in millimetres

ST_v = ventral skin thickness in millimetres.

(note, double fold of skin measured by skin calipers)

This calculated area does not allow for the cross-sectional area of the radius or ulna bones. Astonishingly, this author could find no data relating anthropometric variables to radius or ulnar dimensions. However, in a large study of normal subjects Virtama and Helela (1969) produced standardised age and sex related tables of proximal radius and ulna diameters, derived from standardised radiography. The position of the radiographic measurements was not midway between elbow and wrist joint and is illustrated in Figure 5.2. Their results showed that over the age of 20 there is little variation within sex, bone and laterality. A mean diameter was therefore used for radius and ulna for males and females. These Figures, from tables of Virtama and Helela, are given in Table 5.1. For normal subjects under the age of 20 the age and sex specific diameter was recorded directly from the tables of Virtama and Helela.

Cross-sectional area of both radius and ulna were calculated on the assumption that both were circular in cross-section, clearly a misrepresentation. Horsman (1972) and Horsman and Leach (1974) in a study of 20 cadaveric radius and ulna specimens used different formulae to predict the actual area but found no advantage over an assumption of circularity: generally speaking the estimated were less than the actual measurements. Horsman and Leach (1974) were able to show that the area of the radius is roughly

Figure 5.2

Radiographic sites used by Virtama and Helala (1969).

tuberosity of radius

tuberosity of ulna
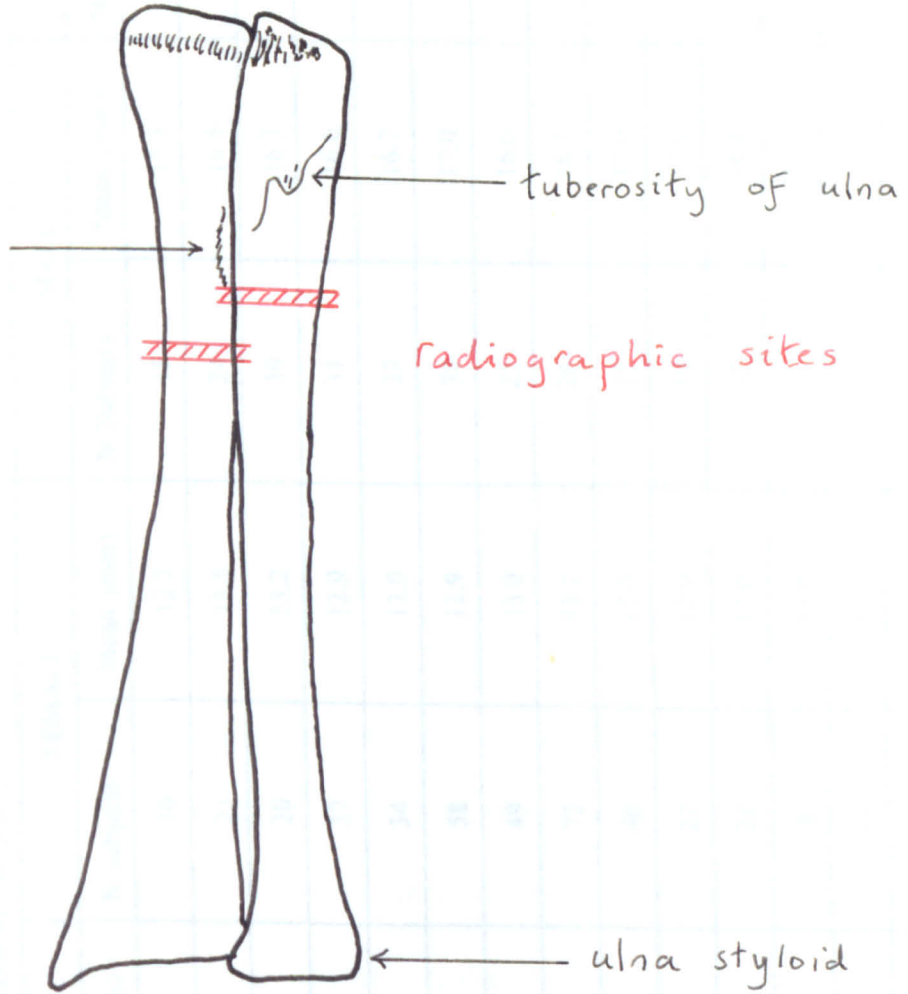
radiographic sites

ulna styloid

Figure 5.2

Table 5.1

Measured diameters of proximal radius and ulna from Virtama and Helela (1972). CSA is calculated on overall mean assuming each bone to be circular.

AGE BAND	PROXIMAL RADIUS				ULNA			
	MALE		FEMALE		MALE		FEMALE	
	N Subjects	Mean (mm)	N subjects	Mean (mm)	N Subjects	Mean (mm)	N Subjects	Mean (mm)
20 - 25	18	15.3	10	12.7	15	15.3	10	13.5
25 - 30	26	14.9	21	13.5	24	16.5	17	13.6
30 - 35	50	15.4	20	13.2	39	16.3	18	13.4
35 - 40	34	15.7	37	12.9	31	16.6	20	13.7
40 - 45	42	15.9	34	13.0	37	16.7	22	13.9
45 - 50	65	15.6	58	12.9	38	17.0	31	14.0
50 - 55	53	15.2	49	13.0	25	16.6	36	13.8
55 - 60	46	15.4	72	13.2	26	16.7	40	13.7
60 - 65	38	15.5	46	13.0	25	17.0	40	14.3
65 - 70	26	15.6	27	12.9	19	17.9	12	13.6
70 - 75	17	15.9	24	13.0	12	18.4	17	14.0
75 - 80	4	16.8	8	13.6	-	-	4	14.3
80 - 85	3	16.6	13	12.9	-	-	7	13.9
MEAN		15.68		13.06		16.82		13.82
STD. DEVN.		0.531		0.253		0.808		0.280
C.S.A.(cm^2)		1.93		1.34		2.22		1.50

constant between 20% and 80% of its length as measured from the distal end, although the ulnar is less constant showing an increase in area of about 50% over the same length.

In order to check the accuracy of the estimates of muscle cross-sectional area in this study, in a series of subjects' computed tomographic scans were performed as a single slice at mid forearm level. From the CT slice it was possible to outline areas of interest using a light pen and screen, and to obtain the required areas by subtraction. The results of this study in 7 subjects are presented in Table 5.2 and are illustrated graphically in Figure 5.3. It can be seen that the correlation obtained between these 2 figures was good throughout a wide range of cross-sectional areas (r = 0.9) and the regression equation was:

$$\text{estimated CSA (cm}^2) = 10 + 0.95 \text{ actual CSA (cm}^2)$$

It can be seen from Table 5.2 that the main inaccuracies derive from the measurements of skin thickness but, because the layer of skin and subcutaneous tissue is not even around the whole circumference of the arm, this was a difficult measurement to take from the CT scan. In any case the errors that result from the inaccuracies in these measurements are minimal. The results justified the assumption of a circular cross-section for the forearm and the radius and ulna. The former assumption is further justified by the observation that when the cloth tape is applied to the forearm and tightened sufficiently to make the measurement of forearm circumference then the forearm assumes a circular outline.

Table 5.2

Estimated and actual (from computed tomography) forearm cross-sectional areas.

*   total CSA of forearm
+   total CSA of forearm corrected for skin and sub-cutaneous tissue.
**   ulna and radius CSA estimated from bone diameters given by Virtama and Helela in table 5.1.

SUBJECTS	1	2	3	4	5	6	7
Age (y)	45	51	57	40	66	65	77
Sex	M	F	F	F	F	F	M
Diagnosis	Normal	RA	RA	RA	RA	RA	RA
Duration of disease (y)	-	10	9	27	13	7	3
Maximum grip strength (N)	418	34	40	32	45	64	54
Maximum pinch strength (N)	122	22	22	18	45	17	41
ANTHROPOMETRIC VARIABLES							
FOREARM CIRCUMFERENCE (cm)	26.0	21.1	21.0	21.0	17.0	19.0	24.0
SKIN THICKNESS (mm) - DORSAL	3.8	12.6	14.0	18.4	2.8	6.0	7.0
- VENTRAL	3.6	13.8	14.0	20.2	6.8	11.8	11.0
- MEAN	3.7	13.2	14.0	19.3	4.8	8.9	9.0
CROSS-SECTIONAL AREA (cm^2)							
- TOTAL *	53.79	35.4	35.09	35.09	23.0	28.73	45.84
- CORRECTED +	49.22	22.87	21.93	19.28	19.10	20.89	35.67
ULNA AREA (cm^2) **	2.27	1.52	1.52	1.50	1.54	1.54	2.40
RADIUS AREA (cm^2) **	1.91	1.37	1.35	1.37	1.31	1.31	1.86
FOREARM MUSCLE (cm^2) CROSS-SECTIONAL AREA	45.04	19.98	19.06	16.41	16.25	18.04	31.41
COMPUTED TOMOGRAPHIC DIMENSIONS							
SKIN THICKNESS (mm) - DORSAL	0.7	7.5	6.0	10.1	2.4	2.0	2.9
- VENTRAL	1.4	6.3	6.0	10.3	5.9	7.5	4.3
- MEAN	1.1	6.9	6.0	10.2	4.2	4.75	3.7
CROSS-SECTIONAL AREA (cm^2)							
- TOTAL *	56.22	36.27	34.13	39.16	25.50	29.24	44.90
- CORRECTED +	51.10	22.69	18.57	18.76	19.40	20.80	35.20
ULNA AREA (cm^2)	2.55	1.82	1.63	1.30	1.86	1.72	2.45
RADIUS AREA (cm^2)	2.74	1.79	1.56	1.38	1.76	1.65	2.00
FOREARM MUSCLE (cm^2) CROSS-SECTIONAL AREA	45.81	19.08	15.38	16.08	15.78	17.43	30.75

Figure 5.3

Relationship between estimated (from anthropometric measurements) forearm muscle cross-sectional area and actual (from computed tomography) forearm muscle cross-sectional area.
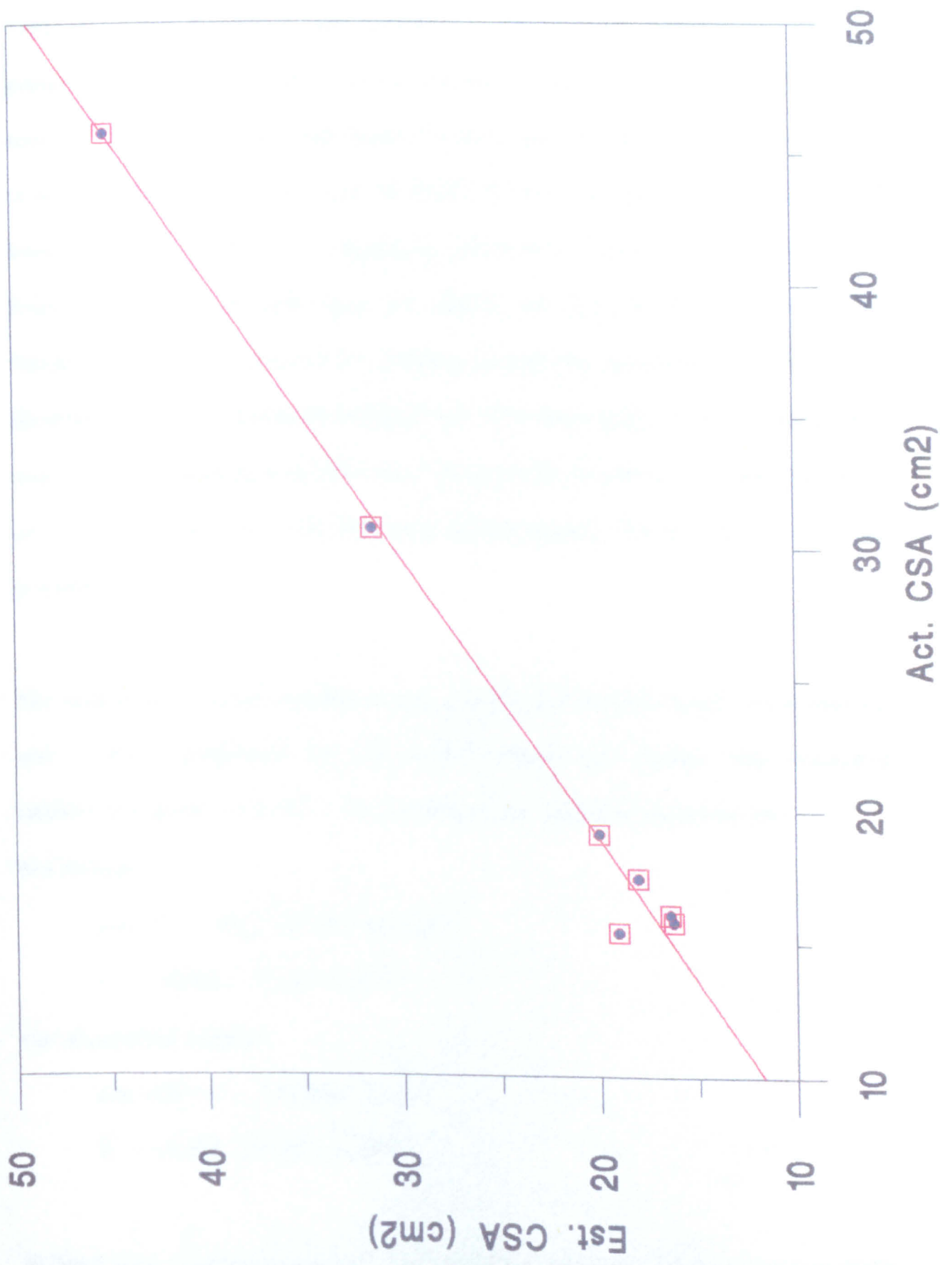
Figure 5.3

Results

Table 5.3 gives the age, height, weight and sex of study participants. The two populations were well matched in terms of these variables. The maximum strength, time to 95% of maximum, and fatigue of both grip and pinch and forearm muscle cross-sectional areas together with the results of a two sample t-test and significance level are given in Table 5.4. Significant differences between the two groups were found for all variables apart from grip fatigue and pinch fatigue. The results for forearm muscle cross-sectional area between normal and rheumatoid arthritis are also illustrated in a 'split' histogram in Figure 5.4. The mean grip/cm² of CSA for normals was:- 7.43, for rheumatoid arthritis was 3.53 (t=13.04, p=0.000). The mean pinch/cm² of CSA for normals was 2.54, the mean for rheumatoid arthritis was 1.60 (t=11.18, p=0.0000).

The relationship between maximum grip strength and forearm muscle cross-sectional area is shown graphically for both normal subjects and subjects with rheumatoid arthritis in Figures 5.5 to 5.7. The corresponding regression equations are:

For normals

grip (N) = -48.7 + 9.15 CSA (cm²)

R^2 = 46.9%, R^2 adj = 46.3

For rheumatoid arthritis

grip (N) = 0 + 3.57 CSA (cm²)

R^2 = 34.1%, R^2 adj = 33.4%

In both these regression equations the coefficient for cross-sectional area was highly significant but the constant was in neither case significant.

Table 5.3

Age, height and weight of normal subjects and patients with rheumatoid arthritis.

	NORMALS n = 100 (32M 68F)				RHEUMATOID ARTHRITIS n = 100 (31M 69F)			
	Mean	Median	Std. Devn.	Range	Mean	Median	Std. Devn.	Range
Age (y)	57.18	62.5	19.99	12 - 93	58.92	59.5	12.94	14 - 84
Height (cm)	165.49	164.74	9.36	146 - 188	163.82	162.56	9.72	131 - 187
Weight (kg)	67.54	66.58	12.94	38.8 - 117.2	66.36	65.0	13.93	37.4 - 107.4

Table 5.4

Grip and pinch strength (- maximum isometric, time to 95% maximum, and fatigue over 4.4 secs) and forearm muscle cross-sectional area in normal subjects (n = 100) and subjects with rheumatoid arthritis (n = 100).

GRIP	NORMALS	RHEUMATOID ARTHRITIS	t	P
Maximum (N)	223.1 ± 100.5	92.64 ± 58.13	11.24	0.0000
T-95 max (secs)	0.88 ± 0.69	1.20 ± 0.89	- 2.84	0.0049
Fatigue (%)	9.36 ± 7.92	10.46 ± 9.22	- 0.90	0.37
PINCH				
Maximum (N)	74.7 ± 22.32	40.81 ± 19.99	11.30	0.0000
T95 max (secs)	0.63 ± 0.66	1.21 ± 0.96	- 4.96	0.0000
Fatigue (%)	12.80 ± 8.31	14.31 ± 13.65	- 0.94	0.35
Forearm Muscle CSA (cm^2)	29.71 ± 7.52	25.96 ± 9.51	3.09	0.002

Figure 5.4

Split histogram of forearm muscle cross-sectional area in normal subjects and in rheumatoid arthritis.

CSA (cm2)

RA
NORMAL

number of patients
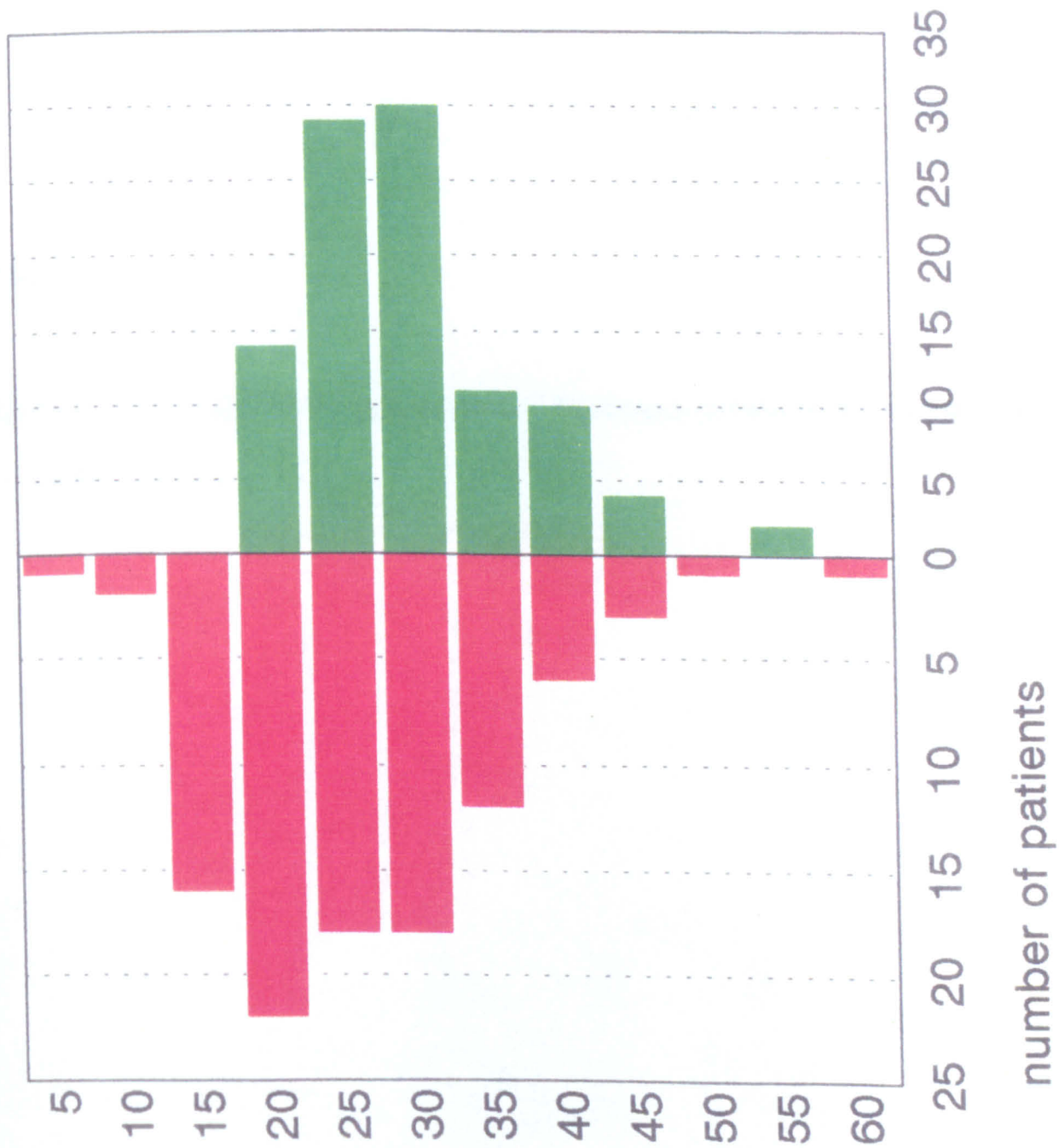
Figure 5.4

Figure 5.5

Relationship between maximum grip strength and forearm muscle cross-sectional area in normal subjects.

Figure 5.5

Relationship between maximum grip strength and forearm muscle cross-sectional area in rheumatoid arthritis.

Figure 5.6

Relationship between maximum grip strength and forearm muscle cross-sectional area in rheumatoid arthritis.

Figure 5.6

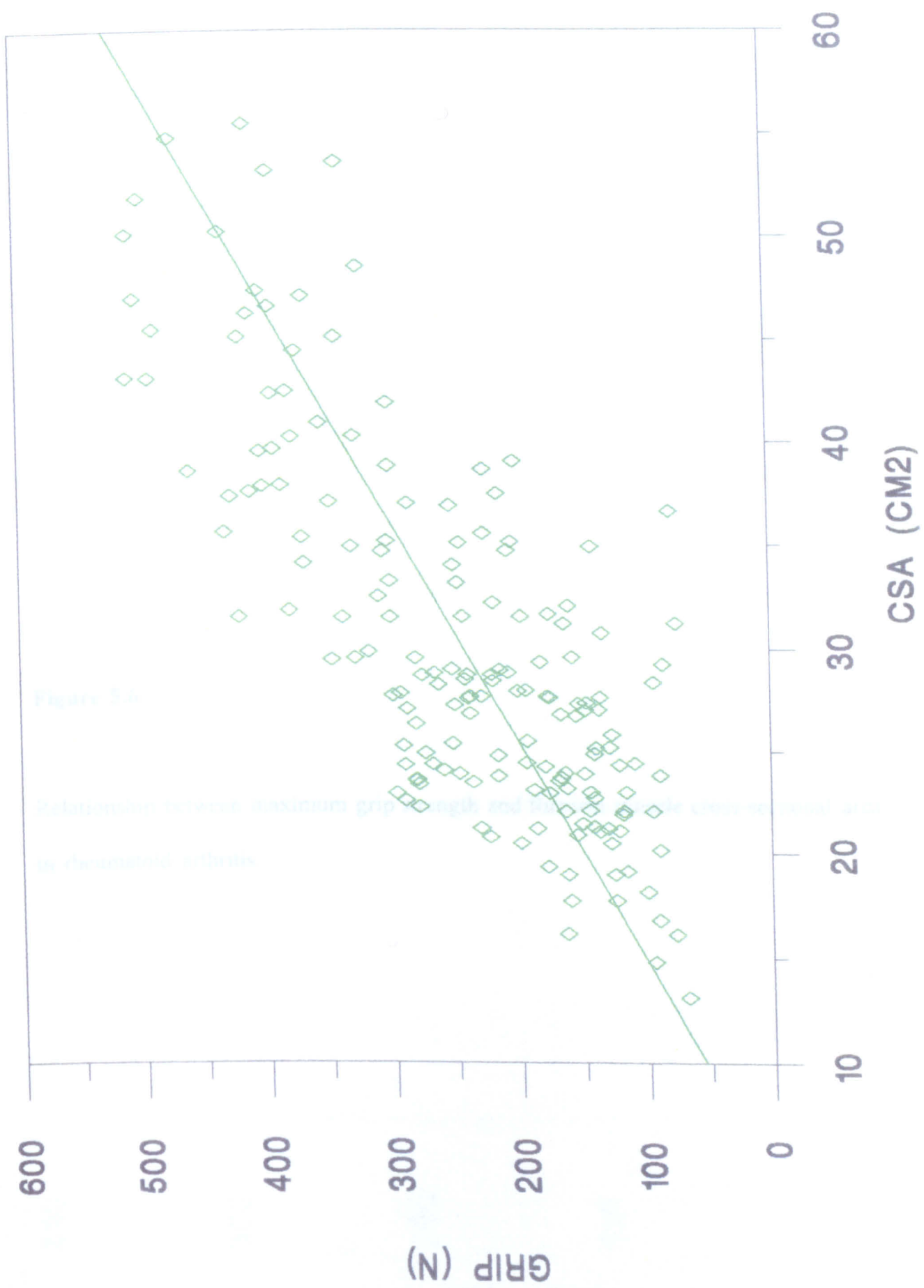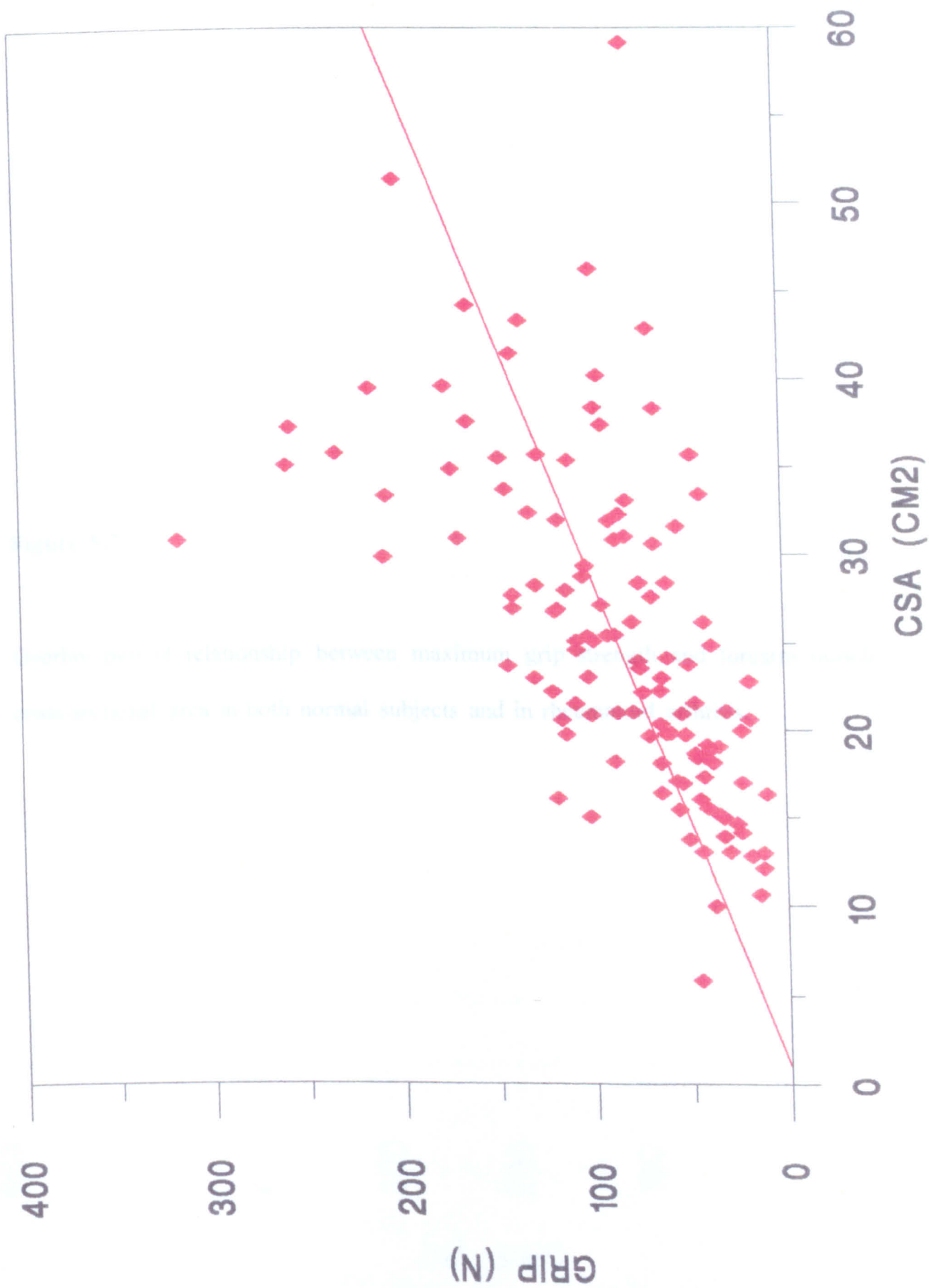**Figure 5.7**

Overlay plot of relationship between maximum grip strength and forearm muscle cross-sectional area in both normal subjects and in rheumatoid arthritis.
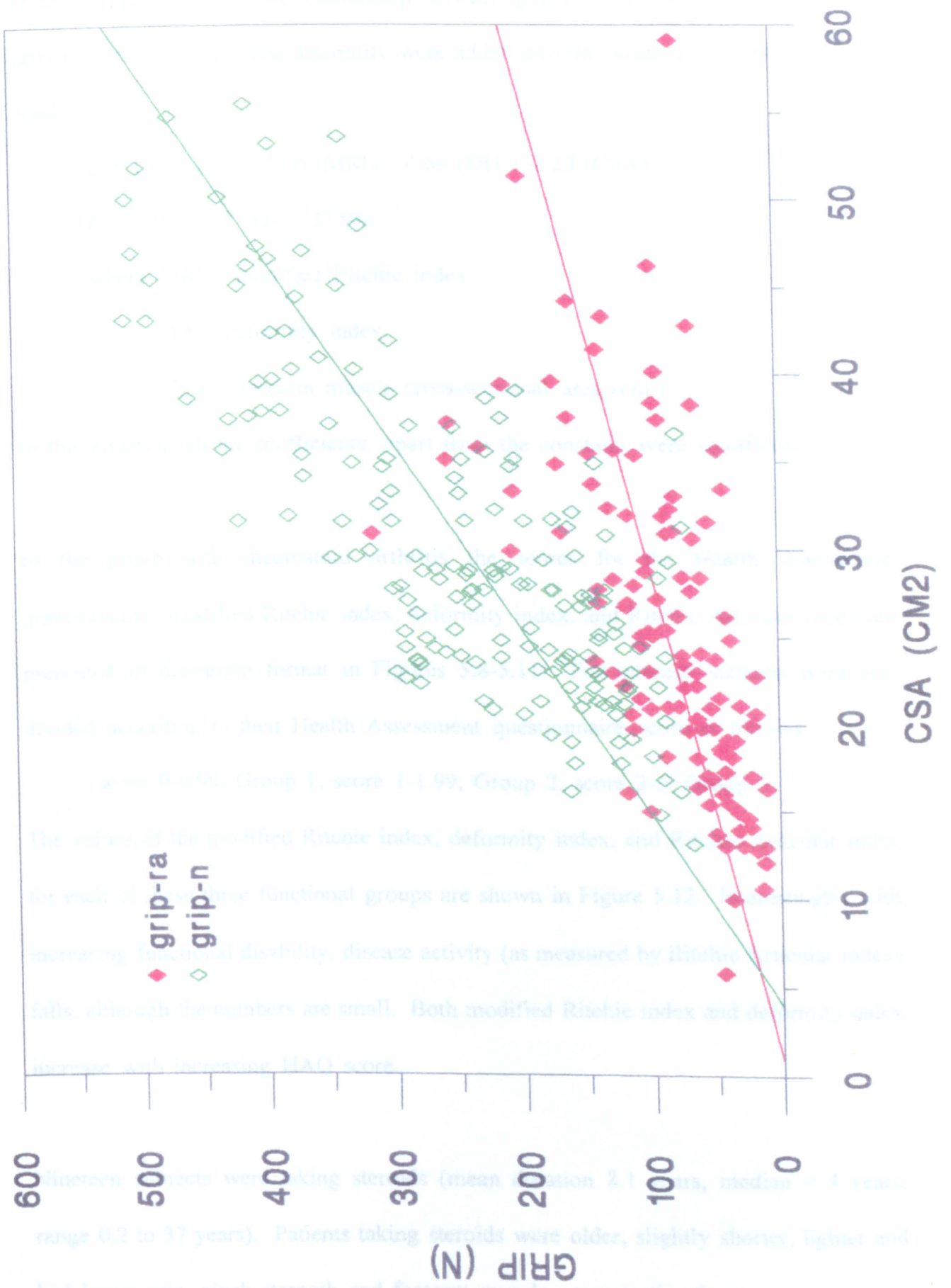
Figure 5.7

In an attempt to improve the relationship between grip strength and CSA in rheumatoid arthritis factors for pain and deformity were added into the equation with the following result:

grip (N) = 63.2 - 5.06 (MRI) - 4.66 (DI) + 2.20 (CSA)

$R^2 = 39.9\%$, R^2 adj $= 37.9\%$

where MRI = modified Ritchie index

DI = deformity index

CSA = forearm muscle cross-sectional area (cm^2)

In this equation all the coefficients, apart from the constant, were significant.

In the group with rheumatoid arthritis the scores for the Health Assessment questionnaire, modified Ritchie index, deformity index, and Ritchie Articular index are presented in histogram format in Figures 5.8-5.11. For interest, subjects were also divided according to their Health Assessment questionnaire score as follows:

score 0-0.99, Group 1; score 1-1.99, Group 2; score 2-3, Group 3.

The values of the modified Ritchie index, deformity index, and Ritchie Articular index for each of these three functional groups are shown in Figure 5.12. Interestingly, with increasing functional disability, disease activity (as measured by Ritchie Articular index) falls, although the numbers are small. Both modified Ritchie index and deformity index increase with increasing HAQ score.

Nineteen subjects were taking steroids (mean duration 8.1 years, median = 4 years, range 0.2 to 37 years). Patients taking steroids were older, slightly shorter, lighter and had lower grip, pinch strength and forearm muscle cross-sectional area:

Figure 5.8

Histogram of scores on health assessment questionnaire in rheumatoid arthritis group.

(n = 68).
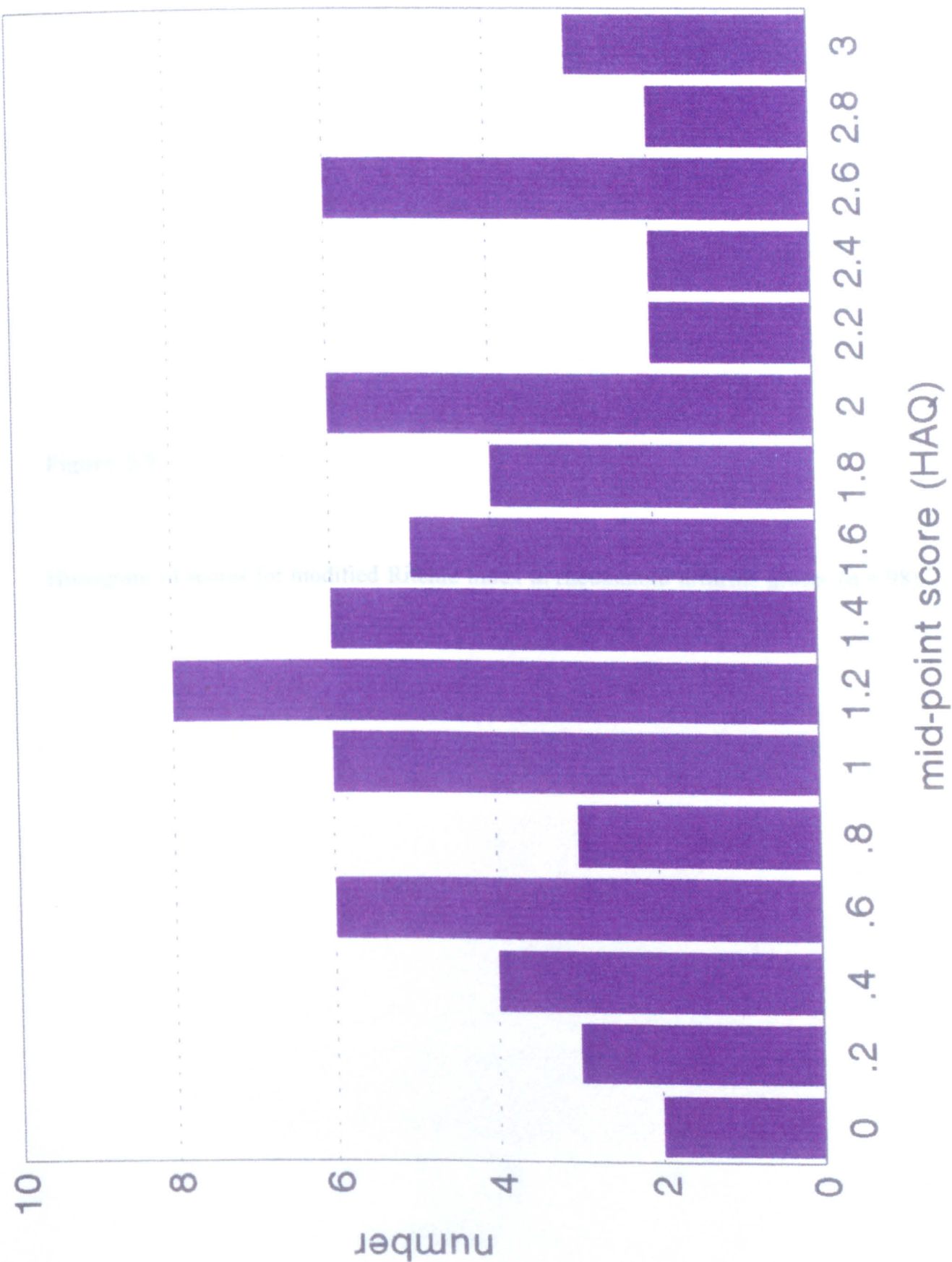
Figure 5.8

Figure 5.9

Histogram of scores for modified Ritchie index in rheumatoid arthritis group. (n = 98).

Figure 5.9

Figure 5.10

Histogram of scores for deformity index in rheumatoid arthritis group. (n = 98).
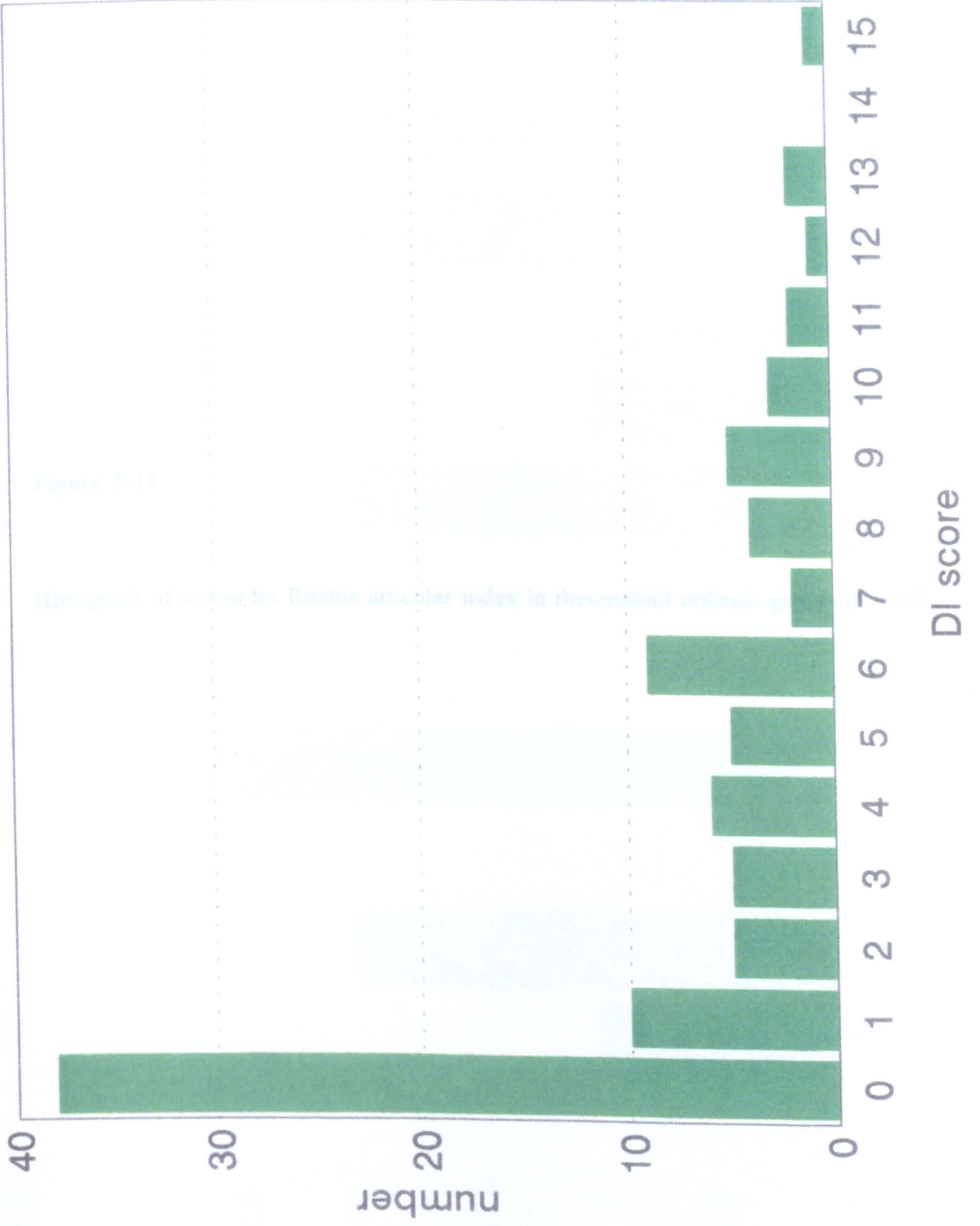
Figure 5.10

Figure 5.11

Histogram of scores for Ritchie articular index in rheumatoid arthritis group. (n = 15).
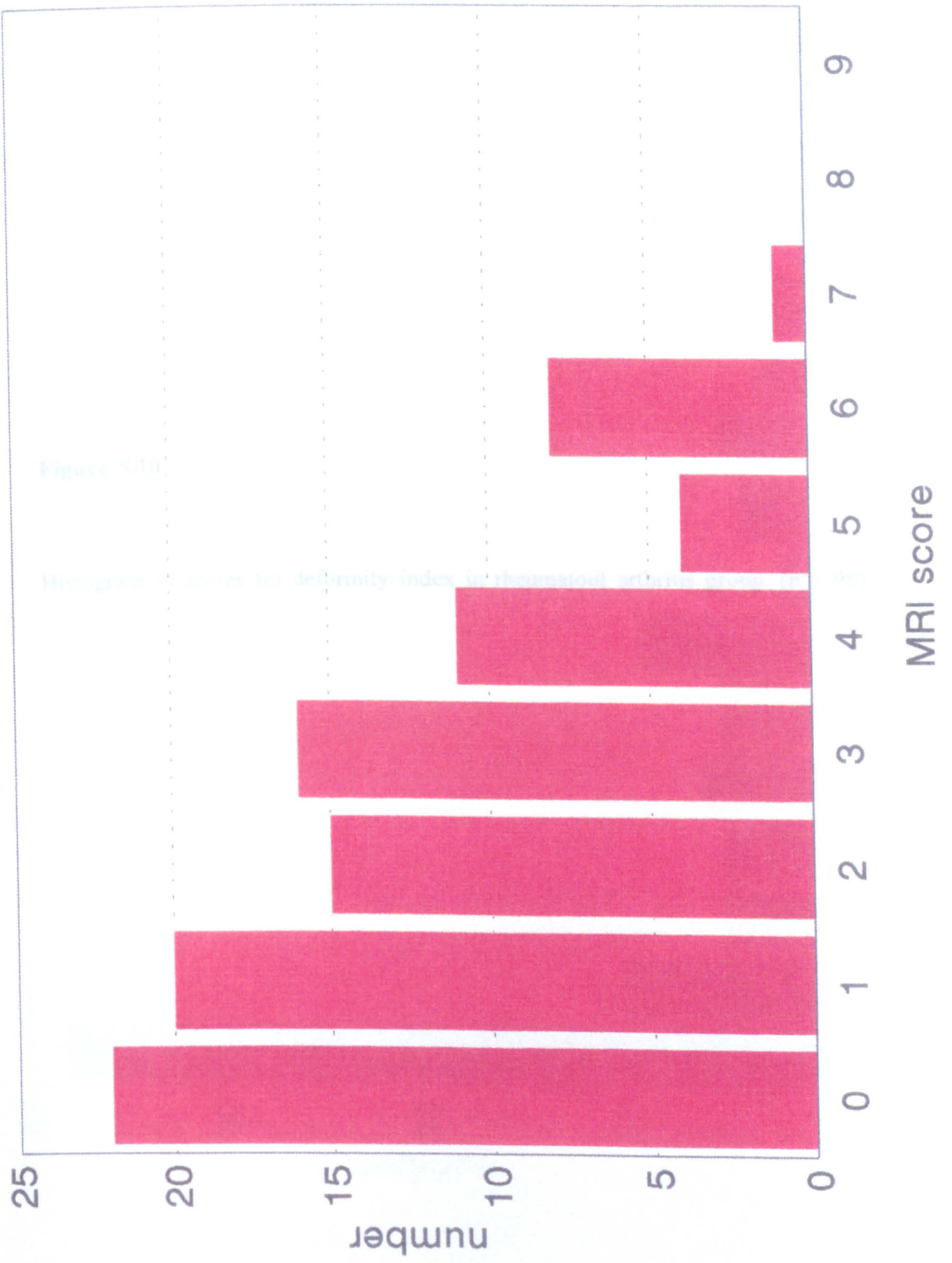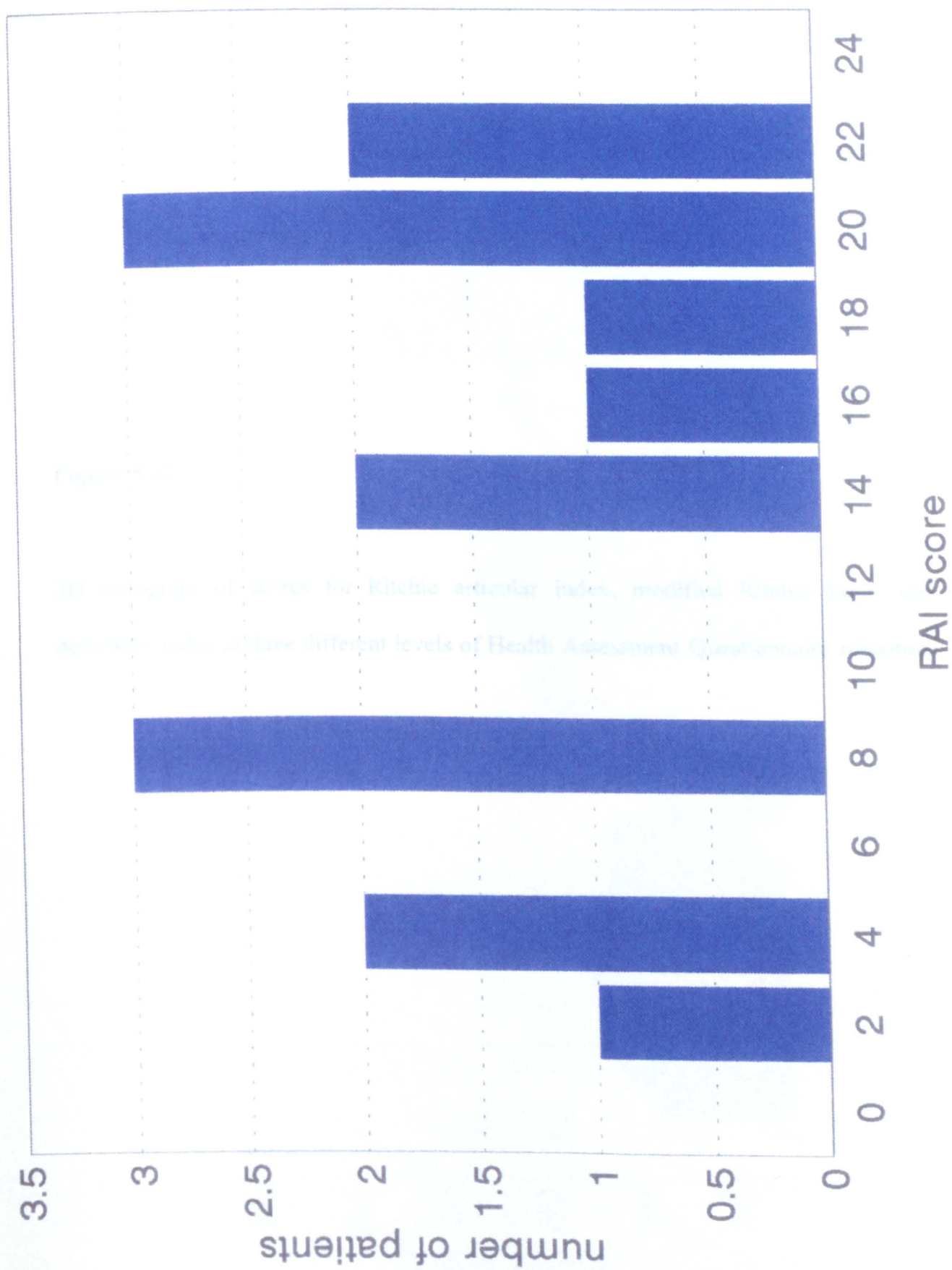
Figure 5.11

Figure 5.12

3D histogram of scores for Ritchie articular index, modified Ritchie index and

deformity index at three different levels of Health Assessment Questionnaire response.
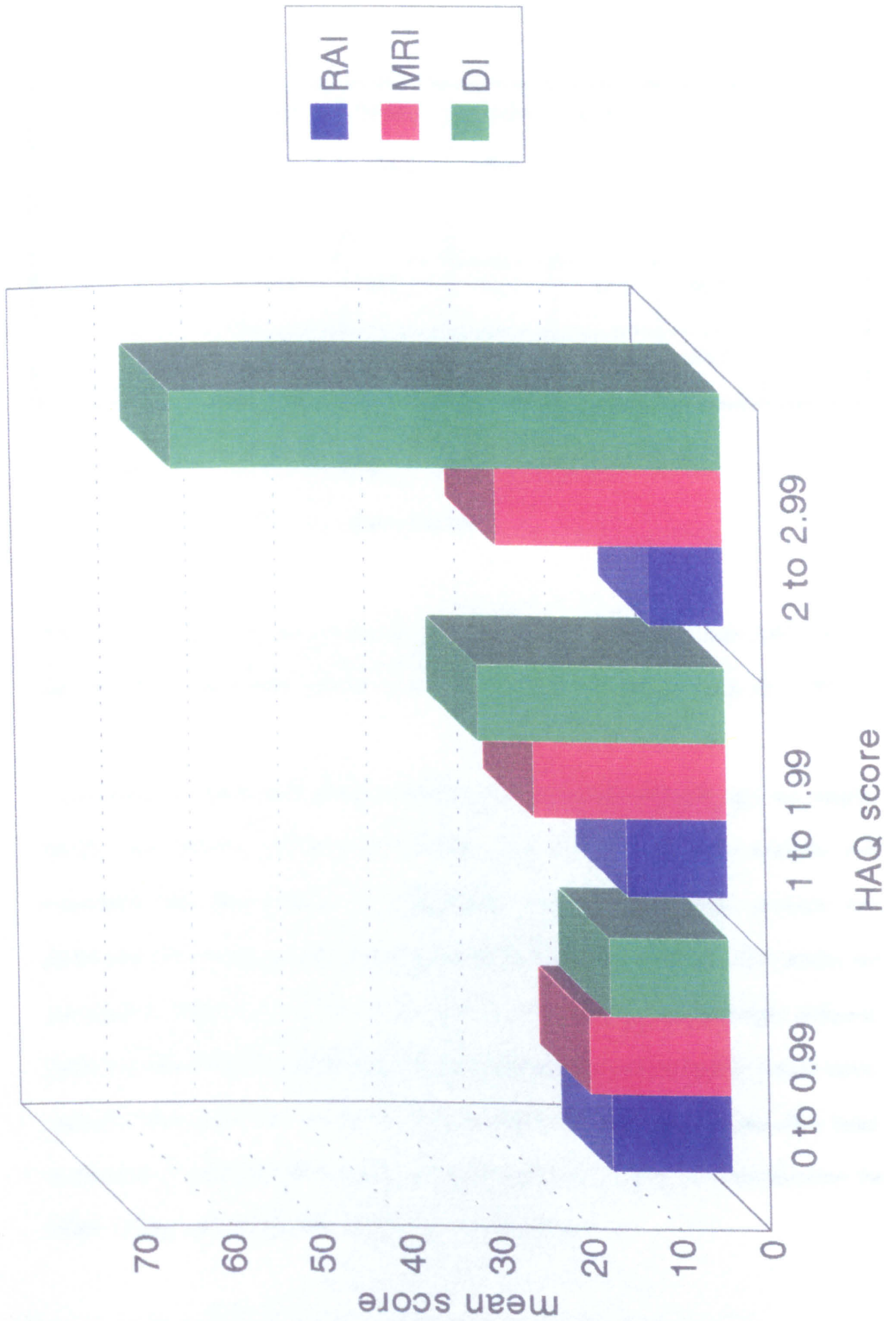
Figure 5.12

	N	Age (y)	height (cm)	weight (Kg)	grip (N)	pinch (N)	CSA (cm^2)
S	19	62.2	161.2	62.4	57.7	30.5	19.91
N	81	58.2	164.4	67.3	100.8	43.2	27.38

where S = patients on steroids

N = patients not taking steroids

The grip force per unit cross-sectional area for patients on steroids was 2.975 N/cm^2 and for patients not taking steroids was 3.65 N/cm^2 (t = -1.59, p = 0.12, df = 98).

To establish the relationship between maximum isometric grip strength, age, sex, height, weight, and forearm muscle cross-sectional area multiple regression analysis was performed with grip strength as a dependant variable. A separate analysis was performed for normal subjects and subjects with rheumatoid arthritis. The results are presented in Tables 5.5 and 5.6. It can be seen that the results are strikingly different. Table 5.5 shows that in normal subjects, even allowing for differences in muscle cross-sectional area, there is a significant effect of height, sex and age. On the other hand, in rheumatoid arthritis, when muscle cross-sectional area is taken into consideration the effect of age, sex, height and weight are not significant.

In an attempt to obtain predictive variables for cross-sectional area, multiple regression

Table 5.5

Multiple Regression Analysis for normal subjects. Maximum isometric grip strength as dependent variable. R^2 = 76%. R^2 adj. = 74.7%. Residual std. devn. = 49.49.

Predictor	Coefficient	Std. deviation	t ratio	P
Constant	- 28.7	142.1	- 0.20	0.841
Age (y)	- 2.459	0.279	- 8.83	0.000
Sex (m=1,F=2)	- 57.89	16.33	- 3.54	0.001
Height (cm)	2.333	0.767	2.91	0.004
Weight (kg)	0.142	0.679	0.21	0.835
CSA (cm^2)	3.719	1.281	2.90	0.005

Table 5.6

Multiple Regression Analysis for subjects with rheumatoid arthritis. Maximum isometric grip strength as dependent variable. R^2 = 38.6%; R^2 adj. = 35.3%. Residual std. devn. = 45.79.

Predictor	Coefficient	Std. deviation	t ratio	P
Constant	- 121.7	120.3	- 1.01	0.314
Age (y)	- 0.099	0.388	- 0.26	0.799
Sex (m=1,F=2)	- 13.80	14.23	- 0.97	0.335
Height (cm)	1.310	0.67	1.97	0.052
Weight (kg)	- 1.015	0.62	- 1.64	0.103
CSA (cm^2)	3.707	0.755	4.91	0.000

Table 5.7

Multiple Regression Analysis for normal subjects. Forearm muscle CSA is dependent variable. $R^2 = 60.6\%$. R^2 adj. $= 59.3\%$. Residual std. devn. $= 4.72$.

Predictor	Coefficient	Std. deviation	t ratio	P
Constant	3.216	8.983	0.36	0.721
Age (y)	- 0.149	0.023	- 5.67	0.000
Sex (m=1,F=2)	- 5.495	1.345	- 4.09	0.000
Finger Circumference (mm)	0.802	0.142	5.67	0.000

Table 5.8

Multiple Regression Analysis for subjects with rheumatoid arthritis. Forearm muscle CSA is dependent variable. $R^2 = 52.2\%$. R^2 adj. 50.2%. Residual std. devn. $= 6.61$.

Predictor	Coefficient	Std. deviation	t ratio	P
Constant	7.11	12.120	0.59	0.559
Age (y)	- 0.126	0.053	- 2.39	0.019
Sex (m=1,F=2)	- 3.625	2.061	- 1.76	0.082
Finger Circumference (mm)	0.450	0.152	2.96	0.004
Grip (N)	0.068	0.029	5.31	0.000

analysis was undertaken using cross-sectional area as the dependant variable and, in the case of rheumatoid arthritis, age, sex, grip strength and finger circumference as the independent variables. In the normal group only age, sex and finger circumference were used as independent variables. The reason for this was as follows. In order to re-analyse previously published results of stiffness in rheumatoid arthritis (Helliwell et al, 1988a) some measure of muscle wasting is necessary. Since grip strength in rheumatoid arthritis is not purely a function of muscle cross-sectional area, then it is not possible to use grip strength alone as a measure of muscle wasting: the additional variables of age, sex and finger circumference were added to improve the estimate (as measured by R^2). Unfortunately, previously published normative data on arthrograph stiffness in the MCP joints (Howe et al, 1985) recorded only height, weight and finger circumference in addition to stiffness data. The results for both these analyses are presented in Tables 5.7 and 5.8. All three independent variables are significant predictors of cross-sectional area in normal subjects. These three variables explain 60% of the variation in cross-sectional area, the associated r value being 0.77, sufficient to use as a predictive equation for cross-sectional area. In the subjects with rheumatoid arthritis age, finger circumference and maximum grip strength are all significant independent predictors, although sex just fails to reach significance in this population (p=0.08). The amount of variation in CSA explained by these variables is slightly less, 50%, but with an acceptable r value of 0.71.

Discussion

Ikai and Fukanaga (1968) found no difference between males and females or in the effect of age when grip strength was standardised for muscle cross-sectional area. In the 100 normal subjects in this study, (allowing for muscle cross-sectional area), age,

sex and height were still independent predictors (see Table 5.5). Fortunately our two populations were matched for age, sex, height and weight (see Table 5.3) and so the significant differences in forearm muscle cross-sectional area between the two groups can be regarded as reliable.

This result is not consistent with previously published results by Yung et al (1986). It is interesting to compare the forearm circumferences recorded by Yung et al with those recorded in this study and other published results in normal populations (see Table 5.9). The forearm circumference in the current study for the normal population is lower than that recorded in all the other studies, probably because the majority of the others were measured in younger populations and at the point of maximum forearm circumference rather than the mid-point. It is difficult to explain why Yung et al could not find a reduction in forearm circumference in patients with rheumatoid arthritis, unless their patients had less severe disease.

The marked differences in the regressions seen between subjects with rheumatoid arthritis and normal subjects recorded in Tables 5.5 and 5.6 are perhaps explicable on the basis of disease. Rheumatoid arthritis is likely to make the effects of gender and age much less important in terms of isometric grip strength. An example is a 34 year old male who had developed rheumatoid arthritis just 3 months prior to this study. He works as a mortician and his job involves a lot of heavy lifting. His forearm muscle cross-sectional area was 59 cm^2 yet his maximum grip strength was only 78 Newtons.

Nevertheless, the finding of a significant effect of age, sex and height on grip strength is not in agreement with previously published results (eg. Ikai and Fukanaga, 1969;

Table 5.9

Forearm anthropometry (cm) in different studies.

	Forearm Length (cm)			Forearm Circumference (cm)		
	R	mean	L	R	mean	L
Laubach & McConville (1967)	25.56	25.59	25.61	26.54	26.27	25.99
Wilmore & Behnke (1969) (males)				27.90		27.30
Wilmore & Behnke (1970) (female)				23.51		23.50
MEAN (M & F)				25.70	25.55	25.40
Pheasant (1986) Males Females Mean					27.0 24.0 25.50	
Yung et al (1986) Normal RA					22.29 22.61	
Helliwell (present study) Normal RA		24.4 24.18			23.19 21.75	

Schantz et al. 1983; Segal and Wolf, 1990). The results of multiple regression analysis can be misleading when the independent variables are strongly inter-correlated. Because of this two other analyses were performed: multiple regression using CSA and only one other predictor as independent variables (eg. age, sex or height); and an analysis of covariation using grip strength as the dependent variable, CSA, sex, age and height as the covariates and a grouping variable generated by dividing the normal group into two equal halves of 50 subjects each. In both cases, the results were unchanged. It appears, therefore, that sex and age have a genuine effect on grip strength, independent of muscle CSA, in this population. The effect of height is presumably related to hand size and mechanical efficiency when grasping the bars of the torque dynamometer.

It is difficult to gauge the effect of corticosteroids in this study. Patients taking corticosteroids, (19% in this population), are likely to have more severe disease. It is also notable that some patients with rheumatoid arthritis in this study have been inherited from a general physician whose practice was to give long-term steroids in the more severe cases. The differences in forearm CSA between the patients on steroids and those not taking steroids could therefore be due to steroid therapy but also could be due to differences in disease severity.

The calculated force per unit cross-sectional area for normal subjects is of the same order as that found in other studies: these are recorded below (all in N/cm^2)

Ikai and Fukunaga (1968)	Upper arm	9.4
Maughan and Nimmo (1984)	Thigh	8.9
Davies et al (1986)	Calf	10.6

Bruce et al (1989a)	Thumb	35.7 (18.5)
Fiatarone et al (1990)	Thigh	4.7
Helliwell (present study)	Forearm	7.4

The differences are, in part, explained by the different sampling frames. For example, Fiatarone et al studied frail, elderly institutionalised subjects. The method used by Bruce et al to estimate adductor policis CSA was, by their admission, an underestimate and the 'corrected' ratio is given in brackets.

Clearly the reduction in cross-sectional area seen in the group of patients with rheumatoid arthritis does not entirely explain the loss of grip and pinch strength recorded. Pain and deformity in the joints of the hand are likely to be responsible for part of this discrepancy and an attempt was made to record this mathematically by multiple regression analysis. However, it is difficult to assess whether these variables explain all of the reduction in grip strength. Certainly multiple regression analysis suggests that the 3 independent variables of pain, deformity and cross-sectional area only account for about 35% of the variation in grip strength in this group. Spiegel et al (1987) felt that joint deformity was the strongest predictor of reduced grip in rheumatoid arthritis. Bruce et al (1989b) and Stevens et al (1992) both suggest that intrinsic muscle wasting of the hand in the elderly is due to qualitative as well as quantitative deficiencies in the muscle and it must be supposed that some qualitative defect either in the neuromuscular efficiency or in the muscle cells is present in rheumatoid arthritis.

Summary

Significant muscle wasting has been found in a group of patients with rheumatoid

arthritis compared to age and sex matched normal subjects.

Some of the reduction in grip and pinch strength found in rheumatoid arthritis is attributable to this muscle wasting, but there is a 60% decrease in maximum isometric grip strength, a 45% reduction in maximum pinch strength yet only a 13% reduction in muscle cross-sectional area.

Some of this difference can be attributable to pain and deformity in the joints of the hand, but it is hypothesised that qualitative differences in the neuromuscular system of patients with rheumatoid arthritis are present.

CHAPTER 6

THE INFLUENCE OF MUSCLE ON JOINT STIFFNESS

Introduction

Literature survey

    Arthrographs used to measure spasticity

    Modelling muscle mechanics

Induced short-term changes in joint stiffness due to muscles

Joint stiffness as a function of muscle activation

Discussion

Summary

Introduction

Stiffness, defined as resistance to passive movement at a joint, cannot distinguish between articular stiffness and stiffness of extra-articular structures which are inevitably linked to joint movement. Of these extra-articular structures, muscles and their associated tendons are of paramount importance. It is of interest that a parallel and sometimes overlapping literature has developed as a result of research attempting to quantify spasticity using devices identical to the arthrographs. Moreover, in the field of muscle physiology, sinusoidal motion has been imposed on joints in order to test biomechanical and electro-mechanical models of muscles, the assumption being that the mechanical properties of the intact joint are entirely related to the associated muscle mechanics (Nichols, 1987).

In this chapter, the literature relevant to measuring spasticity and bio-mechanical modelling of muscles will be discussed and the relevance of this to measuring joint stiffness in arthritic disease will be argued. Experimental work will be presented which attempts to assess the contribution of muscle to joint stiffness in both normal subjects and patients with rheumatoid arthritis. In addition, an assessment will be made of the quality of muscular contraction in rheumatoid arthritis compared to normals.

Arthrographs used to measure spasticity

Apparatus identical to that of Wright and Johns (1960a, 1960b) was employed by Long et al (1964) to measure resting muscle tone in spasticity. They recorded hysteresis loops in six normal subjects while concurrently measuring EMG from the forearm muscles; the lack of EMG activity during the test led them to conclude that resting muscle tone is due to properties inherent in the muscle. In spasticity a marked increase

in the area of the hysteresis loop was found.

Fenn and Garvey (1934) designed a horizontal knee arthrograph for the quantification of spasticity. The angular velocity varied from very slow to 1.2 radians/sec over a 60 degree range. Marked increases in elastic and viscous torque were seen in spasticity.

Webster (1964) used a similar horizontal knee arthrograph for the quantification of spasticity. The lower leg was placed on a large horizontal turntable which oscillated through 100° of amplitude at a rate of approximately 20 to 24 degrees per second. The area of the hysteresis loop was increased in hemiplegia and in Parkinson's disease, and they were able to show an effect of pharmacological therapy on the area of the hysteresis loop in these two conditions.

In the elbow, Jones et al (1982) used a horizontal arthrograph imposing sinusoidal motion at 15° per second with a potential amplitude of movement of 100°: the area of the hysteresis loops obtained were used as a measure of spasticity as well as demonstrating the asymmetrical tonic neck reflex in the hemiplegic arm; they were also able to demonstrate that the area of the loop increased with simple mental arithmetic.

At the ankle, Rebersek et al (1986) developed an arthrograph to quantify spasticity in hemiplegic limbs. Again, sinusoidal motion was used at frequencies varying from 0.1 to 2Hz with maximum amplitude of 15° imposed at different angles of dorsiflexion and plantar flexion of the ankle. They did not present results compared to normals, but found that the measured stiffness was highly dependent on the initial muscle length.

Gajdosik et al (1990) measured the passive resistance to extension of the knee as a measure of compliance and length of the hamstring muscles in order to quantify the straight-leg raising test. They found steep increases in torque as the knee was extended, but the slope of the initial curve (with a knee angle of about 50 - 70°) was linear.

In clinical practice, a bedside measure of spasticity can be used which depends on the behaviour of a joint and its associated muscles as a well damped single degree of freedom mass spring system (Dejong, 1962). It is usually applied to the elbow, shoulder or knee. For the knee, the patient sits on the end of a couch and the leg is allowed to fall and swing to rest without interference by active muscle contractions. The stiffer the system, (i.e. the more spasticity), the higher the frequency of oscillation and the greater the damping. Bajd and Bowman (1982) designed a system to quantify this test and estimated such variables as the amplitude of the initial oscillation, the difference in amplitude between the first and second oscillation, and the time taken from the start of the test to when the leg comes to rest.

The existence of two parallel literatures, in which the same technique is employed to measure, ostensibly, different things exemplifies a preoccupied, partisan approach to research which precludes cross-fertilisation between specialties and hinders the progress of knowledge. Even with latter day computerised cross-indexing many research programmes still proceed in ignorance of each other. The work on muscle spasticity indicates that muscles can make a large contribution to passive resistance at the joint and, in considering the pathophysiology of arthritis, the pathological changes in muscle must be taken into consideration.

Muscle bio-mechanics and modelling

Much of the original work on muscle mechanics is attributable to Hill (Gasser and Hill 1924, Hill 1938). Hill derived a mechanical model based on experiments on isolated cat soleus muscle and, in a series of elegant experiments, was able to link physicochemical and mechanical processes. The so-called phenomenological model of Hill continues to be used by bio-engineers, although muscle bio-physicists have developed more complex models based on the cross-bridge theory of A F Huxley: some authors combine the features of both models, eg: see Zahalak (1990). The model suggested by Hill is shown in Fig. 6.1, the essential features of which are a contractile element (CE) in a series with an elastic element (SE); at rest an alternative model was represented by the addition of a parallel elastic element, indicated by PE in Fig. 6.1. Within the contractile element is a viscous internal resisting force (Pv) and an active state force (Po). It is important to note that the contractile element embodies the process of chemo-mechanical energy conversion, and experiments were able to relate tension and velocity by two constants, as shown in the following formula.

$(a + P) V = b (Po - P)$

where, P = force: 'after load'.

Po = steady isometric force.

V = velocity of shortening.

a = constant, 'heat of shortening'.

b = constant.

This equation related both physical and chemical processes and established a relationship between purely mechanical variables, P and V; this relationship, in an isotonic quick release test with an isolated cat soleus muscle under tetanic stimulation, is shown in Fig. 6.2. It is important to note that the series elastic element (SE)

Figure 6.1

The 1938 Hill model for muscle.

SE = series elastic element.

CE = contractile element.

PE = parallel elastic element (added to model the passive elastic properties of unstimulated muscle).

P_o = the active state force.
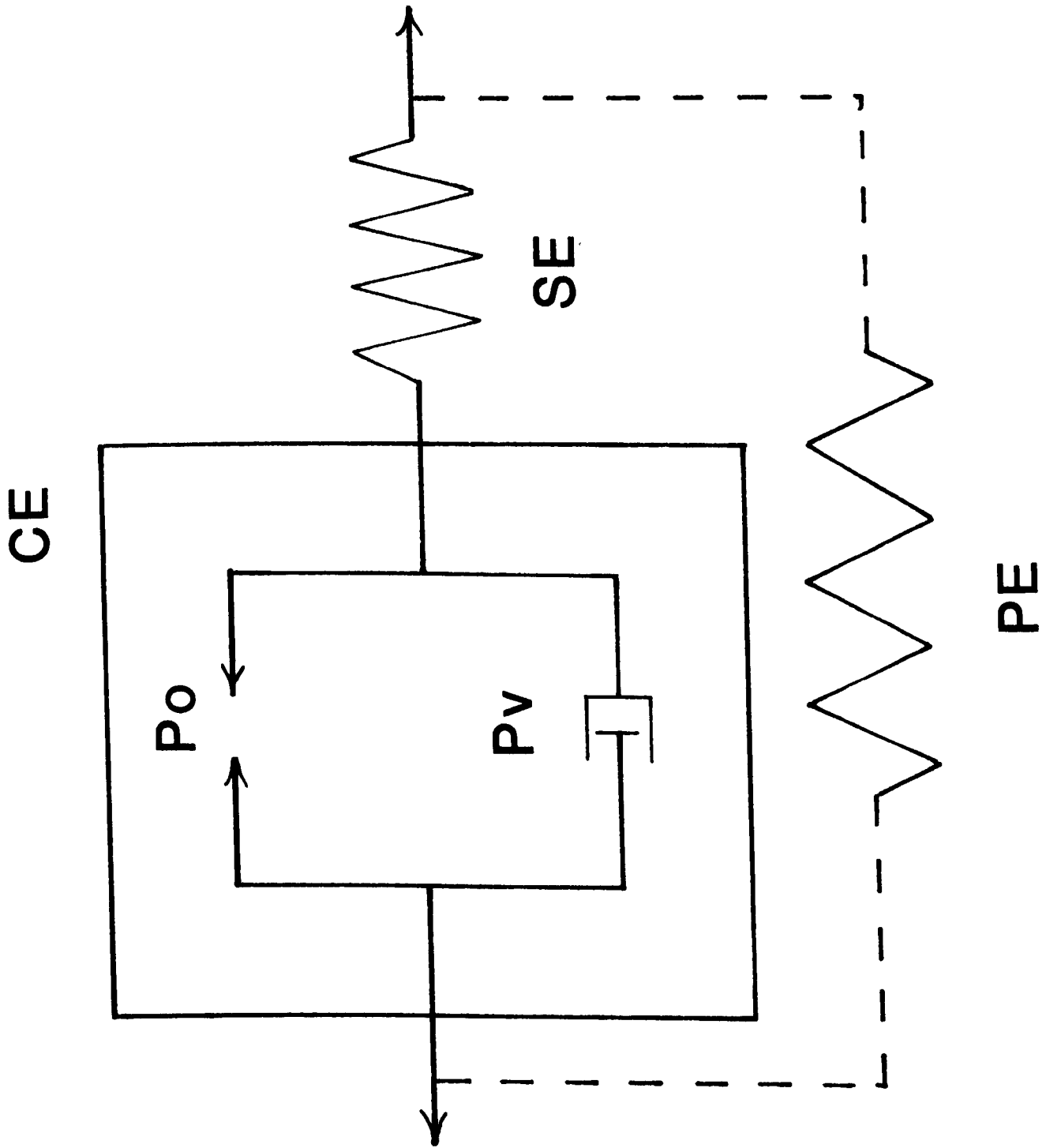
P_v = the viscous internal resisting force.

Figure 6.1

Figure 6.2

Hill (1938) studied cat soleus muscle undergoing quick release tests. Graph of afterload as a function of the steady velocity of shortening in the release phase.

P = force.

V = velocity.
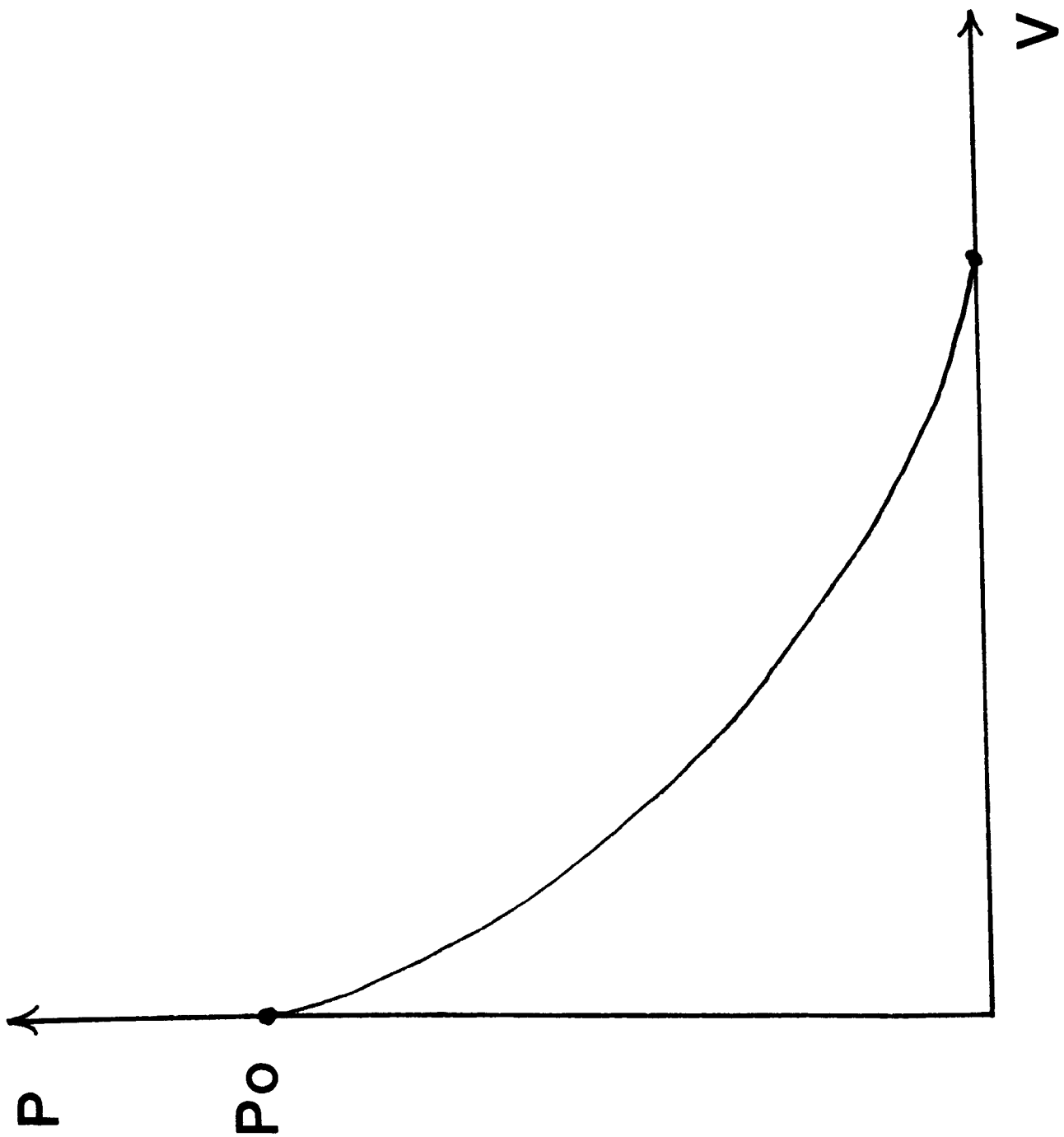
P_O = steady isometric force (active state force).

Figure 6.2

represented in Fig. 6.1 does not represent any particular anatomical structure (such as the tendon), but is embodied within cross-bridges between actin and myosin, (Zahalak 1990).

The advantages of the Hill model are that there is a large body of evidence derived using such models, and that Po, a and b are known for many muscles and that there is a good, although not complete, fit between in vitro muscle behaviour and this model. The disadvantages of using the Hill model are that the elements are purely conceptual and that the stiffness of the contractile element in reality is equal to the number of cross-bridges between actin and myosin which, it is known, are a function of the preceding history of muscle length and contractility (Zahalak 1990).

Muscle/joint system modelling has assumed major importance in the field of robotics and prosthetics. In this situation, experiments on isolated cat soleus muscle are of limited value and many research groups are now deriving fundamental information on the control of joint position, muscle stiffness and posture, from experiments on intact humans. A feature common to these experiments is the imposition of perturbations about a joint with varying external loads and varying levels of contraction or co-contraction of agonist and antagonist muscles. As Winters et al (1988) have pointed out, in such experiments there are three input/output ports: (i) neural port (desired level of contraction), (ii) torque port (resistance of the muscle joint system), and (iii) kinematic port (velocity or length of the system). In these experiments, it is sometimes useful to maintain one of these variables constant and to measure the resultant relationship between the other two. In this way, in the elbow in flexion/extension, Winters et al (1988) were able to show that according to the input characteristics

(relaxed or with varying degrees of co-contraction of flexors and extensors) either inertia, viscosity or elasticity predominated.

Moffatt et al (1969) used a vertical knee arthrograph, similar to that used by Goddard et al (1969) but with a mathematical correction for inertia, to supply sinusoidal motion to the knees of normal subjects. They measured resultant torque and modelled the muscles around the knee on the basis of their results, concluding that muscles obey a Maxwellian model with a variable two element fluid according to the knee joint angle and muscle tension. Interestingly, at rest, over an angle of 50° the angular stiffness they recorded was 423 Nm/deg. (compare with other recorded knee stiffness in Table 2.2). Tennant (1971) performed experiments on the human forearm flexors, using tetanic stimulation and measured the force developed according to several external applied loads. This author, who was an employee of the National Aeronautics and Space Administration, was interested in the control of bio-prostheses and the use of external stimulation of paralysed muscles in hemiplegia. He confirmed many of the known properties of muscle: EMG is related to muscle force potential only under isometric conditions; in neuro-muscular control the frequency signal specifies length, the amplitude signal force; the force developed depends on the initial muscle length; servo control of the muscle is via a gamma efferent system; and externally applied loads may terminate the displacement response to a standard neural input.

Experiments on the response of the muscle/joint system to perturbations is not only of use in terms of theoretical modelling and robotics, but is of importance in predicting and explaining the optimisation of movement trajectories (both loaded and unloaded), the reflex regulation of muscle and joint stiffness, and the prediction of behaviour of

muscle/joint systems in human activities. Both Nichols (1987) and Hassan (1986) point out that the mechanical properties of the intact joint are related entirely to the associated muscle stiffness and the overriding assumption is that joint stiffness is variable and entirely a function of coactivation of agonist/antagonist muscles. The variability in stiffness that results from co-contraction may play an important role in minimising the effort associated with unperturbed movement and in static posture control. As discussed in chapter 4, a number of articular (heterogenic) and muscular (autogenic) reflexes serve to control muscle activation (and therefore stiffness), in addition to cortical input and passive muscle properties. Walsh (Lakie et al 1979, Walsh 1987) has described the importance of thixotropy in the maintenance of static postural control, and it will be discussed further in the next section. Thixotropy does, however, appear to be an entirely passive property of the intact muscle. There are obvious advantages to the thixotropic effect in maintaining posture and in activities such as writing where the small amplitudes incurred will tend to stiffen the hand/arm unit and therefore enable better control.

In designing experiments to test the relative contribution of elastic stiffness and viscous damping to quadriceps muscle function in jumping and running, Cavagna (1970) and Green and McMahon (1979) have used a similar experimental design. Cavagna determined elastic stiffness and damping in four human subjects jumping onto a force platform with the knees extended. Elastic stiffness was derived from the frequency of oscillation of the body, measured on the force platform, and damping by the rate of decay of oscillations. Green and McMahon studied humans bouncing on long planks while carrying weights of different magnitudes. The stiffness of the system decreased with increasing knee angle and increased with increasing weight carried.

The mechanical characteristics of damped oscillating systems have been used extensively in studies of motion control and control of joint and muscle stiffness. Joyce and Rack (1974) imposed flexion/extension perturbations on the elbow while the subject exerted a flexion force against different loads. They were able to show an increase in spring stiffness of the system with an increase in frequency of perturbation and hypothesised that the tendency to oscillation may be an advantage in, for example, hopping and running, especially if the resonant frequency can be altered to suit the activity. They also pointed out that multiple linkage joint systems will have a lower resonant frequency so that resonance may not interfere with movements where fine control is required, and adding an external load will decrease the amplitude of displacement, although there must be an optimal magnitude for this effect.

Agarwal and Gottlieb (1977) observed driven oscillations of the ankle joint in plantar flexion and dorsiflexion with a maximum amplitude of 15° and frequency variation of 3 to 30 Hz: they found the resonant frequency at rest to be 4 Hz and with co-contraction this increased to 8.5 Hz. The dynamics of the human ankle have also been studied by Hunter and Kearney (1982) who found that both dynamic ankle stiffness, angular elasticity and resonant frequency increased linearly with levels of muscle activation, although no change in viscosity or inertia were seen. A similar result was obtained in the elbow by Laquaniti et al (1982), and Cannon and Zahalak (1982) who found the principal effect of increasing the neural input (ie: contraction level) was to increase the resonant frequency and elastic stiffness of the system. Both these researchers found that viscosity of the system decreased proportionately with increased co-contraction level and at rest was approximately 1.5% (Laqauniti et al) and 12% (Cannon and Zahalak) of elastic stiffness.

A novel application of the technique relating resonant frequency, stiffness and muscle contraction has recently been reported (McNair et al 1992). This group studied the stiffness of the hamstring muscle in relationship to internal knee derangement (anterior cruciate ligament rupture). Subjects were tested lying prone with the lower leg horizontal: weights were attached to the lower leg according to the maximum voluntary capacity of each subject and, while the muscle was loaded, a small perturbation was applied to the lower leg and the response recorded by an accelerometer. In this way, the authors were able to measure the stiffness of the system modelled as a slightly damped single degree of freedom mass spring system. They were able to test their subjects at 30%, 45% and 60% of maximum voluntary contraction and found a non-linear increase in stiffness. Interestingly, there were no significant differences between the measured stiffness of the injured and non-injured leg at all muscle activation levels, and they explained this finding on the basis of differential muscle wasting with internal knee derangement (the quadriceps being predominantly the affected muscle).

Although the above experiments are more concerned with the 'active' properties of the muscle/joint complex than the behaviour of this system passively, they do provide a useful reminder that muscles have an important influence on stiffness of the system as a whole. Indeed, joints and their associated muscles spend a large part of the 24 hr cycle in the 'active' state and it may be as important to study the mechanics and behaviour of the system 'activated' as it is the passive properties of joints and muscles.

Induced short-term changes in joint stiffness due to muscles

The work of Walsh and Lakie in Edinburgh will be recalled from chapter 2. Their experiments involved investigating the passive compliance of the wrist joint by imposing sinusoidal displacement at varying torques and measuring the displacement. An increase in resonant frequency (and hence stiffness) was seen with small sinusoidal torques at a frequency of 2.5 Hz: this could be abolished by a single large displacement but would return if the displacing torque was discontinued for three cycles or more (more than one second). This effect they called thixotropy (Lakie et al 1979b). A similar effect was described at the hip joint in a later paper by Walsh (1987) in the elbow by MacKay et al (1986) and in the McP joint by Helliwell (1987). Walsh hypothesised that this effect was purely passive property of muscle and was important in postural control, negating the requirement for reflex changes in muscle stiffness as a result of small perturbations in joint position. Walsh (personal communication) has been unable to detect thixotropy in the eye muscle, and clearly, because of the functional requirements of small saccadic eye movements, the phenomenon would be disadvantageous in this muscle. Thixotropy is also seen in many household substances such as non-drip paint and tomato ketchup ("its shake and shake the ketchup bottle, none will come and then a lot'll").

Fig. 6.3 illustrates this effect in a normal human subject. The subject was 40, male, without any evidence of joint disease in the hand. Stiffness was measured with the Leeds microprocessor controlled arthrograph at 8 different amplitudes at a frequency of 0.5 Hz. Elastic stiffness is represented by the mean slope of the hysteresis loop and 'viscosity' by the area of the loop. When this effect was first noted, in 1985, the sequence of tests was thought to be important: starting at a higher amplitude and then

Figure 6.3

Thixotropy.

Relationship between amplitude (peak to peak) of displacing cycle and (a) mean slope, (b) area.

Measurements were made starting at an amplitude of 4° peak to peak and increasing to 32° (up) and, during a separate test procedure, starting at an amplitude of 32° and decreasing to an amplitude of 4° (down).
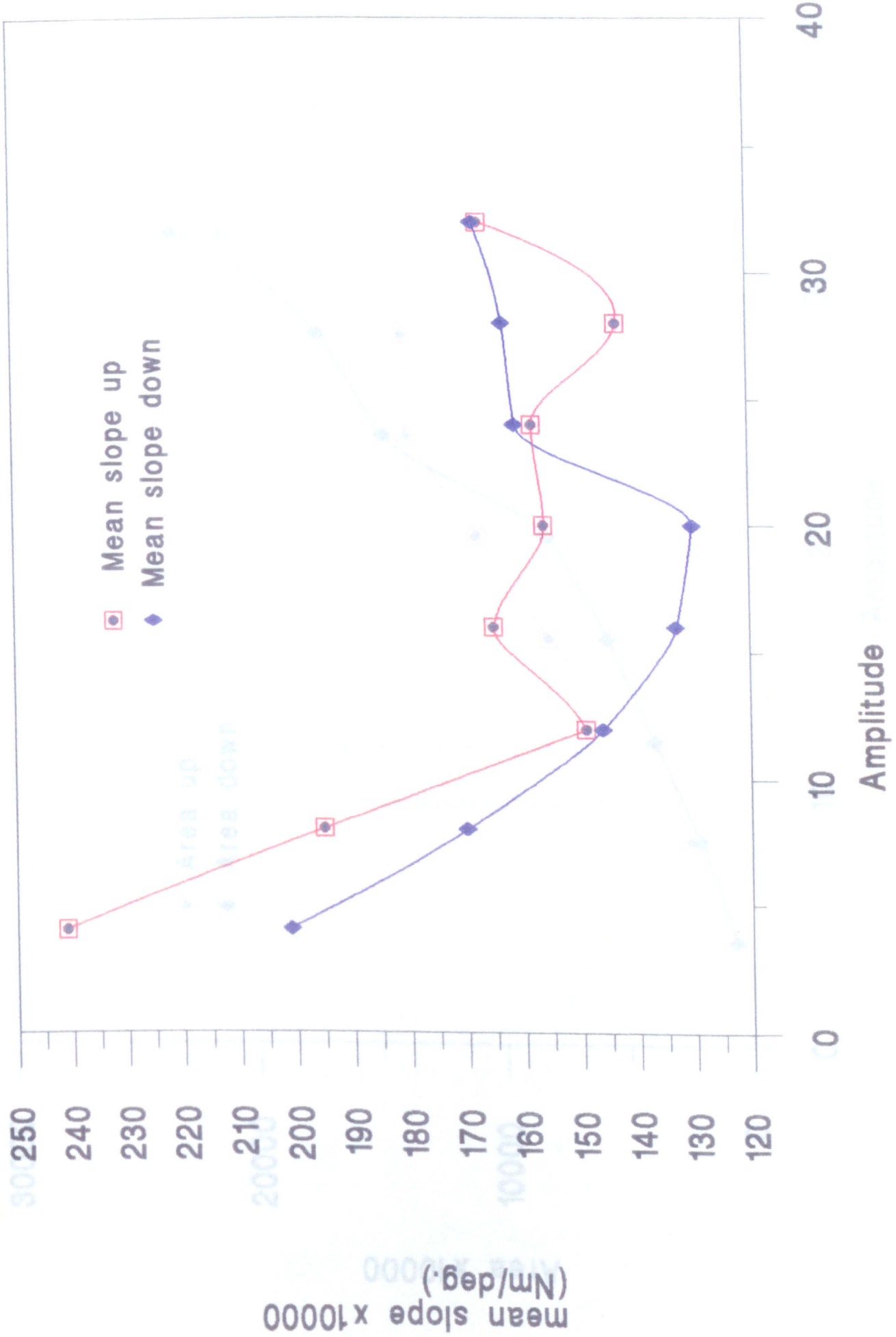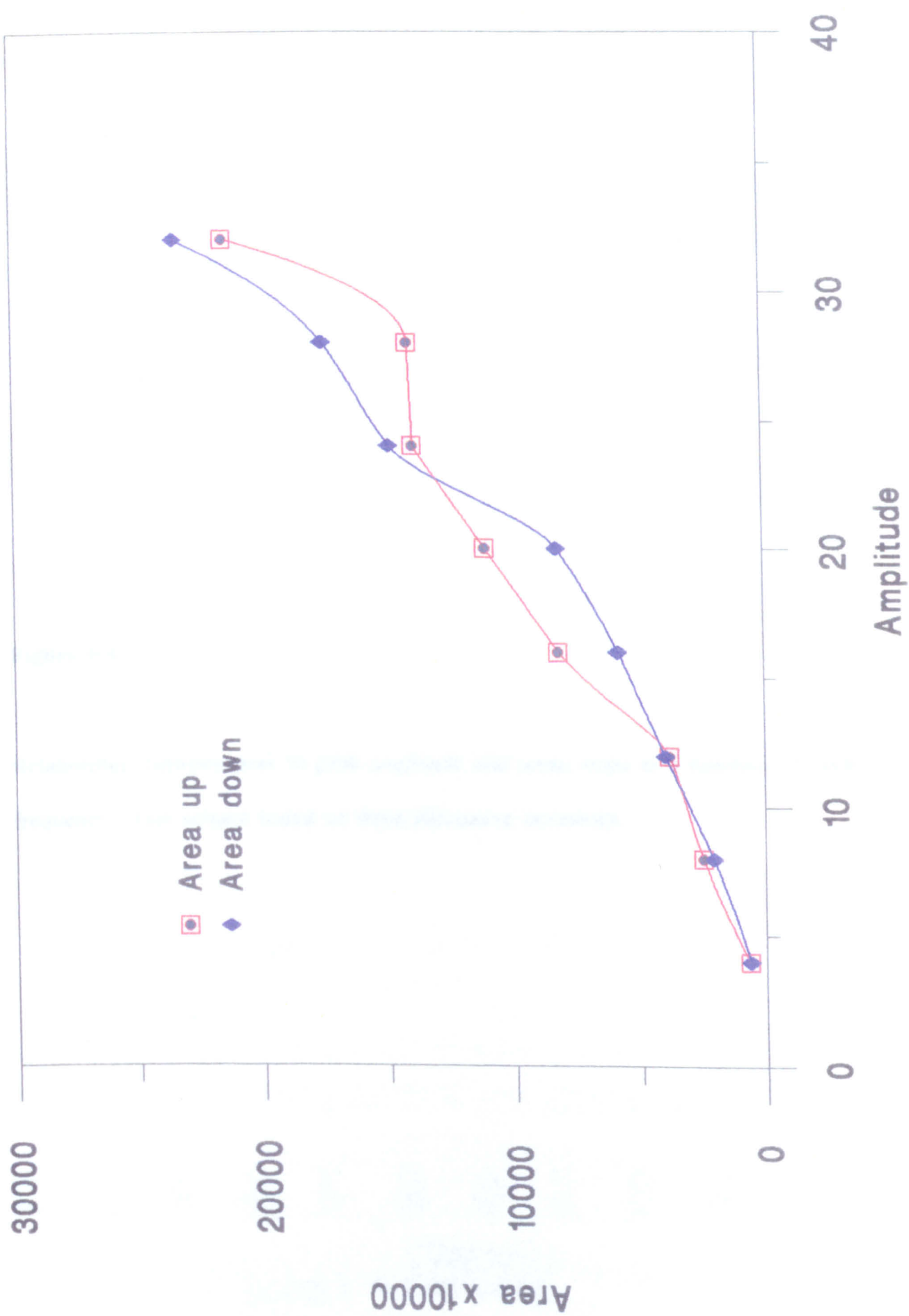
Figure 6.3a

Figure 6.3b

Figure 6.4

Relationship between peak to peak amplitude and mean slope as a function of cycle frequency. One subject tested on three successive occasions.
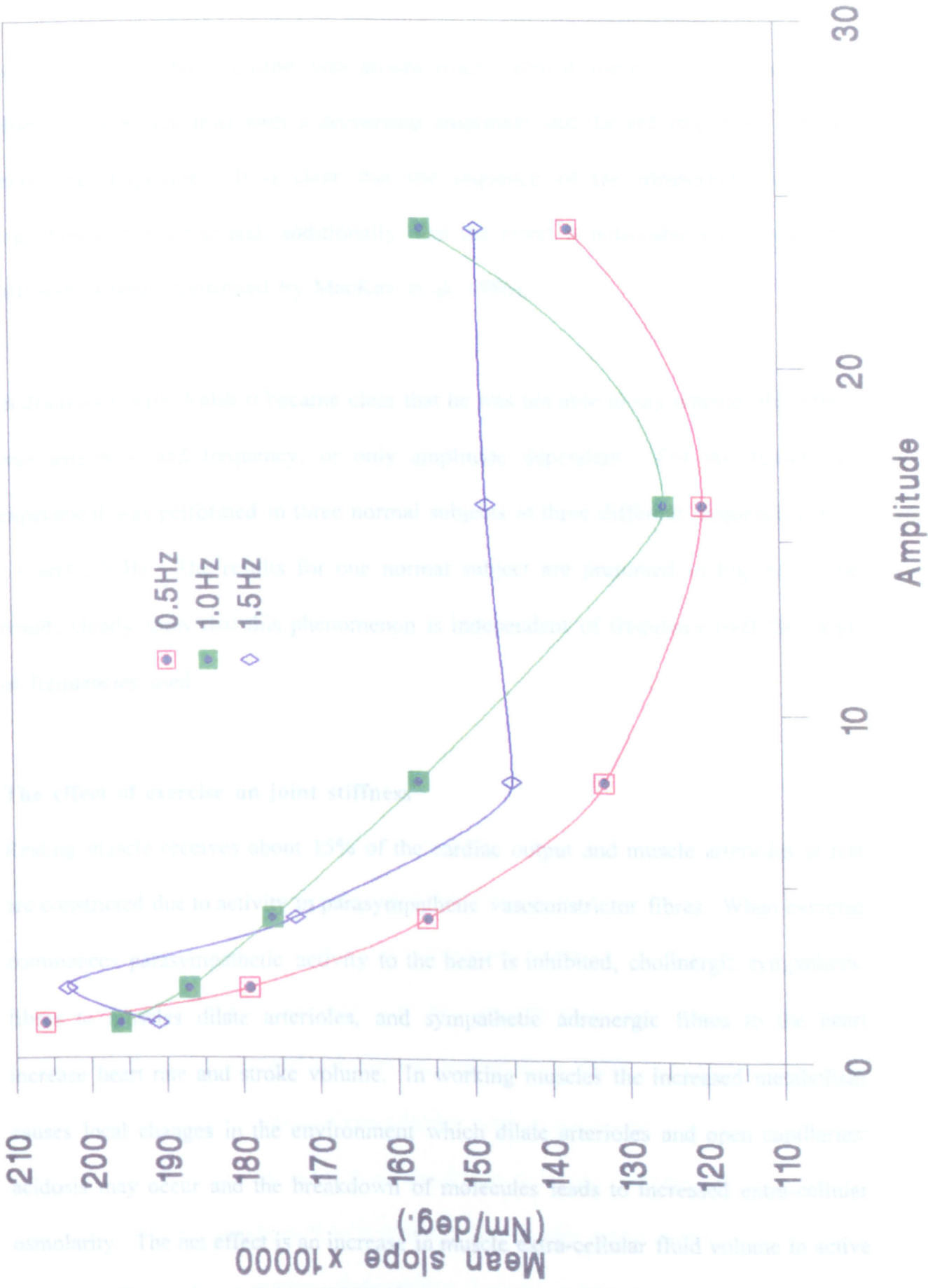
Figure 6.4

decreasing rather than the other way around might abolish the effect. In Fig. 6.3 the blue lines represent tests with a decreasing amplitude and the red lines tests with an increasing amplitude. It is clear that the sequence of the measurements is not important in this effect and, additionally, that the effect is noticeable only for elastic stiffness (a result confirmed by MacKay et al, 1986).

In discussion with Walsh it became clear that he was not able to say whether this effect was amplitude and frequency, or only amplitude dependent. For this reason, an experiment was performed in three normal subjects at three different frequencies: 0.5, 1.0 and 1.5 Hz. The results for one normal subject are presented in Fig. 6.4. The results clearly show that this phenomenon is independent of frequency over the range of frequencies used.

The effect of exercise on joint stiffness

Resting muscle receives about 15% of the cardiac output and muscle arterioles at rest are constricted due to activity in parasympathetic vasoconstrictor fibres. When exercise commences parasympathetic activity to the heart is inhibited, cholinergic sympathetic fibres to muscles dilate arterioles, and sympathetic adrenergic fibres to the heart increase heart rate and stroke volume. In working muscles the increased metabolism causes local changes in the environment which dilate arterioles and open capillaries: acidosis may occur and the breakdown of molecules leads to increased extra-cellular osmolarity. The net effect is an increase in muscle extra-cellular fluid volume in active muscles. Sjogaard and Saltin (1982) found an increase in muscle extra-cellular fluid of approximately 100% in short-term intensive exercise. It may take as long as 50 to 60 minutes before the plasma volume is restored (Astrand and Rodahl 1986).

The ability of muscle to maintain force, and the effect of fatigue, are dependent upon the blood flow, (and therefore the accumulation of metabolites), through the muscle. A maximal contraction can be sustained for only a few seconds. In isometric contractions where the force exerted is less than 15% of maximum and there are appropriately spaced pauses, blood flow can secure a supply of oxygen and remove the formed metabolites. However, at heavier loads there is impaired blood flow, accumulation of metabolites and the onset of fatigue. The imbalance between oxygen delivery and energy production is reflected by the accumulation of lactic acid due to anaerobic metabolism. The peak muscle concentration of lactate following an intense period of exercise occurs just at the end of exercise but the peak blood concentration of lactate occurs several minutes later. (Astrand and Rodahl 1986): the point at which the two curves cross is between 5 and 7 minutes.

An experiment was designed to demonstrate the short-term changes in extracelluar fluid and blood volume seen in exercising muscles using the Leeds microprocessor controlled arthrograph. Four normal subjects were studied, mean age 32 years, three males, one female. The results reflect experiments on the dominant arm in two subjects, of the left arm of one subject on two successive occasions, and on each arm of one subject on two successive occasions, a total of six tests. Isometric grip strength was measured using a pneumodynomometer and subjects were asked to perform repeated isometric exercise at 50% of maximum voluntary contraction until fatigue occurred. An approximate contraction frequency of 1Hz was requested and the time to fatigue was about 4 minutes. Fatigue was deemed to have occurred when subjects were no longer able to achieve 50% of maximum voluntary contraction due to pain and cramp-like feelings in their forearm muscles. Stiffness was measured immediately after

Figure 6.5

The effect of isometric forearm exercise on mean slope and area measured by the finger arthrograph. Mean of six tests on four subjects, (see text for details).
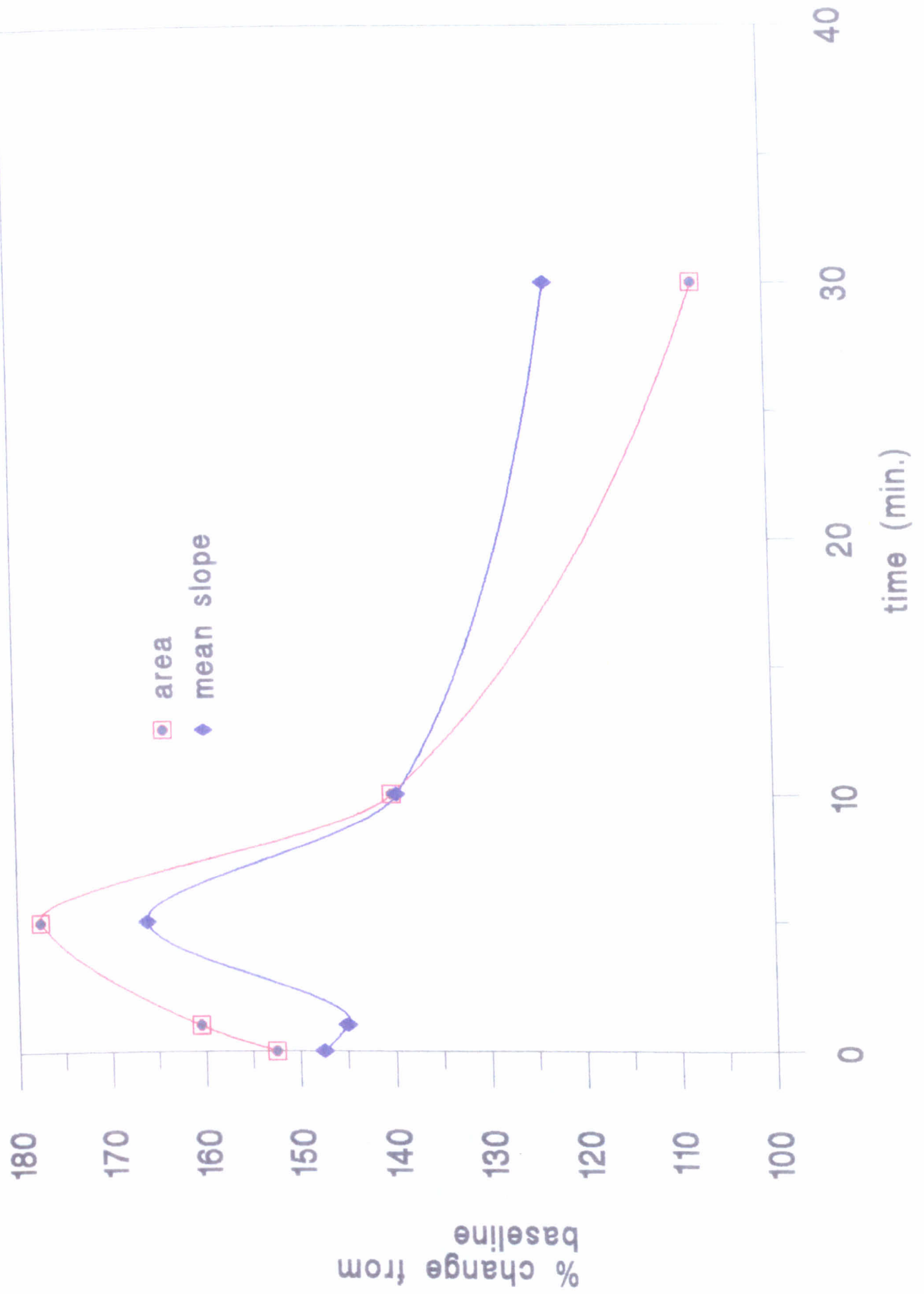
Figure 6.5

immediately after cessation of exercise, at 1 minute, 5 minutes, 10 minutes, and 30 minutes following cessation of exercise.

The results are presented in Fig. 6.5. Without sufficient data points it is difficult to say at what point peak stiffness occurred, but there is a clear increase in stiffness, up to 150% of resting values in one subject, with exercise and this gradually returns towards the normal resting level by 30 minutes after exercise. There are striking similarities between these figures and those obtained from blood lactate levels following a short period of intensive exercise (see for example page 321, Astrand and Rodahl, 1986).

Joint stiffness as a function of muscle activation

Theoretical considerations

All collagenous structures display length and velocity dependent stiffness, that is elastic and viscous stiffness respectively. The simplest phenomenological model to describe this behaviour is the Kelvin body, essentially a spring and dashpot in parallel. The structures acting across the joint can be modelled in this way. In Fig. 6.6, I have described the muscle/joint system as a group of modelled elements each member of the group representing an anatomical structure. Thus, of the three members, I have represented the contractile element of muscle (C) as a variable stiffness spring, the anatomical counterpart of which are the actin and myosin filaments of the muscle: this arrangement is simplified to the extent that the contractile elements of muscle also demonstrate variable non-elastic stiffness properties but the magnitude of the non-elastic stiffness is small compared to total stiffness, particularly when the muscle is contracting. Nevertheless, the non-elastic stiffness properties of the contractile element are important functionally, particularly with regard to the shock-absorbing properties

Figure 6.6

Diagram of model used in this study.

C = variable stiffness spring of contractile muscle elements.

P = parallel Kelvin element representing non-contractile elements of muscle.

S = series Kelvin element representing non-contractile elements in series with muscle (tendon and articular structures).
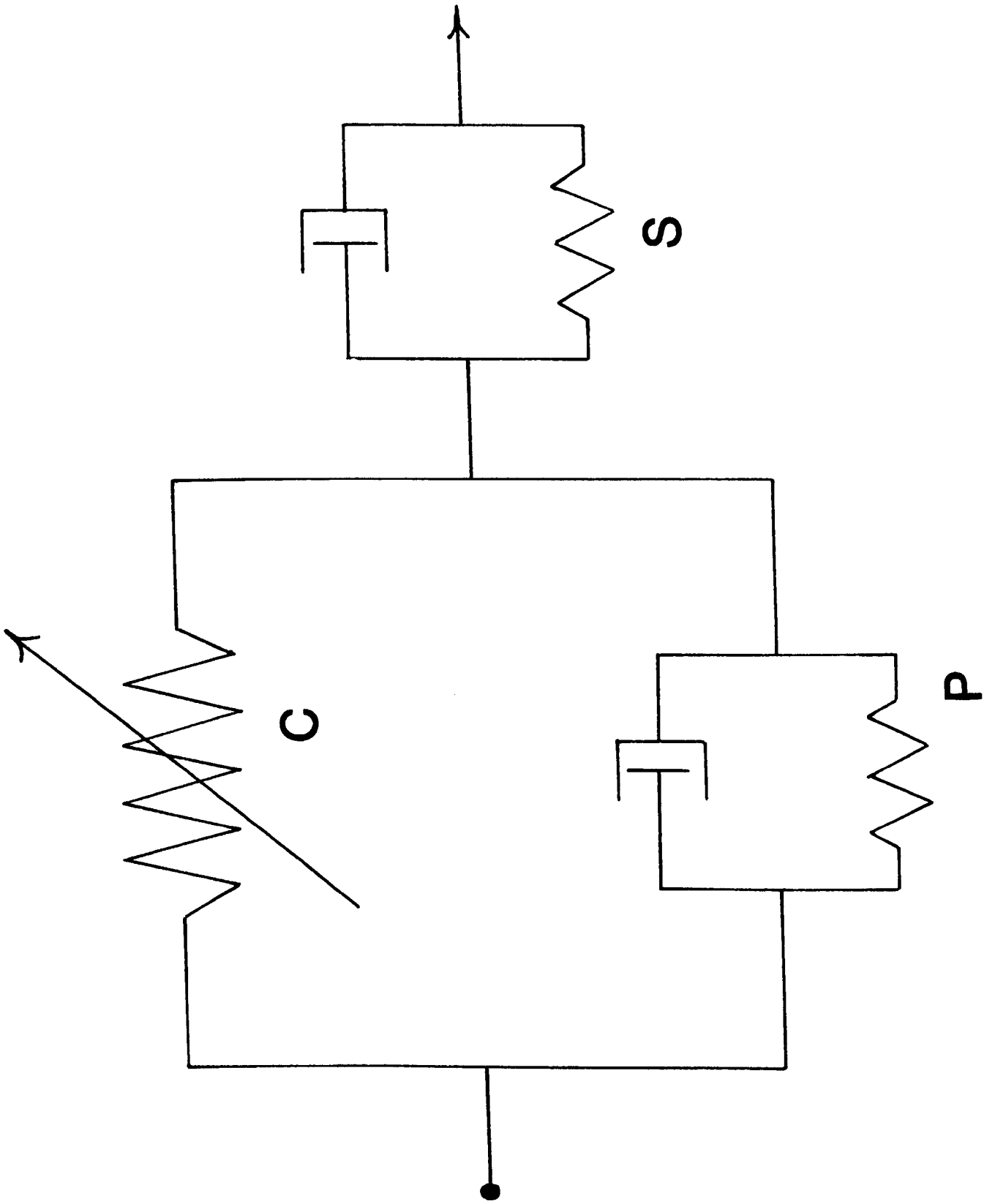
Figure 6.6

of contracting muscles. Secondly, I have represented the non-contractile tissues of the muscle, the perimysium, the epimysium and interseptal connective tissue, by a Kelvin body (P) in parallel with the contractile element; and a Kelvin body in series (S) which represents muscle tendon and articular connective tissue such as the capsule and periarticular ligaments.

Let the elastic stiffness of the contractile element at rest (K_c-rest) be proportional to the number of muscle fibres (k) and their diameter (d), given by:

K_C - rest α d.k

This will be an approximation only because the number of cross bridges formed at rest is not constant and is dependent on the history of previous stretch and activation.

The term 'd.k' in the above equation is equivalent to the physiological cross sectional area of the muscle.

The total elastic stiffness (K_T) at rest is a function of K_C - rest, the elastic stiffness of the parallel element (K_P) and the elastic stiffness of the series element (K_S).

Previous work (Johns and Wright, 1962; Helliwell, 1987) has shown that, at rest:

$K_S > K_C$ - rest + K_P

On contraction of the muscle:

K_C - contracting $>> K_S > K_P$

There is some evidence that the stiffness of non-contractile elements within the muscle can change with muscle activation (Ker 1981), but for the purposes of this discussion

this has been ignored. The terms K_S and K_P are assumed, therefore, to remain constant independent of muscle activation, and the proposed relationship between K_T and muscle activation level is shown in Fig. 6.7. The abscissa (muscle activation level) is presented as an arithmetic scale, but it may be that the square root would be better to provide a linear relationship between the K_T and muscle activation (see Winters, 1990).

By studying sufficient numbers, and calculating appropriate regression statistics, confidence intervals for both intercept and slope may be generated. The confidence interval of the intercept reflects the distribution of scores of K_T, this distribution in turn reflecting the distribution of muscle cross sectional areas; (see inset, Fig. 6.7).

The foregoing discussion is of interest in two ways. Firstly, in rheumatoid arthritis, although the relative contribution of K_C - rest, K_P and K_S to total elastic stiffness (K_T) may change, providing the muscles are qualitatively normal the slope of the curve K_T /activation level should be the same as for normal subjects. Secondly, since a measure of K_C - rest can be obtained from anthropometric data, it should be possible to compare K_T at rest (the intercept) between groups by an analysis of covariance using muscle cross-sectional area as covariate.

In order to investigate the relationship between passive stiffness, muscle cross-sectional area and muscle activation level, a departure from the traditional rheumatological method of measuring joint stiffness had to be made. The experiments are based on an adaptation of the technique by McNair et al (1992) but also used by several other investigators, notably Alexander's group in Leeds (Cuming et al 1978). Elastic and

Figure 6.7

Diagrammatic representation of the relationship between stiffness and muscle activation level.

Symbols as in text.

K_T - contracting = total elastic stiffness with forearm muscles co-contracting.

K_T - rest = total elastic stiffness with muscles relaxed.

K_C - rest = elastic stiffness of contractile element at rest.

K_P = elastic stiffness of parallel muscle element.

K_S = elastic stiffness of series element.

The proportional contribution of K_S at rest in the finger is assumed to be approximately 60%. When the forearm muscles co-contract the proportional contribution of the contractile element (K_C - contracting) increases but the absolute contribution from the parallel element (K_P) and the series element (K_S) remains unchanged.

If articular stiffness (K_s) is increased in arthritis this will be apparent as an increase in the intercept, but the magnitude of the intercept will also depend on the associated decrease in the contribution from muscle (K_C and K_P); providing the muscle is functioning normally, the slope of the line should not change.
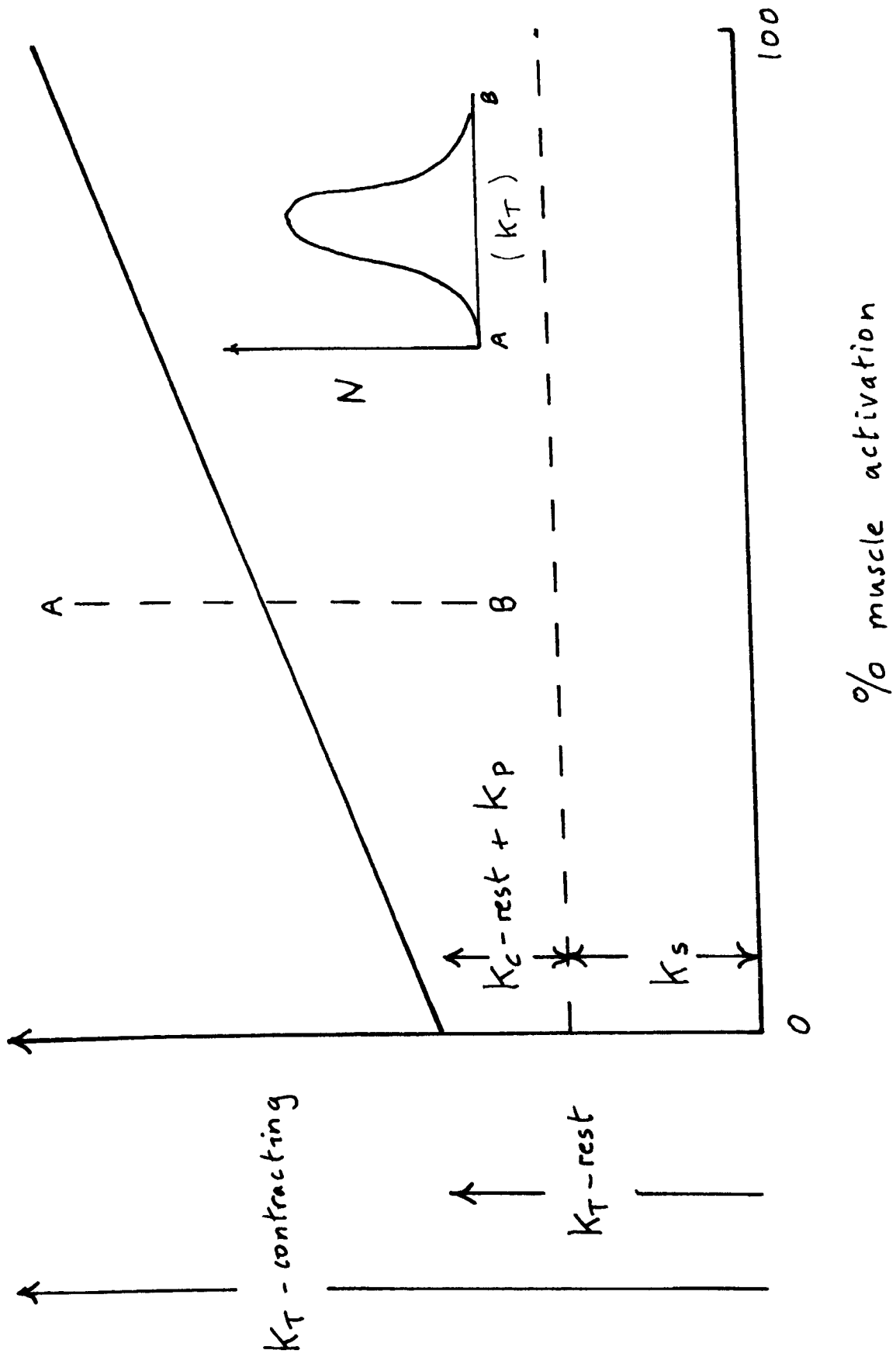
Figure 6.7

viscous stiffness were measured at the wrist with the subject grasping the handles of a strain gauged dynamometer, the output from which was visible to the subject. In this way, muscle activation level was controlled. Stiffness was measured by applying a small perturbation to the system and measuring the subsequent damped frequency response. The experimental system is shown in diagrammatic form in Figs. 6.8 and 6.9. In this system, the stiffness is given by:

$$W_n = \sqrt{(K/J)} \qquad \text{radians/sec}$$

Where W_n = natural angular frequency (radians/sec)

K_T = angular stiffness (Nm. rad^{-1})

J = polar moment of inertia (Kg. m^2)

But:

$$J = mr^2$$

and

$$f_n = W_n/2\pi$$

Where m = mass of hand and dynamometer

r = radius arm (distance between centre of rotation of wrist and accelerometer attached to dynamometer handles)

f_n = resonant frequency of perturbed system,, so that dynamic angular stiffness (K_T) is given by:

$$K_T = JWn^2 \quad \text{Nm. rad}^{-1}$$

$$K_T = f_n. \, 4\pi^2. \, m.r^2 \quad \text{Nm. rad}^{-1}$$

The stiffness due to damping is given by

$$c^2/\,4m$$

Where c is the coefficient of damping, derived from the acceleration/time trace in the

Figure 6.8

Diagram to illustrate methodology in this experiment.

m = mass of hand and dynamometer handles.

r = radius arm of system (measured from the most distal part of ulna styloid to most distal part of palpable fifth metacarpal).

F = fulcrum of system at the wrist.

To the right is shown an idealised response curve following a small perturbation of the system (represented by angle theta in the diagram to the left). The damped frequency response is shown to illustrate the calculation of the damping factor (δ) and the resonant frequency (fn). In practice measurements were usually taken from three cycles and then averaged.
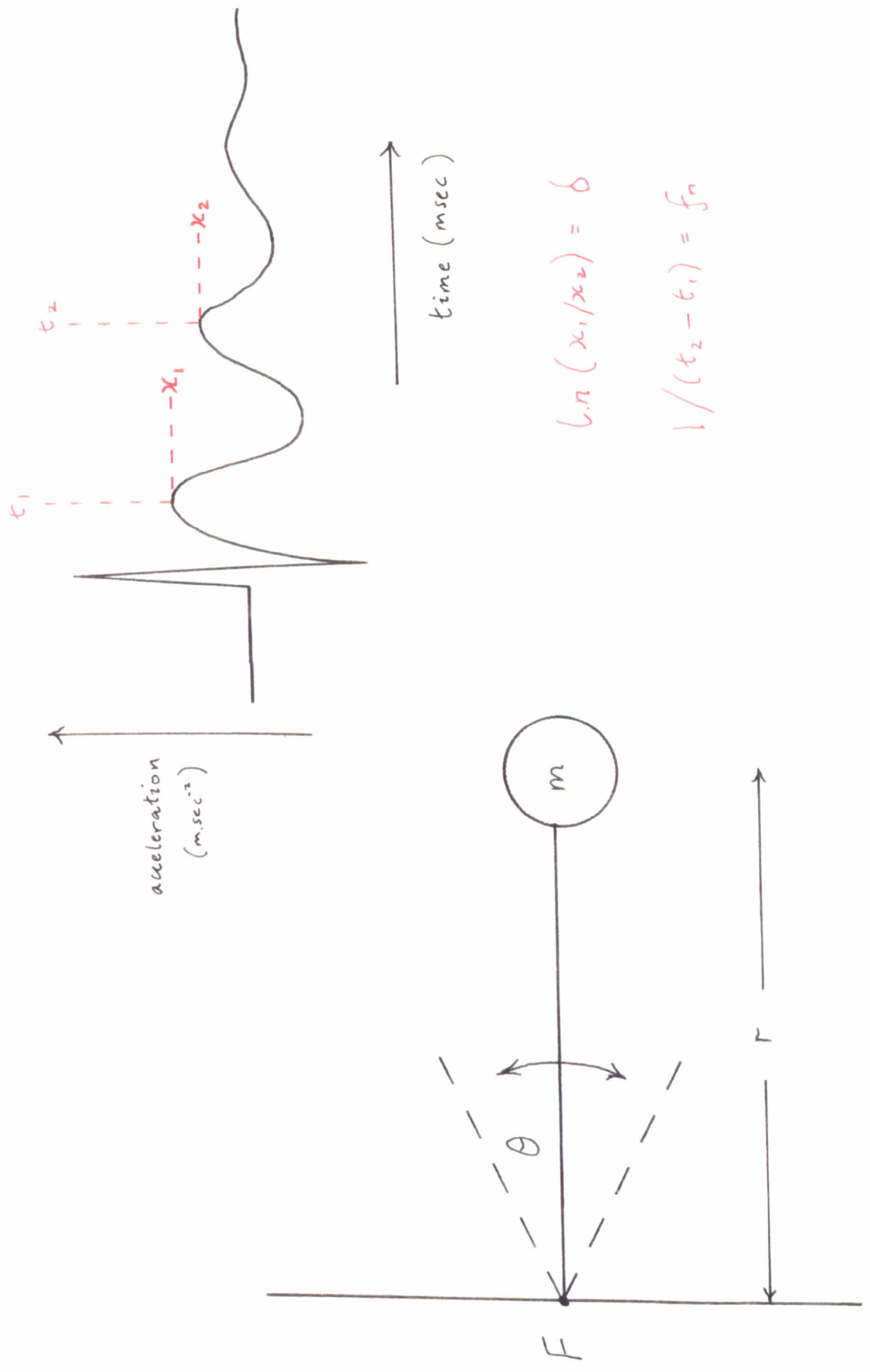
$Ln \left(x_1 / x_2 \right) = \delta$

$1 / \left(t_2 - t_1 \right) = f_n$

Figure 6.8

Figure 6.9

Diagrammatic representation of the experimental arrangement in this part of the study.

Figure 6.9

following way.

The logarithmic decrement is given by:-

$$\delta = L.n. \; x_1/x_2$$

where δ = logarithmic decrement

x_1/x_2 = ratio of two successive oscillations (see inset, Fig. 6.8)
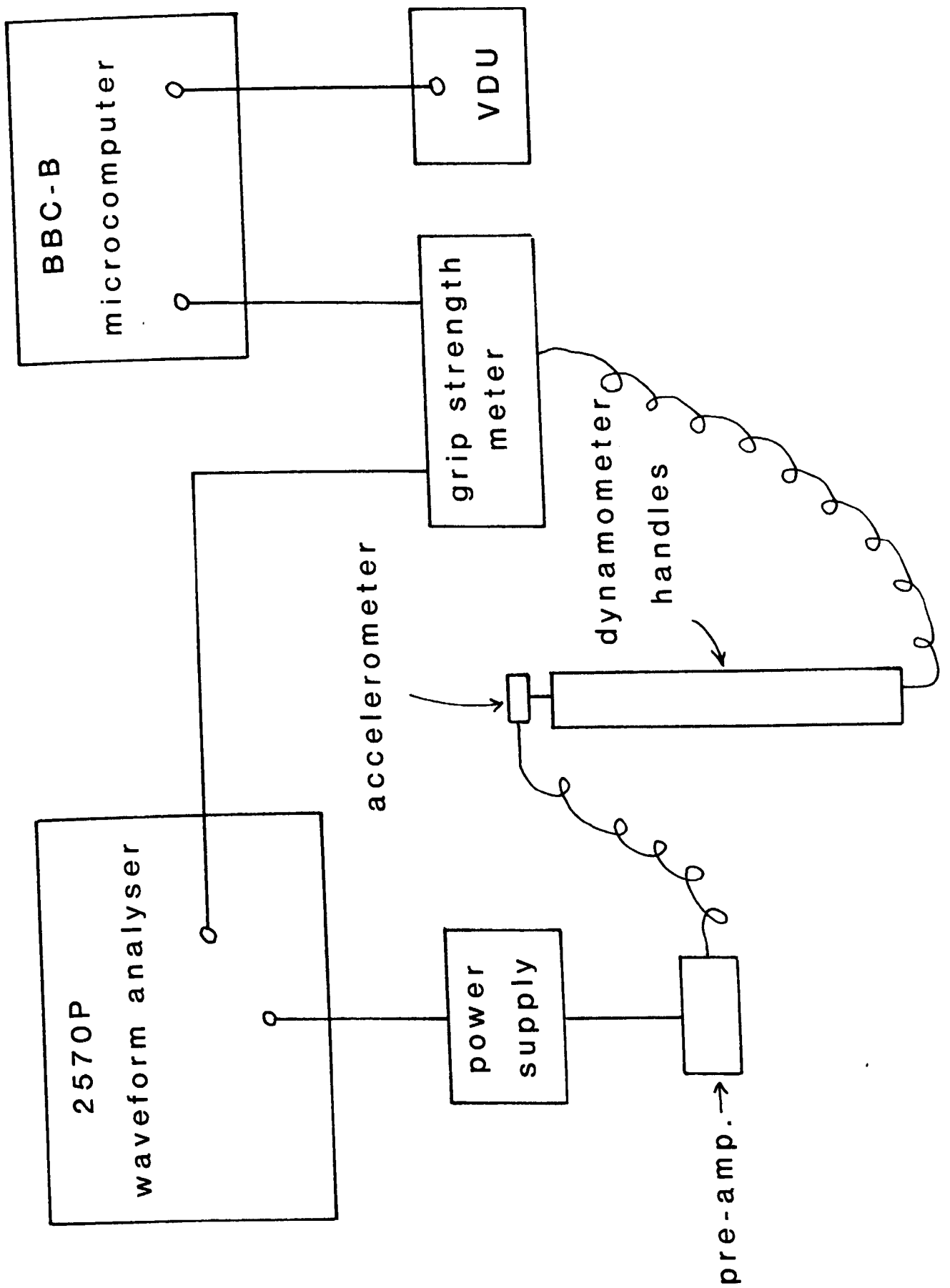
The damping factor (ξ) is given by:-

$$\xi = \frac{\delta}{\sqrt{(2\pi)_2 + \delta^2}}$$

and the coefficient of damping by:-

$$c = 2.m. \; \xi \; W_n$$

If the logarithmic decrement is less than 2 then damping is unlikely to make a significant difference to the stiffness of the system.

The dynamic angular stiffness (K_T) derived above is likely to be very similar to the static elastic stiffness in a system which is not too heavily damped (Cuming et al 1978).

Experimental procedure and reproducibility

The subject sits comfortably with the right forearm resting on a specially adapted chair arm. The arm is restrained by two vertical supporting pillars, one at the posterior end medially and one at the anterior end laterally; from this latter post, a velcro strap can be used to secure the wrist. The forearm is held mid-way between pronation and supination, the wrist joint just extending over the end of the platform. The subject grips a pair of padded handles of a torque dynamometer: these are held vertically and

a small accelerometer is attached to the upper end of the dynamometer handles such that the axis of excitation of the accelerometer is horizontal. The analog output from the dynamometer handles is fed to a digital display and thence to a BBC-B microcomputer. The signal from the accelerometer is fed via a pre-amplifier and power supply to a wave form analyser (2570P N.E. electronics). The arrangement is drawn diagrammatically in Fig. 6.9 and shown in plates 6.1 and 6.2.

The software for data acquisition by the BBC-B microcomputer in response to gripping the dynamometer arms has been described by Helliwell et al (1988). The subject was asked to perform a practice isometric grip for 4.4 seconds and the grip/time curve was then displayed. The subject was then asked to perform another maximal isometric grip and, whilst performing the grip, a small tap was applied to the dynamometer handles. No attempt was made to standardise the perturbation since the small differences likely to occur from one tap to another were unlikely to make any difference to the response of the system to the perturbation. The wave form analyzer receives input from the accelerometer and the dynamometer, both of which have been calibrated prior to the start of the experiments. An instantaneous display of the response to the perturbation was available and, if this was not satisfactory for any reason, it could be repeated.

The subject was then asked to hold the handles lightly in the position that was assumed for performing the maximum grip. It was found that the handles could just be held without slipping at a force of about 6 Newtons, and so subjects were asked to grip at this force using the analog readout of the grip strength meter as a guide. Another small tap was then applied to the handle and the resultant response of the system recorded, as previously.

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Plate 6.1

A normal subject preparing to start the test.

Plate 6.1

Plate 6.2

A closer view of the hand position, dynamometer and accelerometer attachment.
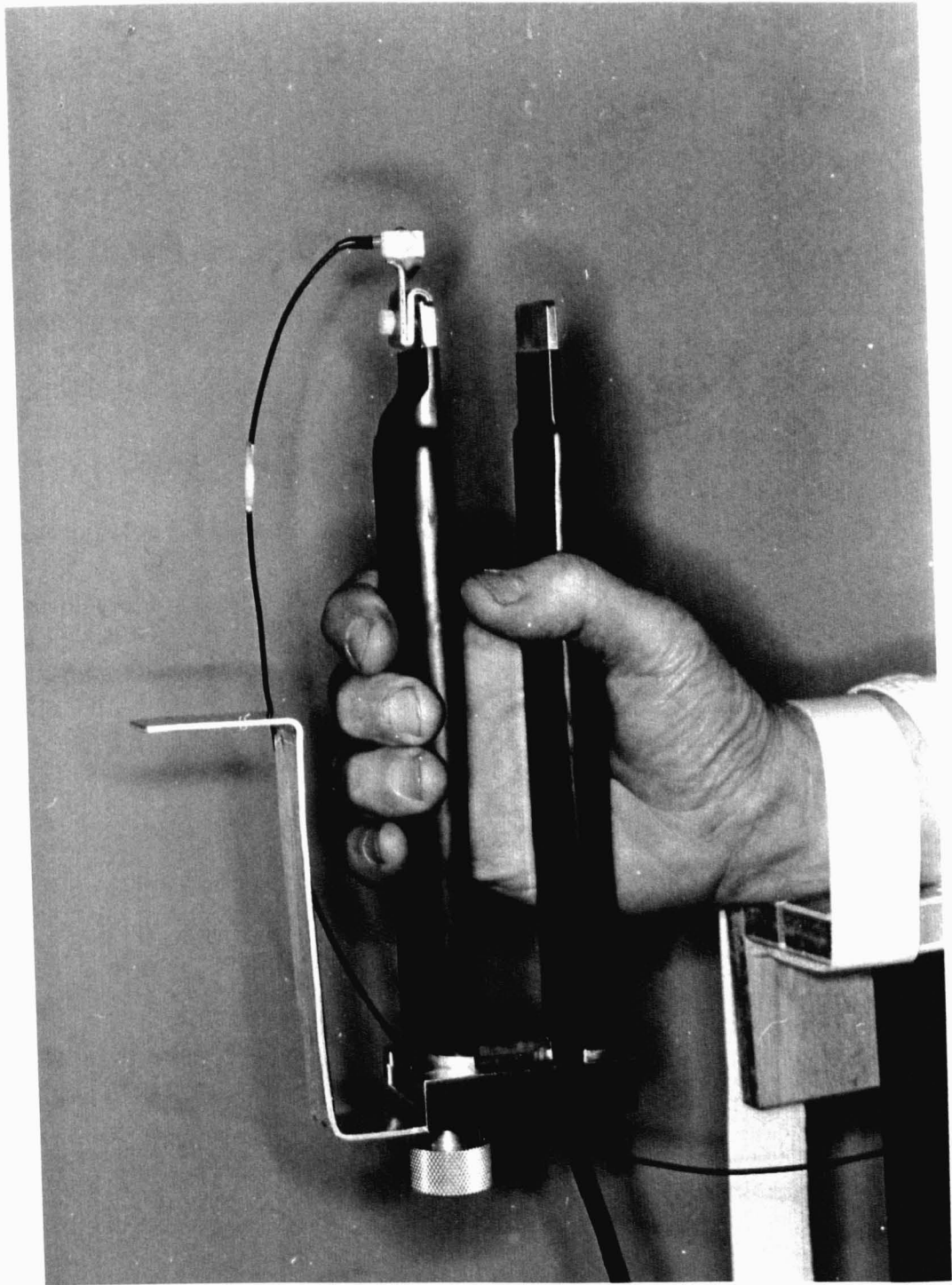
Plate 6.2

Figure 6.10 to 6.13

Simultaneous recording of forearm muscle EMG (electrodes over flexor profundus)

and accelerometer output following a small perturbation with the subject:

- lightly grasping the dynamometer handles (6.10)

- grasping the handles at 20% maximal isometric grip (6.11)

- grasping the handles at 50% maximal isometric grip (6.12)
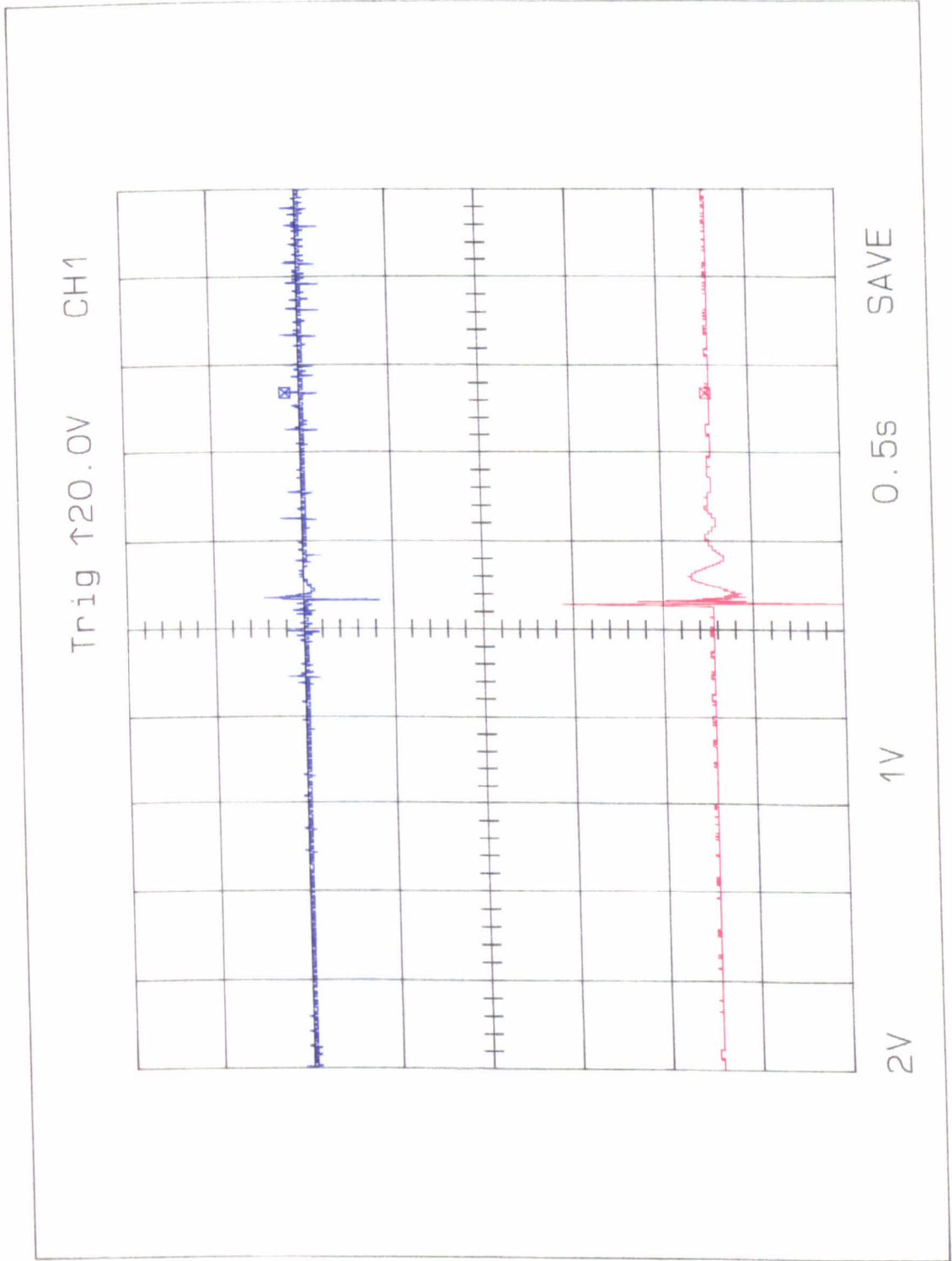
- grasping the handles maximally (6.13)
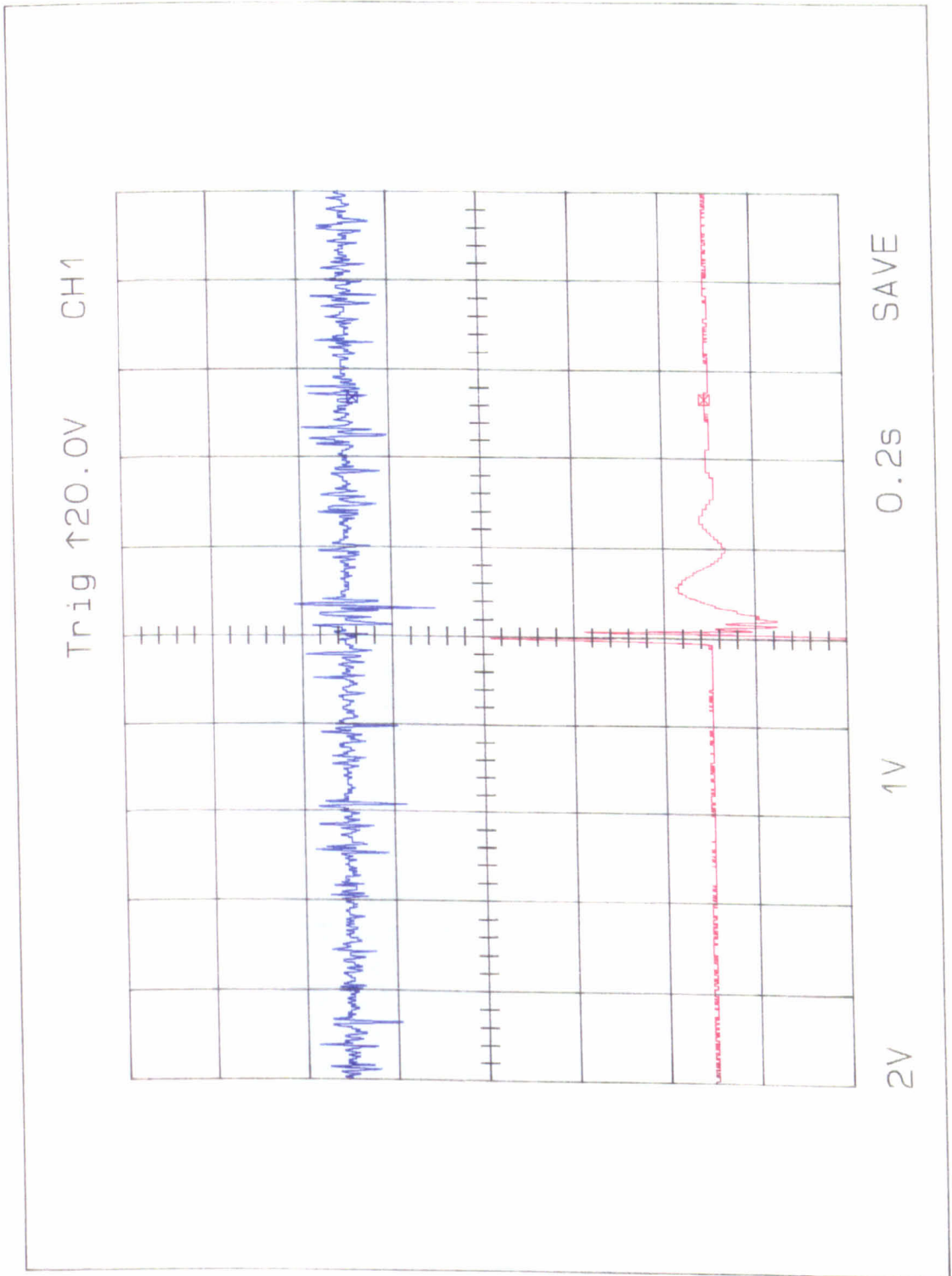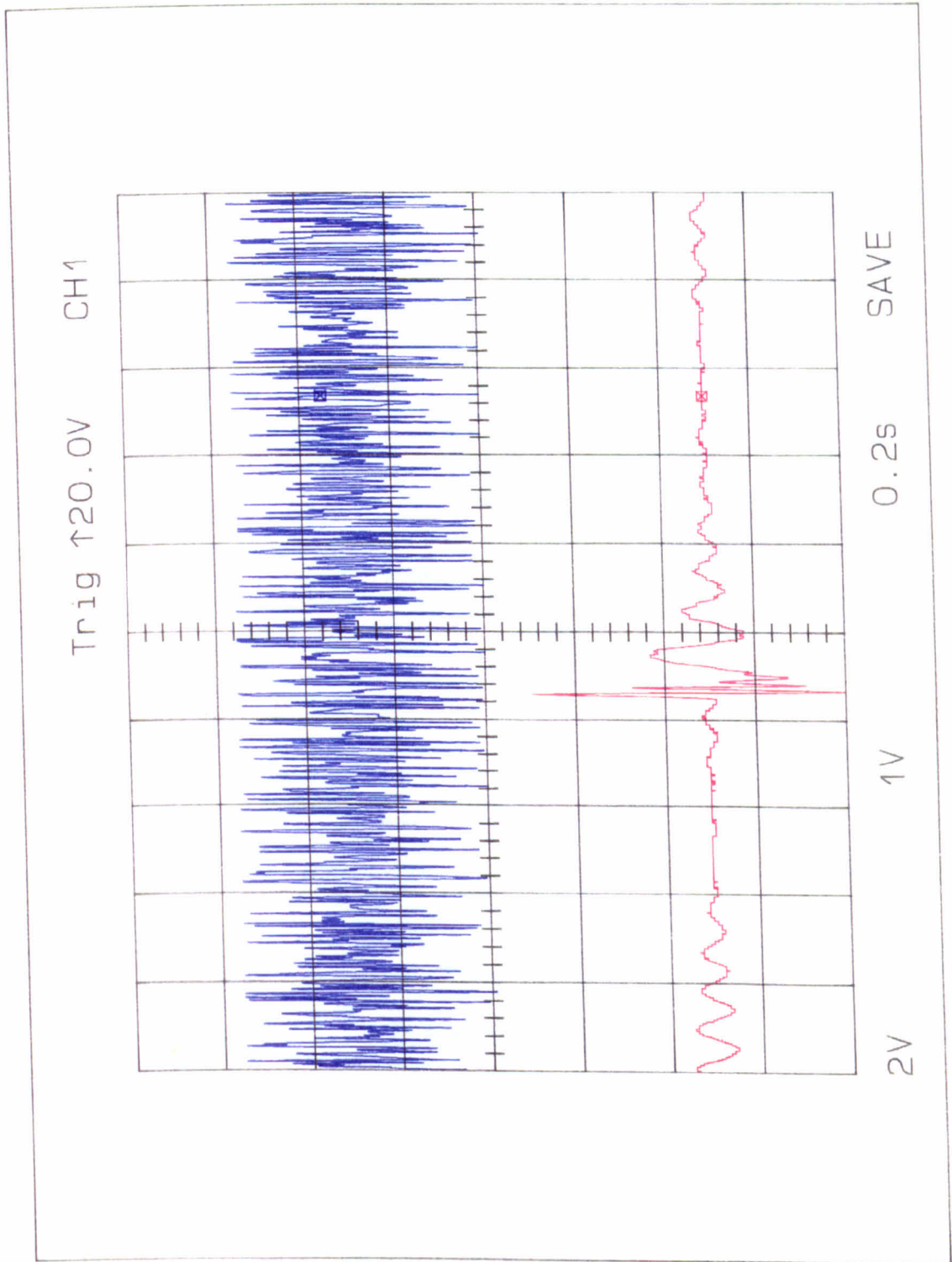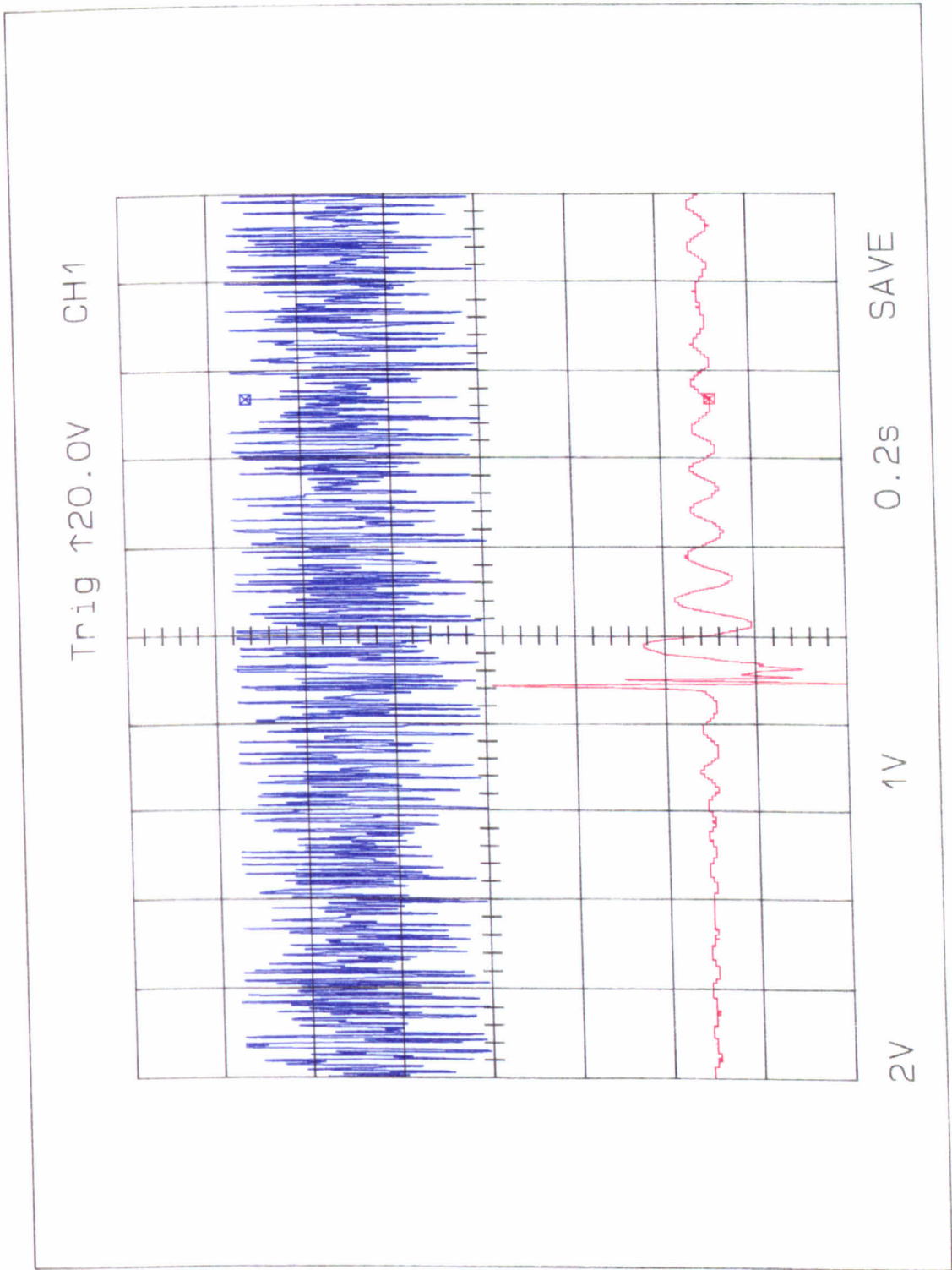
Figure 6.10

Figure 6.11

Figure 6.12

Figure 6.13

Two further conditions were tested: 20% maximum grip strength and 50% maximum grip strength. These values were chosen on the basis of preliminary tests. The grip strength software incorporated an option for measuring grip strength endurance. Essentially subjects were provided with a visual display of their grip, represented by a long column arranged vertically in the middle of the computer screen. Like a thermometer, if the subject squeezed, a thread of colour appeared, the height of the colour corresponding to the strength of grip. A target grip was prescribed and when this was reached the colour within the column changed and remained so as long as that grip was held. A 10% error either side of the target grip was allowed. In this way, subjects were asked to maintain their grip at either 20% or 50% of maximum while further taps were applied to the wrist. The success with which the subjects could hold the grip at this pre-defined level was checked on the wave-form analyser.

At the start of the test, demographic details were obtained such as height, weight, sex, handedness, duration of disease and the anthropometric measurements recorded in the experiments described in Chapter 5: forearm circumference mid-way between the lateral epicondyle and the ulna styloid, skinfold thickness on the dorsal and ventral surface of the forearm, finger circumference, and the distance between the ulnar styloid and the tip of the fifth metacarpal.

On one subject EMG recordings were made while the experimental procedure was performed and these results are displayed in Figures 6.10 - 6.13. It can be seen that when the subject is relaxed, gripping at 6N, following the perturbation there is a small burst of EMG activity with a delay of 20 msec, approximately the required delay for the muscle spindle response to stretch. The response of the muscle is relatively short,

20-40 msec and, as can be seen from the Figure 6.10, it does not interfere with the response of the system to the imposed perturbation. This short burst of activity is not apparent at the higher levels of muscle activation where EMG activity is more marked. In fact, at grips of more than 25N a refractory period is evident following the perturbation.

A diagrammatic representation of the response from the accelerometer following the wrist tap is shown in Figure 6.8, but is also evident in Figures 6.10-6.13. At least the first three cycles were used to estimate the resonant frequency (fn). With the subject relaxed sometimes no more than 2 cycles were recorded (the standard collection time was for 1.2 seconds sampling at 4KHz). An estimate of the logarithmic decrement (δ) is given by the ratio of the amplitude of the first to the third peak. The radius arm (r) is taken as the distance between the ulna styloid and the tip of the 5th metacarpal. The mass of the system is the mass of the dynamometer handles plus the mass of the hand, distal to the wrist joint. This was derived from standard anthropometric tables (Contini, 1985). The volume of the hand is 0.566% of the total body volume and, assuming the density of the human body is almost 1, the mass of the hand was calculated by multiplying the weight of the subject in kilograms by 0.00566.

Although it was felt, on theoretical grounds, that the contribution of damping to the stiffness of the system would be minimal, in 4 subjects the relative contribution of elastic stiffness and damping was calculated for each level of contraction and the results are presented in Table 6.1. It can be seen that logarithmic decrement does not exceed 2.0 in any of the conditions and the maximal percentage contribution that the damping makes is 7%. The contribution of the damping to these measurements was

Table 6.1

Natural frequency of system (Fn) logarithmic decrement (δ) damping factor (c) total angular stiffness of system (K_T) and percentage contribution of damping for four subjects and four levels of muscle co-contraction.

	Activation level	Fn (Hz)	δ	c	K_T x 10^{-3} (Nm/deg)	% contribn. damping
Normal age 39, F Max. grip = 306N Wt = 59.55 Kg	REST	4.9	0.99	8.07	107.94	2.4
	20%	6.7	0.75	8.41	201.81	1.4
	50%	8.0	0.90	12.01	287.72	2.0
	MAXIMUM	8.6	0.48	6.94	332.49	0.6
Normal age 22, F Max. grip = 250N Wt = 73.18 Kg	REST	4.9	1.25	11.00	102.31	3.8
	20%	7.0	0.76	9.67	208.79	1.4
	50%	8.0	0.55	8.02	272.71	0.8
	MAXIMUM	9.3	0.31	5.27	368.54	0.2
R.A. - age 56, F Duration of disease = 1 y Max. grip = 60N Wt = 68.18 Kg	REST	5	0.55	4.88	75.24	0.8
	20%	5.7	1.81	17.67	97.78	7.7
	50%	6.5	0.69	7.95	127.16	1.2
	MAXIMUM	7.2	0.52	6.65	156.02	0.7
R.A. - age 60, F Duration of disease = 24 y Max. grip = 44N Wt = 74.55 Kg	REST	7.0	0.69	8.91	200.40	1.2
	20%	8.0	0.72	10.61	261.74	1.3
	50%	8.9	0.86	14.10	323.95	1.8
	MAXIMUM	9.6	0.35	6.22	376.91	0.3

Table 6.2

Reproducibility of stiffness measurements. Figures are fn (Hz). CV = coefficient of variation (mean/std. devn. x 100).

	Activation level	Week 1	Week 2	Week 3	mean	CV (%)
SUBJECT 1 Male, age 38 Max. grip = 389N	MAXIMUM	11.3	11.3	10.7	11.09	3.1
	25%	8.6	9.0	9.2	8.92	3.2
	50%	8.5	9.9	9.3	9.23	7.6
	REST	5.8	6.4	6.1	6.11	4.9
SUBJECT 2 Male, AGE 42 Max. grip = 502N	MAXIMUM	12.2	11.0	11.4	11.55	5.1
	20%	9.9	10.5	9.3	9.89	6.3
	50%	10.5	10.4	10.3	10.38	1.1
	REST	6.7	7.1	6.2	6.66	6.7
SUBJECT 3 Male, age 42 Max. grip = 516N	MAXIMUM	10.4	12.2	10.7	11.10	8.7
	20%	8.6	7.3	7.4	7.76	9.4
	50%	8.9	10.4	10.2	9.83	8.3
	REST	4.7	4.9	5.5	5.03	8.3
SUBJECT 4 Male, age 29 Max. grip = 250N	MAXIMUM	11.2	11.0	11.4	11.22	2.0
	20%	8.9	9.4	6.4	8.22	19.4
	50%	11.3	10.8	10.4	10.84	4.5
	REST	5.1	4.9	4.8	4.93	3.0

therefore ignored and the values for K_T refer only to the spring-like elastic response of the system.

In order to determine the reproducibility of the system 4 normal subjects were measured on 3 consecutive occasions, the minimum inter-test interval being 7 days. The results are presented in Table 6.2. The coefficient of variation (std. dev. x 100/mean, Snedecor and Cochran, 1980) for the most part does not exceed 10%.

Results

Seventy normal subjects were compared with 20 subjects with rheumatoid arthritis. The two groups were not matched for age, sex, height or weight as can be seen in Table 6.3 which records these characteristics. The essential difference is that the normal subjects are younger than the patients with rheumatoid arthritis. Table 6.4 gives the forearm muscle cross-sectional area, the maximum isometric grip strength, the anthropometric characteristics and the stiffness at each level of muscle contraction. In Figures 6.14 and 6.15 the spread of results for the groups of K_T (maximum grip) and K_T (resting) are given (see also Fig. 6.7: these plots are equivalent to K_T vs N for A-B).

The relationship between forearm muscle cross-sectional area and resting stiffness is given in Figure 6.16 for normals and 6.17 for patients with rheumatoid arthritis and for both groups, as an overlay plot, in Fig. 6.18. The respective regression equations are:

Table 6.3

Demographic characteristics of study population. Mean (median, range).
MRI = modified Ritchie index. DI = deformity index. HAQ = Health Assessment Questionnaire.

	NORMAL n = 70	RHEUMATOID ARTHRITIS n = 20
Age (y)	32.9 (30, 8-72)	62.9 (61.5, 50-84)
Sex	29M 41F	8M 12F
Height (cm)	166.2 (168.3, 119-192)	165.7 (162.6, 152-180)
Weight (Kg)	63.4 (63.9, 19-98)	67.4 (64.8, 44-97)
Duration of disease (y)		12.2 (11.5, 0.5 - 18.5)
Ritchie Index (n=7)		26 (25, 20-36)
M.R.I.		2.6 (2.5, 0-8)
D.I. (n=19)		4.0 (2.0, 0-13)
H.A.Q. (n=6)		1.92 (1.91, 1-3)

Table 6.4

Anthropometric measurements, stiffness, grip and muscle C.S.A. Mean (median, range).

	NORMAL n = 70	RHEUMATOID ARTHRITIS n = 20	t	p
Epicondyle to ulna distance (cm)	25.5 (26, 17-29)	24.8 (24.8, 21-28)	1.38	ns
Forearm circumference (cm)	23.3 (24, 16-29)	21.4 (21.2, 15-27)	2.51	0.014
Max. grip (N)	275 (278, 68-509)	60.3 (49, 12-134)	8.25	0.000
CSA (cm^2)	30.9 (28.8, 13-56)	22.7 (21.3, 12-43)	3.16	0.002
Stiffness (K_T) Nm/deg. Rest 20% grip 50% grip max. grip	100.3 (98, 20-243) 192.1 (171, 48-505) 269.0 (239, 46-598) 365.0 (333, 65-853)	110.8 (100, 35-227) 176.5 (152, 98-463) 227.0 (197, 68-533) 229.0 (241, 43-426)	-0.77 0.59 1.34 4.15	ns ns ns 0.000

Figure 6.14

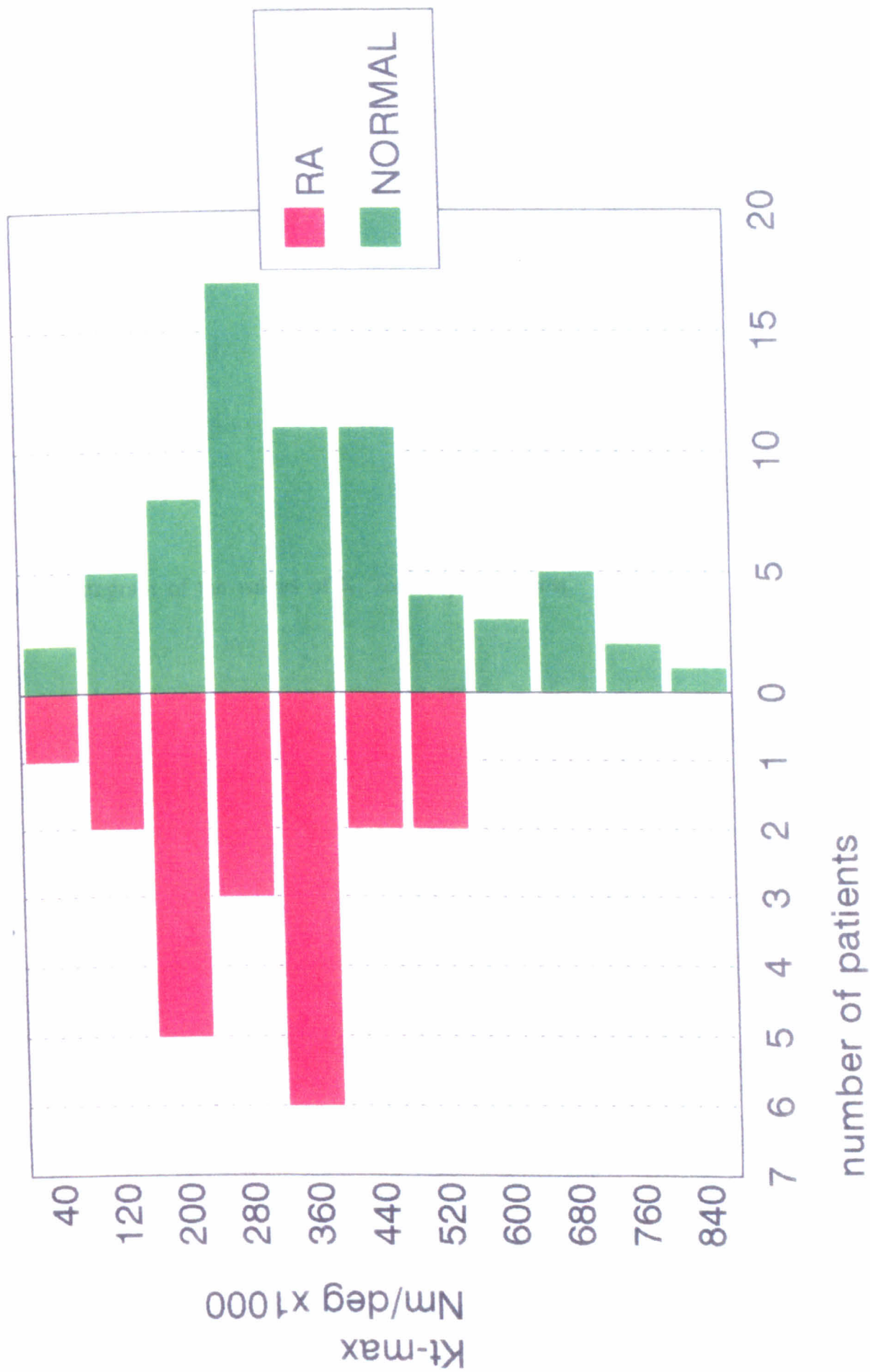Split histogram of the values of K_T for subjects gripping maximally.

Figure 6.14

Figure 6.15

Split histogram of the values of K_T for subjects at rest.
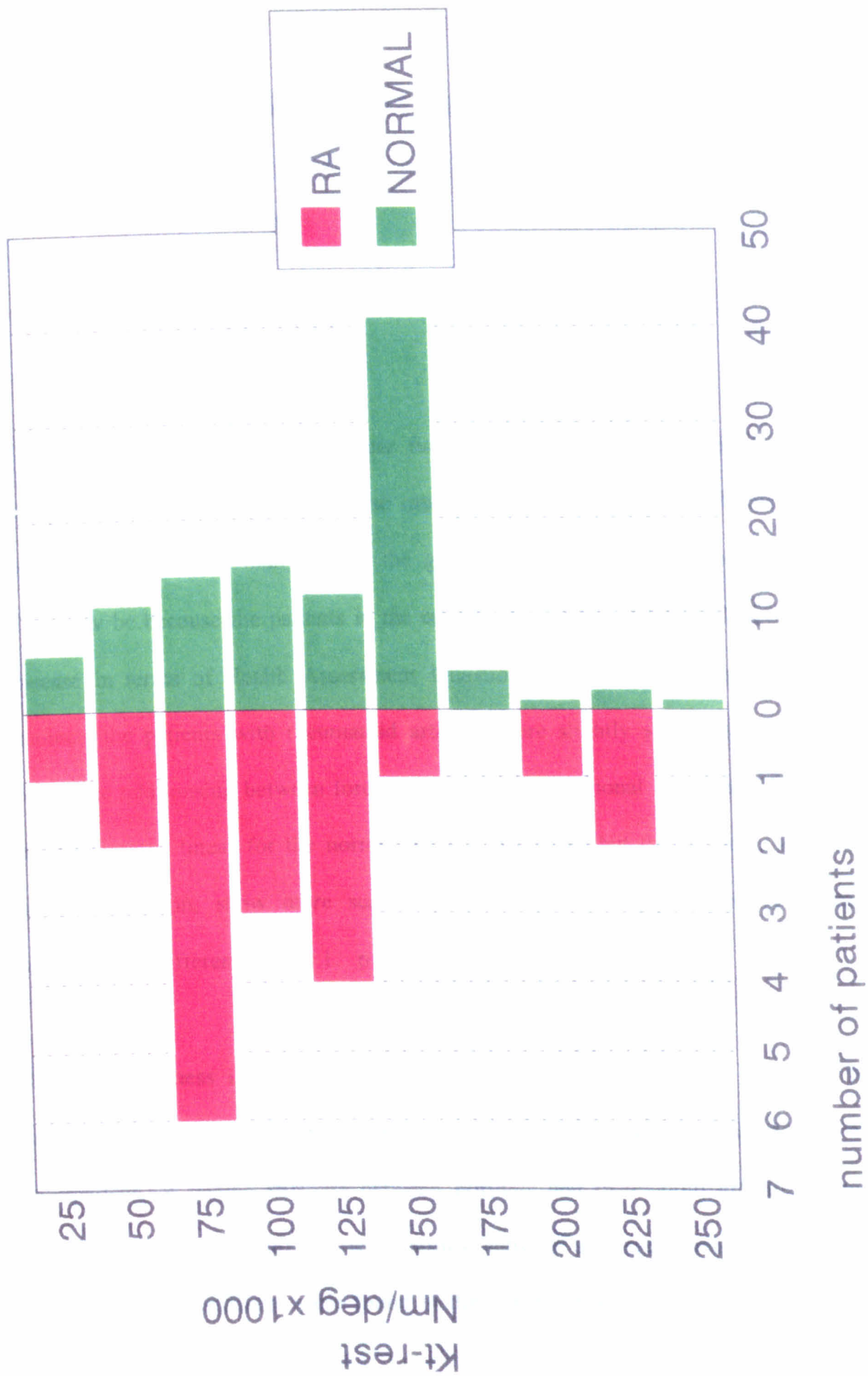
Figure 6.15

For normals,

$$K_T \text{ (rest) (Nm/deg)} = 27.2 + 2.36 \text{ CSA (cm}^2)$$

$$R^2 \text{ adjusted} = 26.3\%$$

For rheumatoid arthritis

$$K_T \text{ (rest) (Nm/deg)} = 66.5 + 1.95 \text{ CSA (cm}^2)$$

$$R^2 \text{ adjusted} = 3.8\%$$

To summarise, at this point, in these two populations the weakness of rheumatoid arthritis has been confirmed and the muscle wasting associated with the disease is perhaps more evident than seen in the group of patients documented in Chapter 5. This may be because the patients in the current study were older and had more severe disease in terms of Health Assessment Questionnaire scores. Compared to normal subjects the patients with rheumatoid arthritis were slightly stiffer at rest (see Table 6.4). The relationship between forearm muscle cross-sectional area and stiffness at rest is significantly linear for the normal group (Fig. 6.16) but the patients, with such a small population, show more scatter (Fig. 6.17). The slopes, however, are not significantly different $(F = 0.1, \; p = 0.75)$.

If resting stiffness is a function of forearm muscle cross-sectional area, and if the significant wasting seen in rheumatoid arthritis can be taken into account, then a true comparison of resting stiffness between normals and rheumatoid arthritis should be possible. However, significant associations between sex, age, forearm cross-sectional area and resting stiffness were found in the normal group as follows:

Figure 6.16

The relationship between resting stiffness and forearm muscle cross-sectional area in normal subjects.

Figure 6.17

The relationship between resting stiffness and forearm muscle cross-sectional area in patients with rheumatoid arthritis.
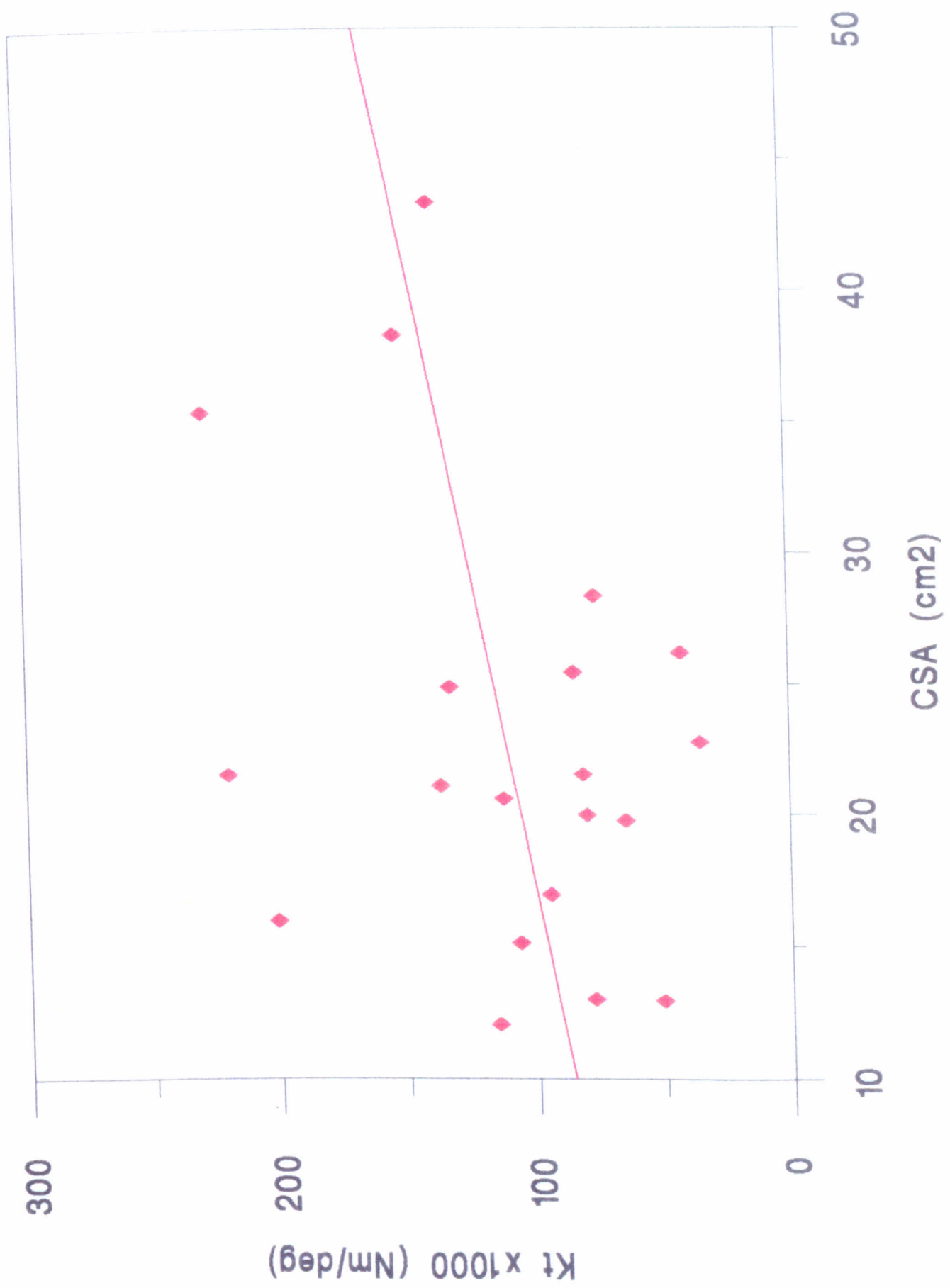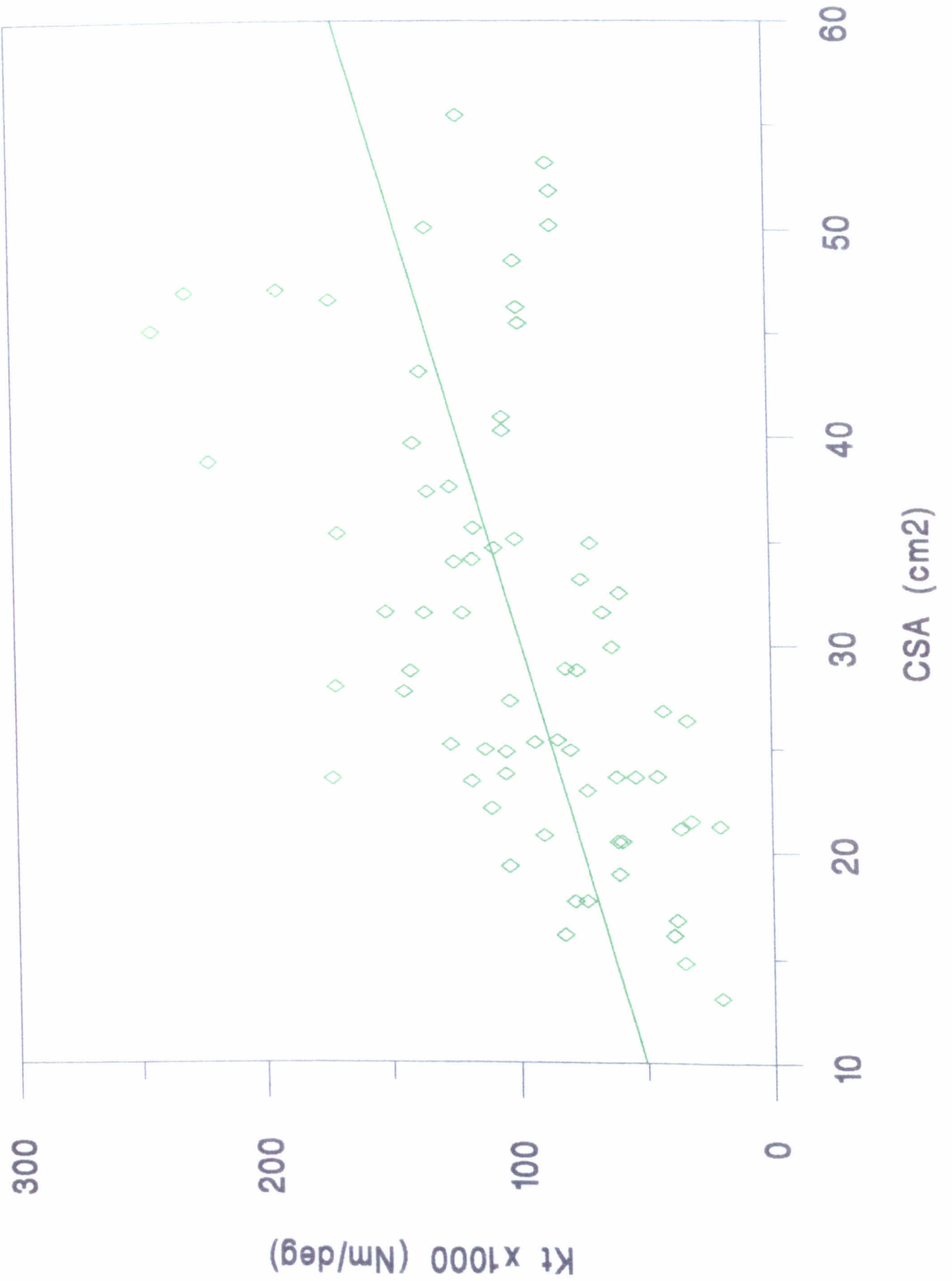
Figure 6.17

Figure 6.16

Figure 6.18

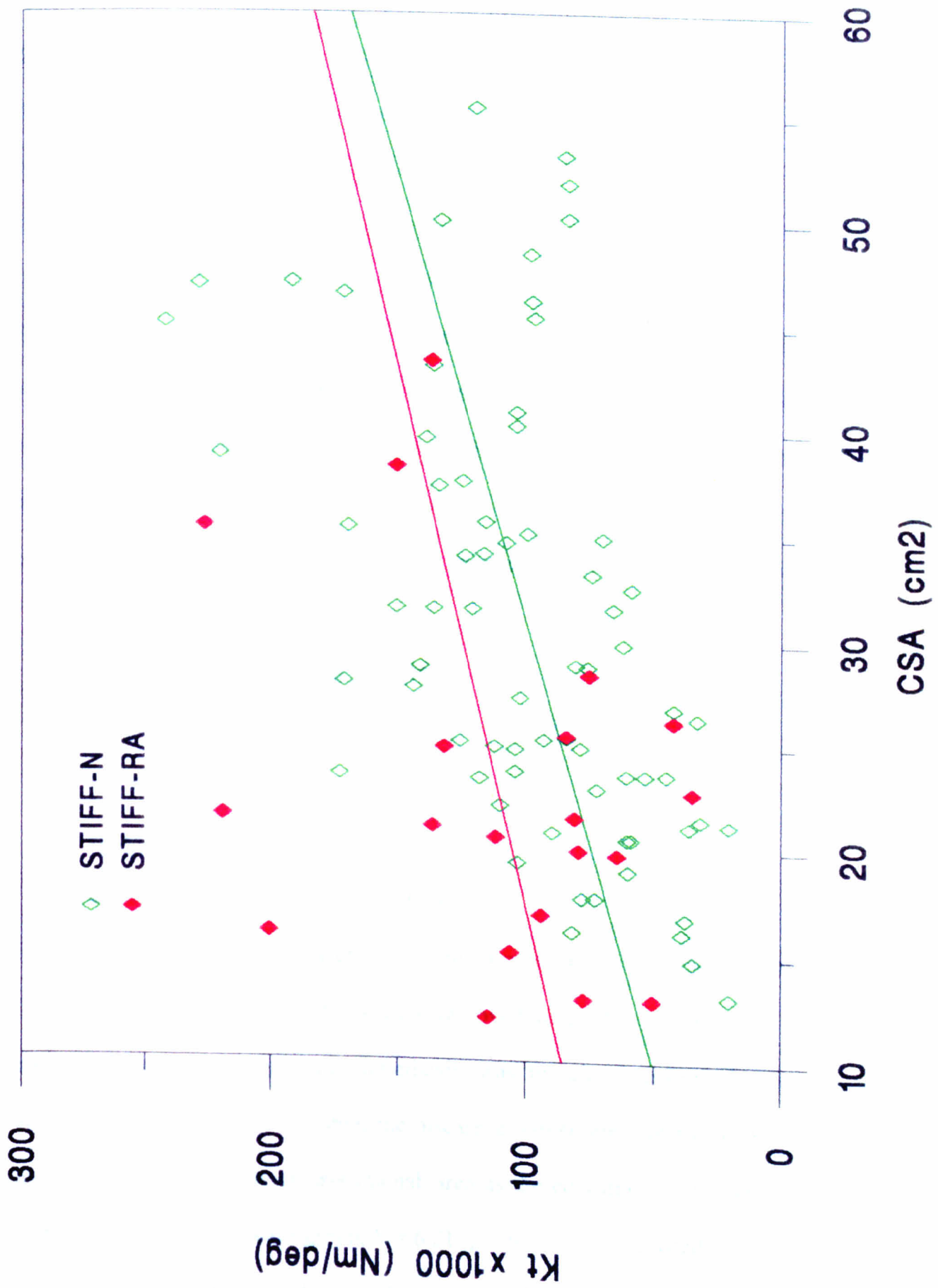Overlay plot of resting stiffness and forearm muscle cross-sectional area in both groups.

Figure 6.18

	Age	Sex	K_T (resting)
Sex	0.008		
K_T (resting)	0.250 [+]	-0.462 *	
CSA	- 0.029	-0.633 *	0.418 *

+ p< 0.001

* p< 0.05

Therefore, a question of concern is whether age and sex are important predictor variables of resting stiffness in addition to forearm muscle cross-sectional area. Each variable, age and sex, was used as a discriminating factor for resting stiffness using cross-sectional area as a co-variate. Age was divided into five bands to provide a categorical variable. The results using co-variance analysis, were as follows:

For age,

effect of age, $F = 1.78$, $p = 0.144$

effect of CSA, $F = 11.78$, $p = 0.001$

For sex,

effect of sex, $F = 3.55$, $p = 0.064$

effect of CSA, $F = 6.33$, $p = 0.014$

In other words the predominant effect was forearm muscle cross-sectional area and the 'significant' effects of age and sex were removed when this variable was taken into consideration. An analysis of co-variance was therefore performed using resting stiffness as the dependent variable, the disease group (normal or rheumatoid arthritis) as the factor, and muscle cross-sectional area as the co-variate. The result showed a significant effect for disease group, $F = 6.21$, $p = 0.015$ with adjusted means for resting stiffness 120.26×10^{-3} Nm/deg for rheumatoid arthritis and 90.84×10^{-3} Nm/deg for

the normal group. These differences are illustrated in Figure 6.21.

To assess muscle qualitatively the relationship between muscle activation and stiffness was examined. In Fig. 6.19 a graph of K_T against the four levels of muscle contraction is given for both patients with rheumatoid arthritis and normals. The median and range are presented in order to avoid the assumption of normality and a non-parametric test is used to assess significance (results given with the Figure caption). Although the two groups are similar at rest the slopes diverge as co-contraction increases, the difference becoming significant at maximum grip. However, if angular stiffness is plotted against actual grip (Fig. 6.20) the slopes of the stiffness/grip curves do not differ, although the results for rheumatoid arthritis are widely scattered. Appropriate regression equations are:

For normals;

angular stiffness (Nm/deg) = 124.29 + 0.964 (grip, N)

R^2 adjusted = 52.4%

For rheumatoid arthritis;

angular stiffness (Nm/deg) = 165 + 1.24 (grip,N)

R^2 adjusted = 12.9%

F (slopes) = 0.36, p = 0.55

F (intercept) = 8.37, p = 0.004

The intercept is an overestimate of the actual resting mean (see Table 6.4). Using the square root of grip as the abscissa, the intercepts are -21.1 x 10^3 Nm/deg and 109 x 10^3 Nm/deg for normal and rheumatoid arthritis respectively,with slightly improved R^2 - adjusted (53.9% for normals, 15.8% for RA).

Figure 6.19

Relationship between K_T and muscle activation levels in normals and in rheumatoid arthritis. At each level of muscle activation the median and range for both groups are displayed. Normal subjects in black and patients with rheumatoid arthritis in red. The following statistics apply:

ACTIVATION LEVEL	95% CI OF DIFFERENCE BETWEEN GROUPS (Mann-Whitney)	SIGNIFICANCE LEVEL
Resting	-18.4 to 32.74	0.534
20% activation	-60.6 to 27.8	0.513
50% activation	-97.4 to 22.6	0.161
Maximal activation	-193.7 to -44.4	0.002

Figure 6.19

Figure 6.20

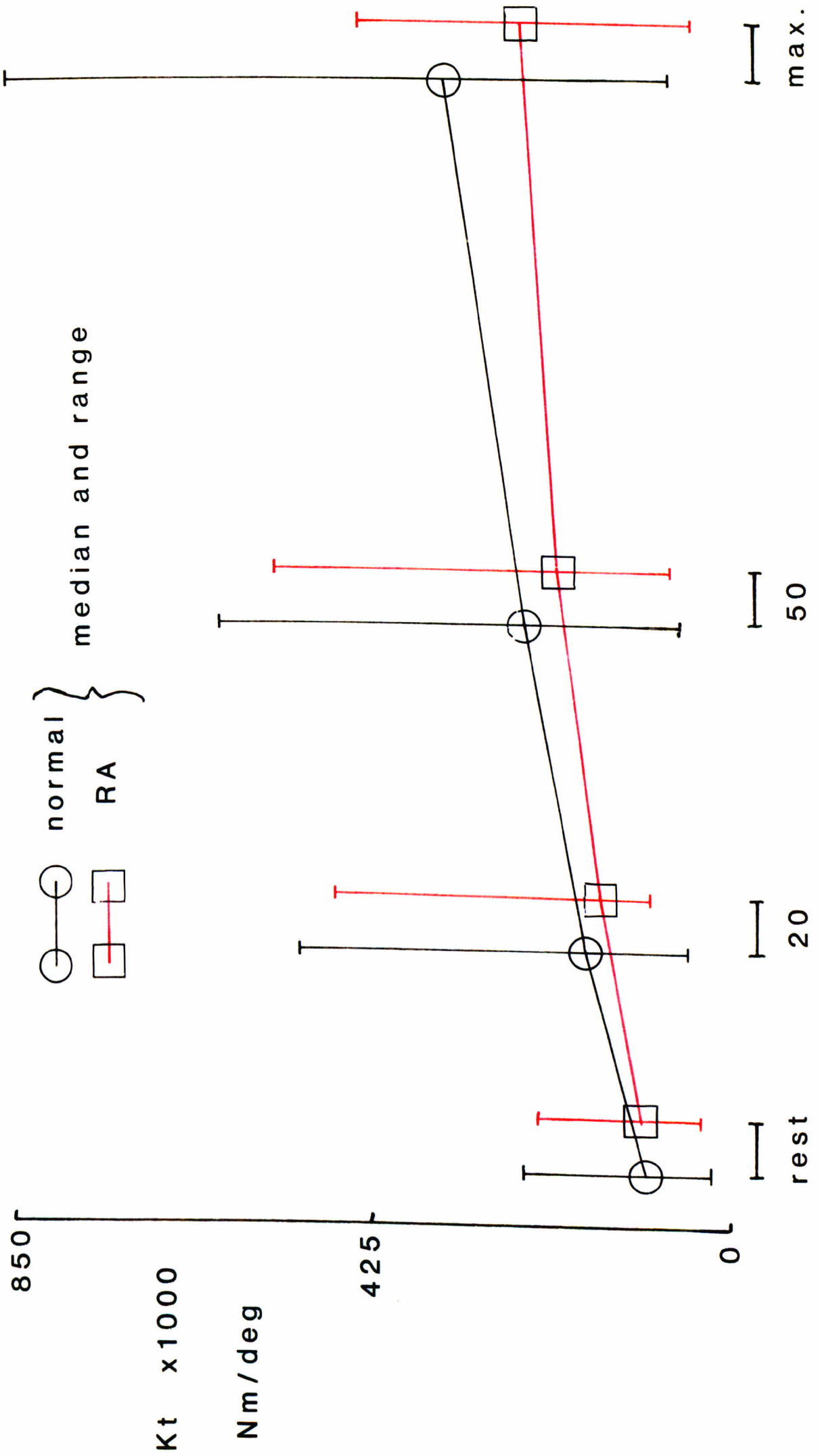The relationship between K_T and grip in both normal subjects and patients with rheumatoid arthritis.
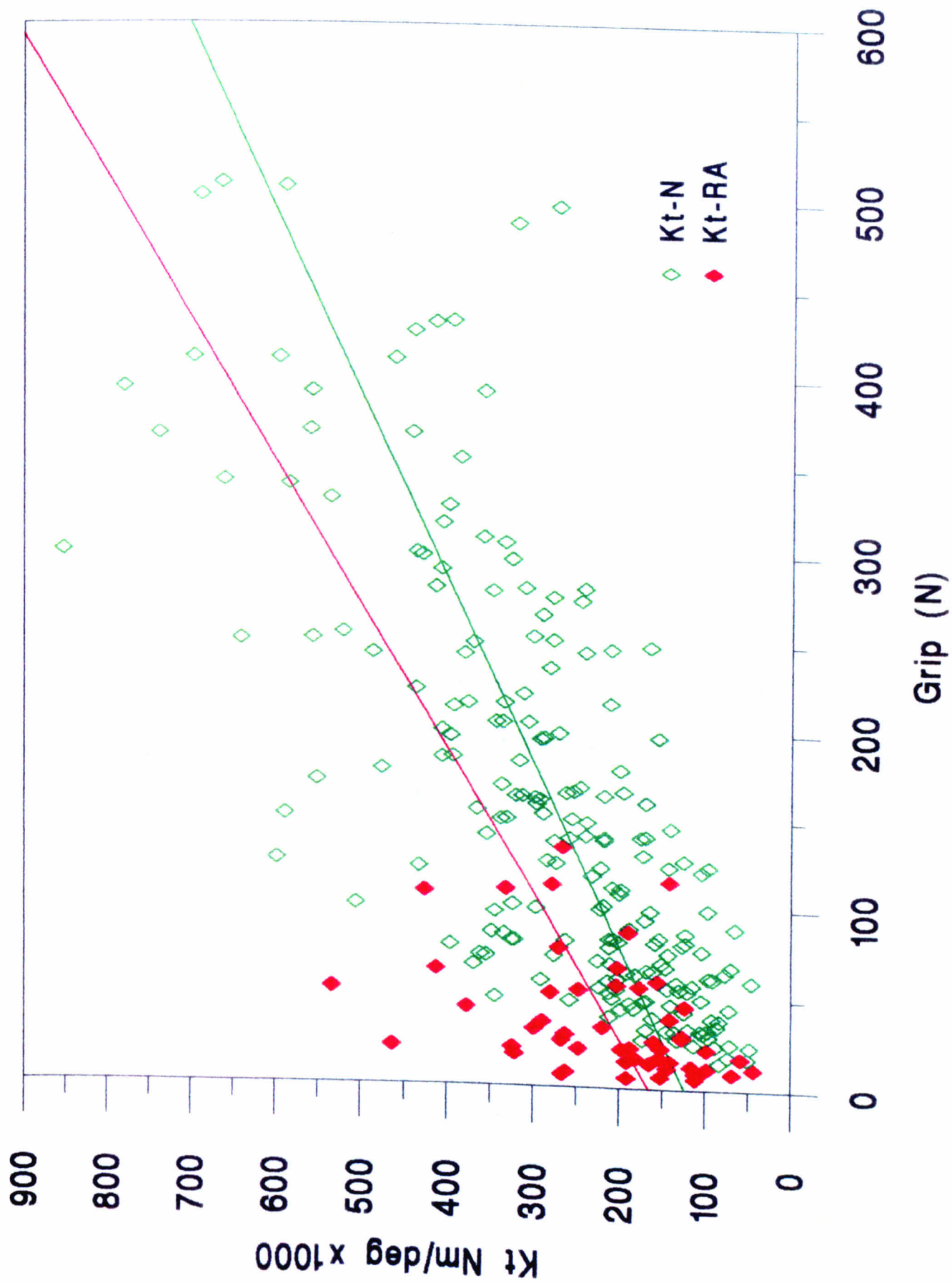
Figure 6.20

Figure 6.21

Histogram depicting corrected (for forearm muscle cross-sectional area) and uncorrected resting stiffness (K_T - rest) for normal subjects and patients with rheumatoid arthritis. The corrected stiffness values are significantly different at 1% level.
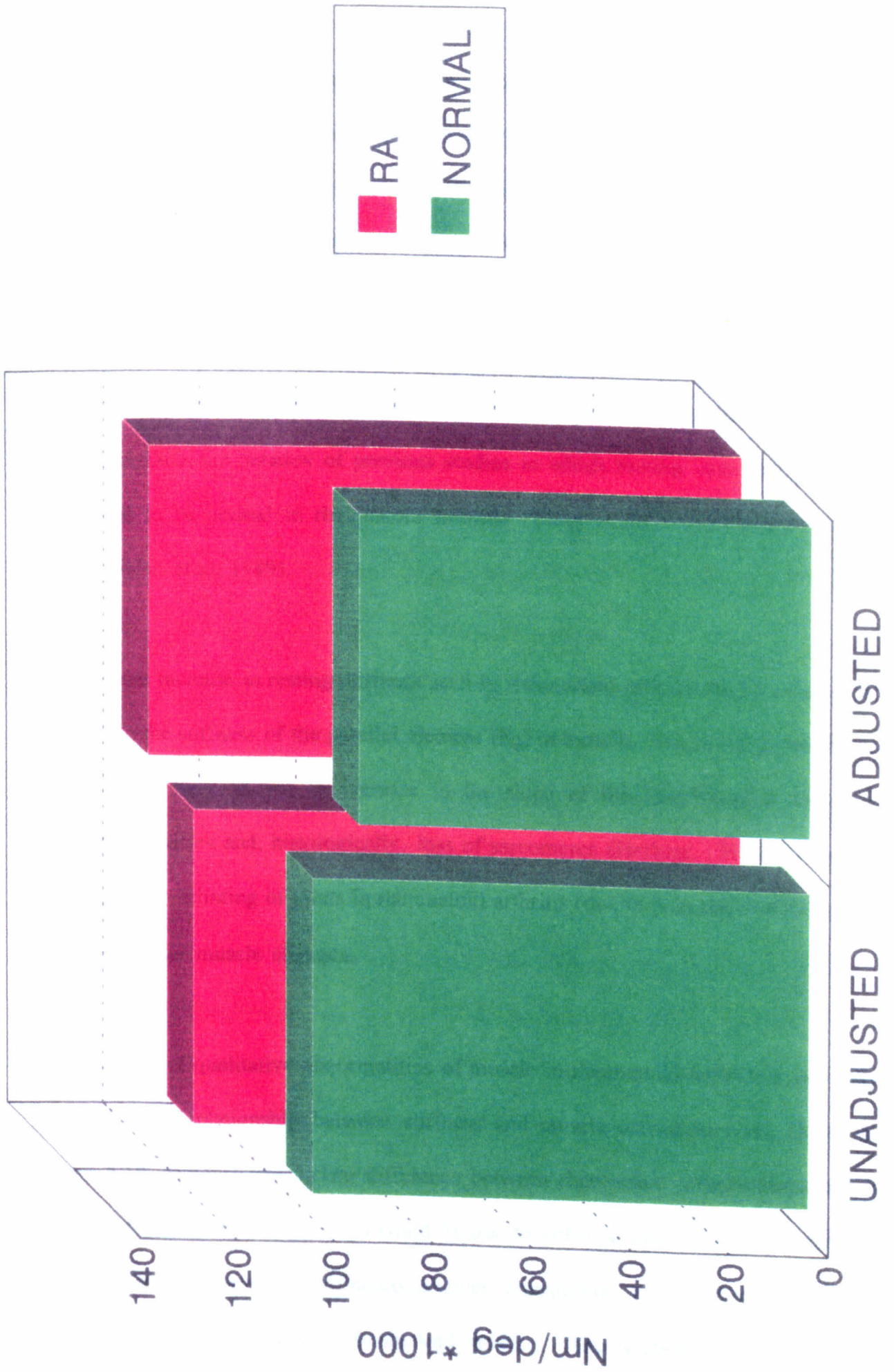
Figure 6.21

Discussion

In this chapter the emphasis has been on the contribution of muscle to passive stiffness measured at the joint. A considerable body of experimental evidence relies on this fact and neglects the contribution of articular tissues to stiffness measured in this way. However, at rest and with normal muscles, we have seen that the contribution of articular tissue to total passive stiffness is significant. Furthermore, in arthritis, the relative contribution of articular tissues to total passive stiffness may be increased. Figure 6.21 reflects this increase when muscle wasting has been accounted for and perhaps explains the paradox of previous studies in which resting 'articular' stiffness was found to be normal in rheumatoid arthritis (Yung et al, 1986; Helliwell et al, 1988a; Walsh et al, 1989).

Some of the increase in resting stiffness seen in rheumatoid arthritis may be due to an increase in the stiffness of the parallel element (K_p) in muscle. Studies of immobilised animal joints have shown an increase in the slope of the length/tension curve of associated muscles and, histologically, loss of sarcomeres (Herbert, 1993). Voluntary or involuntary splinting of joints in rheumatoid arthritis (due to pain and swelling) may result in similar muscle changes.

The question of qualitative abnormalities of muscle in rheumatoid arthritis is not fully resolved. The relationship between stiffness and muscle activation level, shown in Figure 6.19, demonstrates a clear difference between rheumatoid arthritis and normals at maximum co-contraction. This could be due to either a qualitative abnormality of muscle fibres, an abnormality of neuromuscular transmission, or inhibition of maximum grip by pain and deformity in rheumatoid arthritis. The relationship of stiffness to

actual grip, shown in Figure 6.20, suggests that grip-for-grip the muscle in rheumatoid arthritis is qualitatively normal. This result would agree with the results of Lenman and Potter (1966). Presumably the potential for maximum isometric grip strength is never achieved in arthritis due to reflex and voluntary inhibition of alpha motorneurone discharge and, possibly, neuromuscular inefficiency. The pathological changes seen by Haslock et al (1970) and the electromyographic abnormalities found by Steinberg and Wynn-Parry (1961) are presumably not sufficiently severe to cause abnormalities in the stiffness/grip curve in this study nor the voltage/tension curve in the study of Lenman and Potter (1966). The short term increases in grip strength seen in response to (essentially) analgesic therapies such as physiotherapy (Helliwell, 1987) would accord with this finding. Circadian variation in grip strength (Wright, 1959a) seen in rheumatoid arthritis and previously attributable to changes in stiffness (Myers et al, 1980) may merely reflect diurnal variation in pain. Clearly pain is a major symptom in rheumatoid arthritis but patients can usually discriminate between pain and stiffness (see Chapter 3). Pain may well be measured equally by assessment of grip strength as by the usually adopted visual analogue scales - (Helliwell, 1987).

Although the slopes of the relationship between stiffness and grip were similar in normals and in rheumatoid arthritis (Fig. 6.20) the intercepts did not precisely reflect the resting stiffness measured in this group. In fact the values were overestimates (for normals, intercept = 124.3 Nm/deg, actual resting stiffness = 100.3Nm/deg; for rheumatoid arthritis intercept = 165.0 Nm/deg, actual resting stiffness = 100.8 Nm/deg). An underestimate would have been expected since the resting stiffness measurement was not a true resting value, the subjects having to hold the dynamometer handles with a grip of about 6N. However, the overestimate may result from several factors

including (i) the imprecision in the relationship between grip and stiffness due to variation in the 'fixed' elements of the system (e.g. non-linearity - see Winters, 1990); (ii) the relationship between stiffness and grip is not entirely linear - the use of $\sqrt{\text{grip}}$ improved the variation and the intercept, particularly in rheumatoid arthritis; (iii) in rheumatoid arthritis other factors may influence stiffness and these may not be uniform for each level of muscle co-contraction, e.g. joint geometry may change; and (iv) imprecisions in the technique, e.g. - not obtaining true readings of maximum grip, and therefore poor estimates of sub-maximal grips.

The measurement system used in the main experimental section of this chapter was found to be reproducible from week to week (see Table 6.2). In most cases there was no difficulty discerning the frequency response to system perturbation. Occasionally, at maximum grips, the wrist was resonating before a perturbation was applied: this can be seen in Figure 6.13. This effect was rarely seen in patients with rheumatoid arthritis and was most often seen when subjects appeared to be exerting a marked maximal effort. Is this an exaggeration of normal physiological tremor, normally regarded as having a frequency of 8-12 Hz (Pizzuti et al, 1992)? The origin of physiological tremor is still in some doubt the oscillation originally being attributed to the stretch reflex arc, but Brumlik (1962) found that tremor persisted after complete neuromuscular block and he suggested the ballisto-cardiac impulse theory. A ballistocardiograph is a device for recording the mechanical output from the heart and, in operation, relies on vibrations transmitted through the body with each heart beat. Lippold (1970) rejuvenated the reflex-arc theory showing that the EMG is in phase with tremor and that disruption of the loop (e.g. in tabes dorsalis) abolishes the tremor. Pathological tremors have a different frequency, 2 to 3 Hz in Parkinson's disease and

1 to 2 Hz in liver failure; the former originating with extra-pyramidal dysfunction. It is likely that the pre-perturbation resonance seen in certain subjects at maximal grip in this study is not an exaggeration of normal physiological tremor (which generally improves with movement) but resonance already established in a stiff (ie: isometrically contracting) system by small 'internal' perturbations.

The experiments describing variations in short term arthrographic stiffness illustrate the large influence that muscles can have on passive resistance at the joint. The experiments involving isometric exercise provide a clear illustration of the changes in muscle volume in response to exercise and illustrate the effects of muscle oxygen debt in this form of exercise. The time course of the blood lactate concentration would probably have mirrored the changes in muscle stiffness seen. In one subject it was possible to produce a similar result using the technique of measuring the resonant frequency of the wrist, although the changes were only evident for resting stiffness: stiffness at 20% maximum did not exhibit a similar increase following isometric exercise.

The short term amplitude dependent changes in stiffness known as thixotropy are presumably due to increased cross-bridge formation between actin and myosin, a process which is energy (ATP) dependent. Although thixotropy is not dependent on reflex muscle activity, the phenomenon does illustrate history and time dependent changes in resting stiffness of the contractile element (K_c - rest). These factors were not taken into consideration in the study of stiffness and muscle activation but may have influenced the poor correlation between the variables seen in this study and the imprecise estimate of resting stiffness as reflected by the intercept of the stiffness/grip relationship (Fig. 6.20).

Summary

Large (up to 150%) variation in joint stiffness can be seen as result of changes in amplitude (thixotropy) and as a result of isometric exercise.

The resonant frequency of the wrist, as a measure of passive stiffness at the joint, is significantly increased in rheumatoid arthritis, if allowance is made for forearm muscle wasting.

Forearm muscle contractile properties, as measured by the relationship between wrist stiffness and grip strength, are normal in rheumatoid arthritis.

SECTION III

CHAPTER 7

A RE-ANALYSIS OF STIFFNESS MEASUREMENTS OBTAINED WITH THE LEEDS MICROPROCESSOR CONTROLLED ARTHROGRAPH.

Introduction

Methods

Results

Discussion

Summary

Introduction

Previous studies with the Leeds microprocessor controlled arthrograph (Howe et al, 1985; Helliwell 1987; Helliwell et al, 1988a) failed to show any increase in objective stiffness in rheumatoid arthritis. Elsewhere in this thesis it has been suggested that failure to measure objective stiffness in rheumatoid arthritis may have been due to the associated muscle wasting which is an inevitable component of this disease. Although an anthropometric variable was used as a covariate in comparing stiffness variables, it was later felt that finger circumference, measured just distal to the finger web, was a remote and unlikely indicator of muscle wasting. Indeed, this anthropometric variable was employed because it was felt that it would give an indication of tissue volume adjacent to the joint under study, on the assumption that the articular contribution to stiffness would be dominant. Some more relevant measure of muscle wasting was required to correct the measurement of passive articular stiffness. Curiously, Yung et al (1986) could find no evidence of muscle wasting, as measured by forearm circumference in their patients with rheumatoid arthritis.

The experiments described in Chapter 5 confirm the clinical impression of muscle wasting in rheumatoid arthritis and provide a means of predicting forearm muscle cross-sectional area from previous arthrographic studies. The amount of variation in cross-sectional area, explained by the independent variables in the normal group (see Table 5.7), is sufficient to be fairly confident of predicting an 'estimated' cross-sectional area: the correlation coefficient for this equation being 0.8, although independent studies to confirm the predictive accuracy of this regression equation have not been performed. The variation in cross-sectional area, explained by the

independent variables in the rheumatoid arthritis group was less satisfactory. Nevertheless, this chapter describes the application of the predictive equations to previously obtained data in order to provide a more meaningful correction factor for stiffness obtained in rheumatoid arthritis and normal populations.

Methods

Demographic details and stiffness variables were obtained from previous studies (Howe et al, 1985; Helliwell 1988a). The data were still available on computer so application of the regression equations obtained in Chapter 5 was a fairly straightforward procedure. Covariance analysis was performed using stiffness as dependent variable, disease as the grouping factor and estimated cross-sectional area as the covariate. The regression and percentile lines for the normal group were plotted and the results for patients with rheumatoid arthritis added to these normal curves. It will be recalled that stiffness variables from the arthrograph are mean slope (representing elastic stiffness), area (representing energy lost during the cycle), and hysteresis (another term for viscosity, but expressed in such a way as to make the result independent of amplitude of rotation). In accordance with previously published results only normal curves for mean slope and hysteresis were constructed. It should be noted that in Chapter 7 the results for mean slope have been multiplied by 10^4 so that they remain consistent with the previously published results using this device: in Chapter 2 it will be remembered that the multiplication factor was consistently 10^3 throughout.

Further analysis was also carried out on the data relating to a single oral dose of ibuprofen (Helliwell, 1987). It will be recalled from Chapter 2 that the aim of this study was to correlate the clinical and arthrographic response to a single oral dose of ibuprofen with the pharmacokinetic profile of the drug. The subjects were in-patients at the time; all had rheumatoid arthritis; they numbered 8 although both hands were studied in one patient. Seven subjects had clinically active disease in the joint being studied (MCP3); the mean Ritchie Index was 24, mean ESR 32 and the mean duration of disease 9.6 years. The experimental procedure was as follows:

(i)   all NSAID's were stopped 24 hours before the start of the study. No other active treatments were allowed on the two days of the study.

(ii)   On the first day, that is 24 hours after stopping anti-inflammatory drugs, patients had subjective and objective scores over a six hour study period starting at 12.00 noon. This time was chosen as a starting point so that any circadian variation would be minimal during the study period.

(iii)   On the second day, 48 hours after stopping anti-inflammatory drugs, after a baseline reading at 12.00 noon an 800mg oral dose of Ibuprofen was administered and subsequent measurements made over a similar six hour period. Unfortunately, one subject with active arthritis was in so much pain on the first day of the study that the control day was abandoned and the drug was administered on the first day.

(iv)   Analysis of the results was by an analysis of variance calculated for each variable over each of the two days. Despite obvious changes in mean slope, grip and pinch strength during day two compared to day one, the variance of scores was so large that significant changes were not found. It was noted that four of the eight patients responded well and four not at all, but it was not felt justified to analyse these four subjects separately.

In this chapter the re-analysis uses a technique to smooth the variation in scores. For each patient the individual scores were expressed as the standardised normal deviate (z), given by:

$$z = (x_i - \bar{x}) / s$$

z is a useful measure of distribution in normal samples, the magnitude of z relating to the probability of obtaining a value greater than that, the approximate values being: $z = 1.645$, $p = 0.05$, $z = 1.96$, $p = 0.025$. Most statistical textbooks print a table of probabilities associated with values of the standardised deviate.

The values of z were averaged at each time point and plotted for control, experimental and experimental minus control days.

Results

The age, sex, finger circumference, grip strength and stiffness variables and estimated forearm muscle cross-sectional areas for the 135 patients with rheumatoid arthritis and 88 normal subjects are given in Table 7.1. The mean estimated cross-sectional area for the patients with rheumatoid arthritis was similar to that from the group of patients

Table 7.1

Age, sex, finger circumference, maximum grip strength, stiffness variables and estimated forearm muscle cross-sectional area: rheumatoid arthritis compared to normal.

	RHEUMATOID ARTHRITIS n = 135		NORMAL n = 88		t	p
	mean	std. devn.	mean	std. devn.		
Age (y)	59.44	10.95	32.87	16.9		
Sex	35M 100F		46M 42F			
Finger circ. (mm)	57.32	5.06	59.46	5.48	2.91	0.004
Max grip (N)	60.96	41.23	--	--		
Mean slope x $10.^4$ (Nm deg $^{-1}$)	72.93	47.95	85.0	48.06	1.83	0.06
Hysteresis (%)	32.58	8.57	37.98	10.37	4.06	0.0001
Area (x 10^4)	831.4	635.0	1239.8	699.5	4.42	0.0000
CSA - estimated (cm^2)	23.21	5.38	37.88	6.04	18.27	0.0000

studied in Chapters 5 and 6 (n = 100 patients with RA, Chapter 5, CSA = 25.96 cm^2; n = 20 subjects with RA, Chapter 6, CSA = 22.7 cm^2; n = 135 patients with RA from previous studies, estimated CSA = 23.2 cm^2). The estimated cross-sectional area of the normal group was, however, higher than those previously found (n = 100 normals Chapter 5, CSA = 29.71 cm^2; n = 70 normals Chapter 6, CSA = 30.9 cm^2; n = 88 normals from previous arthrographic studies, estimated CSA = 37.9 cm^2).

The age, finger circumference, maximum grip strength, stiffness variables and estimated forearm muscle cross-sectional areas for the rheumatoid arthritis sub-groups are given in Table 7.2. The sub-groups were divided on the basis of the disease locally in the McP3 joint, as previously described. As expected, the arthroplasty and subluxed McP3 joint patients had lower estimated forearm cross-sectional areas than the other three groups. The highest estimated forearm cross-sectional area was found in the group with inactive rheumatoid arthritis, reflecting the greater grip strength of this group.

The regression equations for stiffness variables on estimated forearm cross-sectional area for all rheumatoid arthritis groups and normal subjects, are presented in Table 7.3 and graphically presented in Figs. 7.1 to 7.3. In contrast to the previous findings (Helliwell, 1987) the majority of the patients are above the 50th centile for mean slope, and below the 50th centile for hysteresis.

Table 7.4 gives the results of the analysis of covariance using mean slope and hysteresis as dependent variables, disease group as grouping factor and estimated forearm cross-sectional area as the covariate. Again, unlike previously published

Table 7.2

Age, finger circumference, maximum grip strength, stiffness variables and estimated forearm muscle cross-sectional area - rheumatoid arthritis sub-groups.

	All RA n = 135	Active RA n = 66	Inactive RA n = 32	Subluxed McP n = 32	Arthroplasty n = 5
Age (y)	59.4	56.7	65.0	59.4	59.8
Finger circ. (mm)	57.3	58.3	56.3	56.5	56.8
Max grip (N)	61.0	58.0	87.0	44.0	30.0
Mean slope x $10.^4$ (Nm deg $^{-1}$)	73.0	72.6	96.6	53.4	51.0
Hysteresis (%)	32.6	31.8	32.4	33.9	35.0
Area (x 10^4)	831	800	1089	668	653
CSA - estimated (cm^2)	23.21	23.5	24.6	21.7	20.5

Table 7.3

Regression of area (x 10⁴), mean slope (Nm deg⁻¹ x 10⁴) and hysteresis (%) on estimated forearm cross-sectional area.

* p = 0.001
+ p = 0.01
⊕ p = 0.05

	df	AREA				MEAN SLOPE				HYSTERESIS			
		A	t	B	t	A	t	B	t	A	t	B	t
All RA	133	-136	-0.6	40.7	4.6*	-19.9	-1.2	3.93	5.85*	33.9	10.2*	-0.05	-0.4
Active RA	59	305	1.3	17.8	1.8	9.4	0.4	2.45	2.82+	33.4	6.2*	-0.07	-0.3
Inactive RA	28	312	0.7	33.2	1.95	18.6	0.57	3.33	2.58⊕	33.1	5.8*	-0.03	-0.2
Subluxed McP	29	-967	-1.9	75.8	3.33+	-64.9	-1.94	5.46	3.63+	29.2	4.1*	0.24	0.8
Arthroplasty	2	881	0.5	-7.9	-0.1	21.9	0.25	1.61	0.38	86.5	2.8	-2.45	-1.7
Normals	86	-661	-1.5	50.2	4.46*	-77.5	-2.8+	4.29	5.94*	59.2	8.8*	-0.56	-3.2+

Table 7.4

Analysis of covariance using mean slope (N.m. deg^{-1} x 10^4) and hysteresis (%) as dependent variables, estimated forearm muscle cross-sectional area as covariate and disease (normal vs. RA group) as grouping factor. See text for additional information on statistical procedure.

* p = 0.001
+ p = 0.01
⊕ p = 0.05

	MEAN SLOPE v CSA estimated				HYSTERESIS v CSA estimated			
	F (slopes)	ADJUSTED VARIABLES		F	F (slopes)	ADJUSTED VARIABLES		F
		Disease	Normal			Disease	Normal	
All RA	0.14	95.93	49.63	25.76*	5.33⊕	32.29	42.81	12.74*
Active RA	2.20	99.04	62.75	12.85*	2.50	28.12	40.48	24.22*
Inactive RA	0.49	140.16	71.48	31.24*	2.95	28.27	39.33	15.95*
Subluxed McP	0.51	107.59	65.92	9.40+	4.33⊕	37.12	40.34	8.92+
Arthroplasty	0.17	125.75	81.78	3.36	1.44	26.57	38.42	4.06⊕

Figure 7.1 (a and b)

Normal regression lines, and 2.5, 10, 90, 97.5 percentiles for (a) mean slope and (b) hysteresis as a function of estimated forearm muscle cross-sectional area.
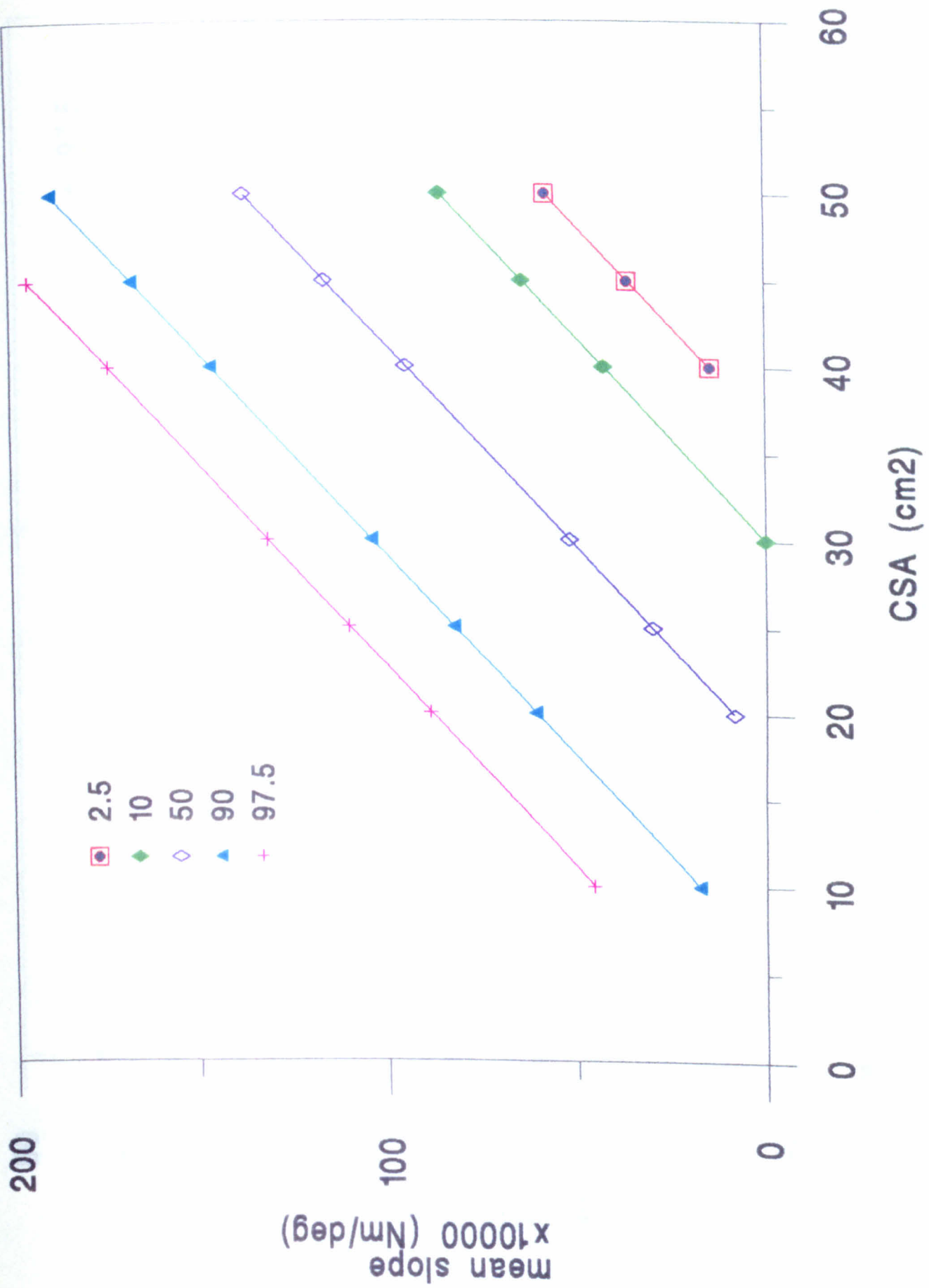
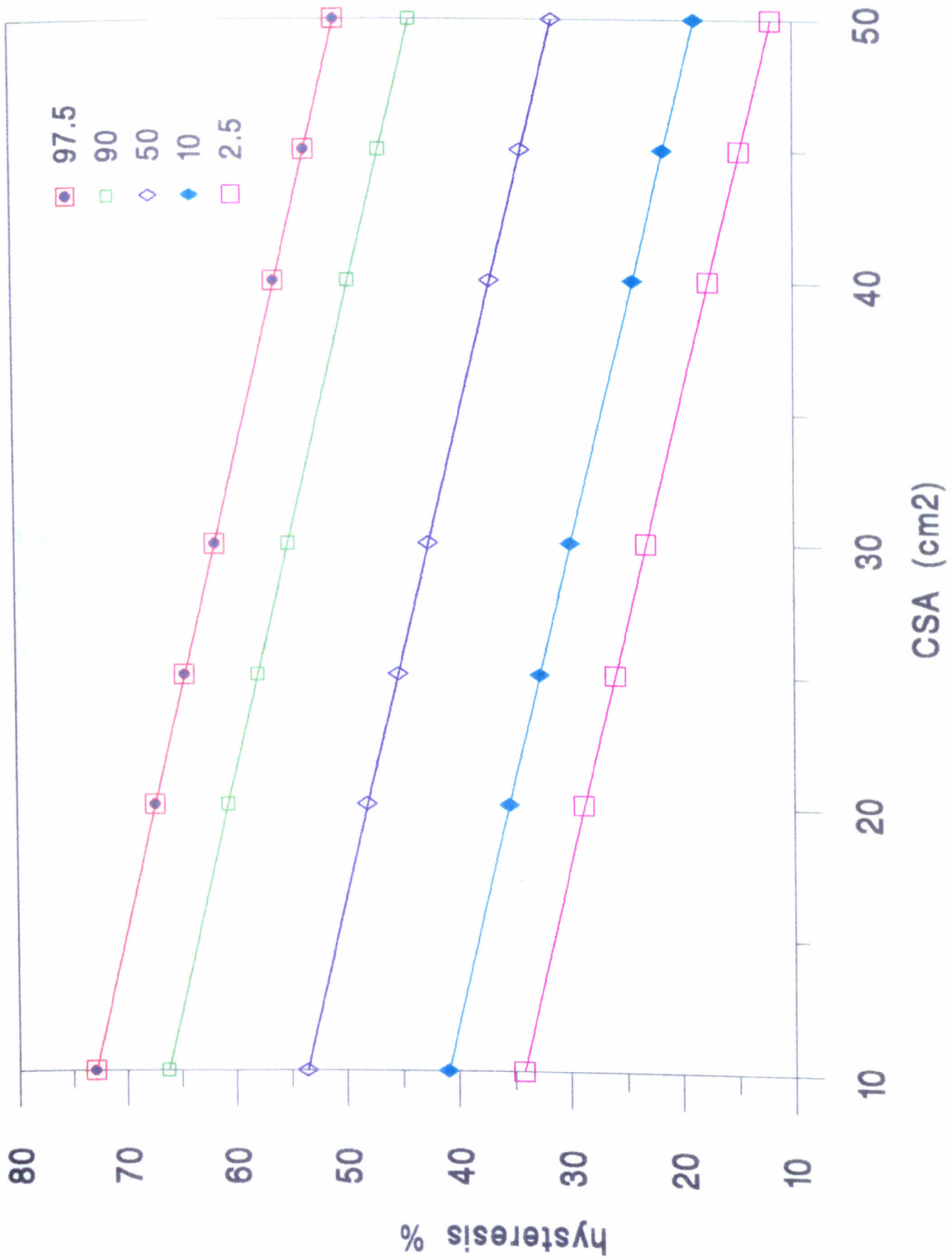Figure 7.1a

Figure 7.1b

Figure 7.2 (a and b)

Normal regression lines, and associated percentile lines, for (a) mean slope and (b)

hysteresis with results for patients with rheumatoid arthritis (n = 128) superimposed.

Figure 7.2a

Figure 7.2b

Figure 7.3 (a and b)
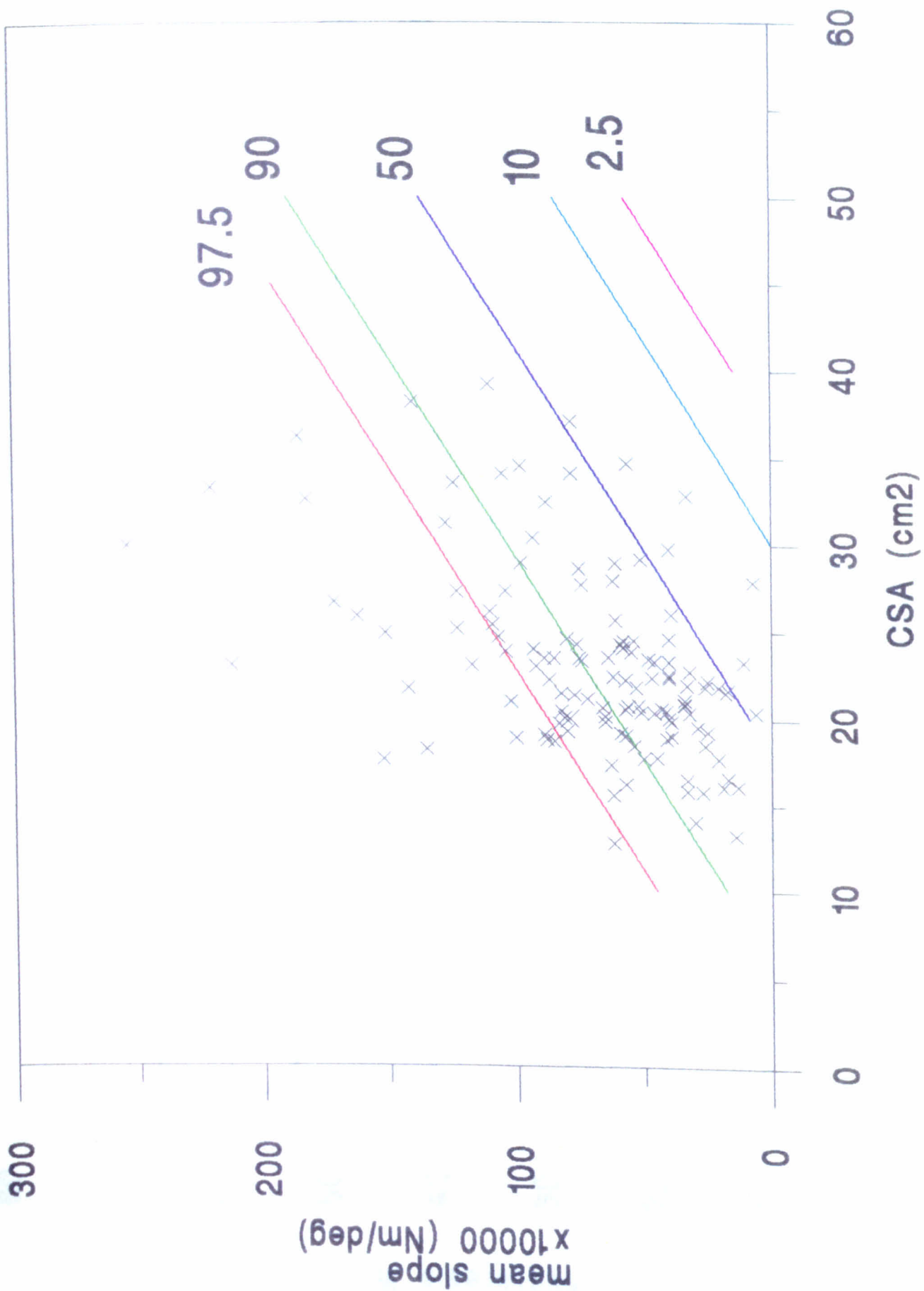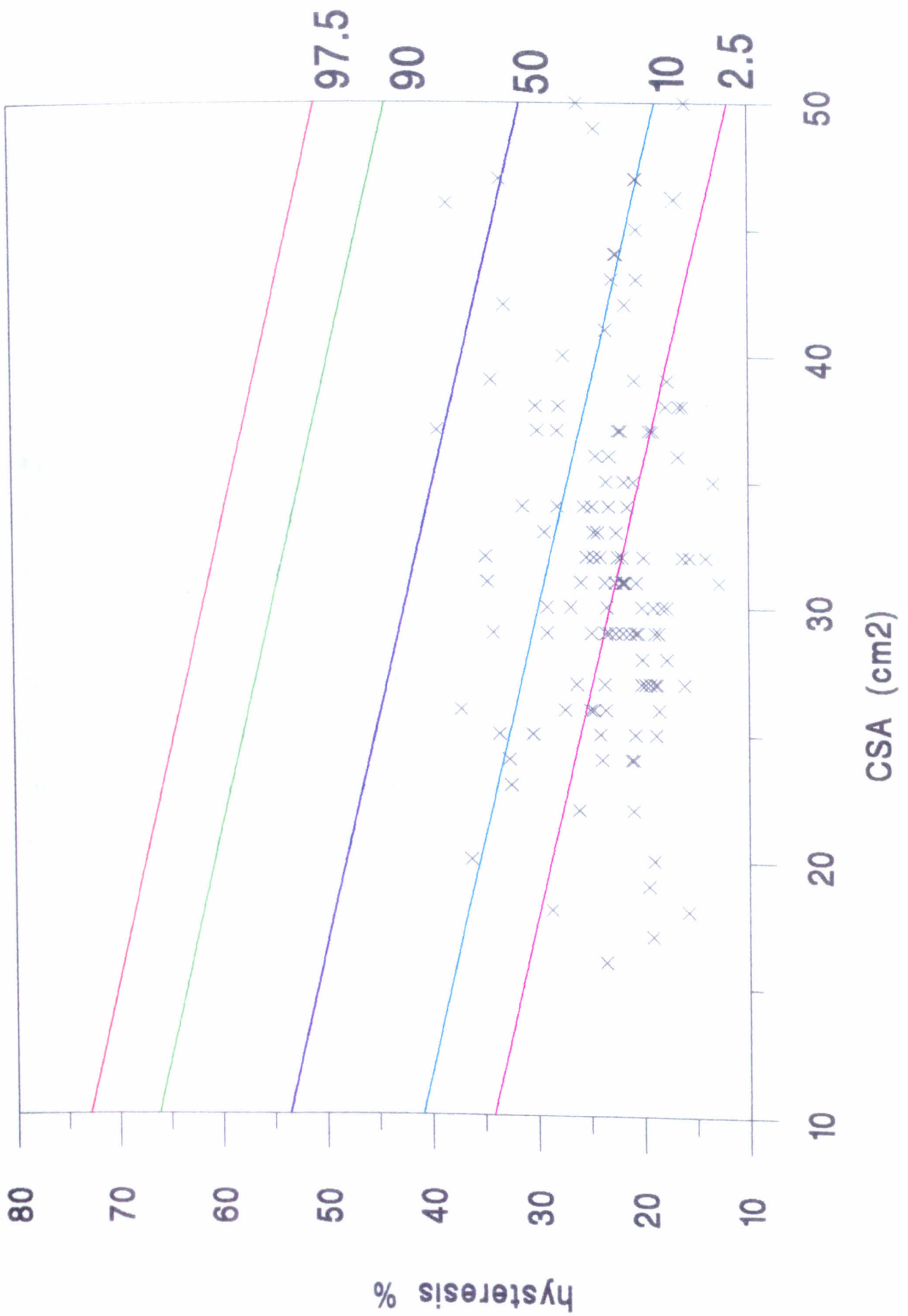
Normal regression lines and associated percentile lines for (a) mean slope and (b) hysteresis with mean values for rheumatoid arthritis superimposed.

N = mean value for all normals (n = 88)

RA = mean value for all rheumatoid arthritis (n = 128)

iRA = mean value for mastic rheumatoid arthritis (n = 32)

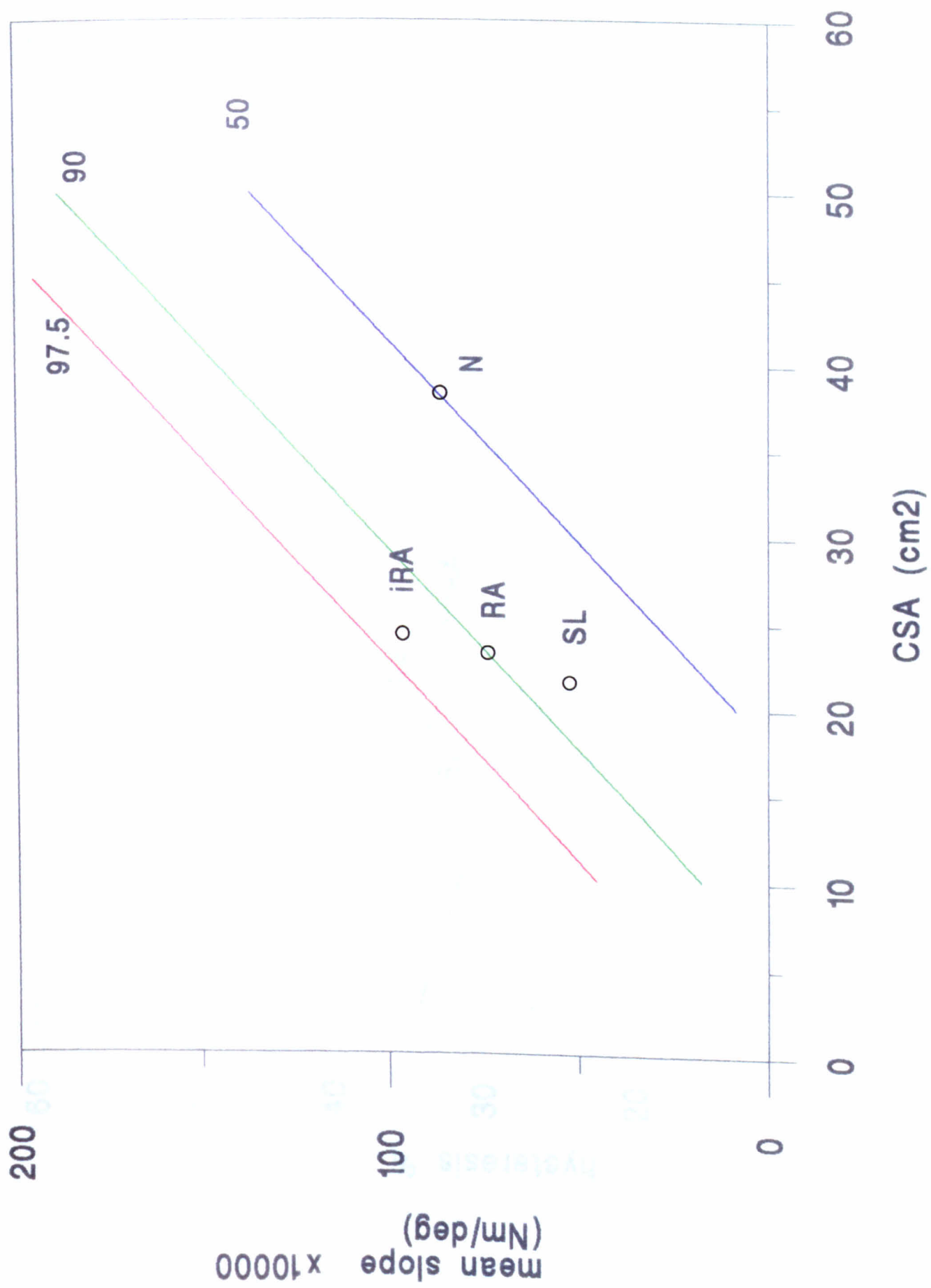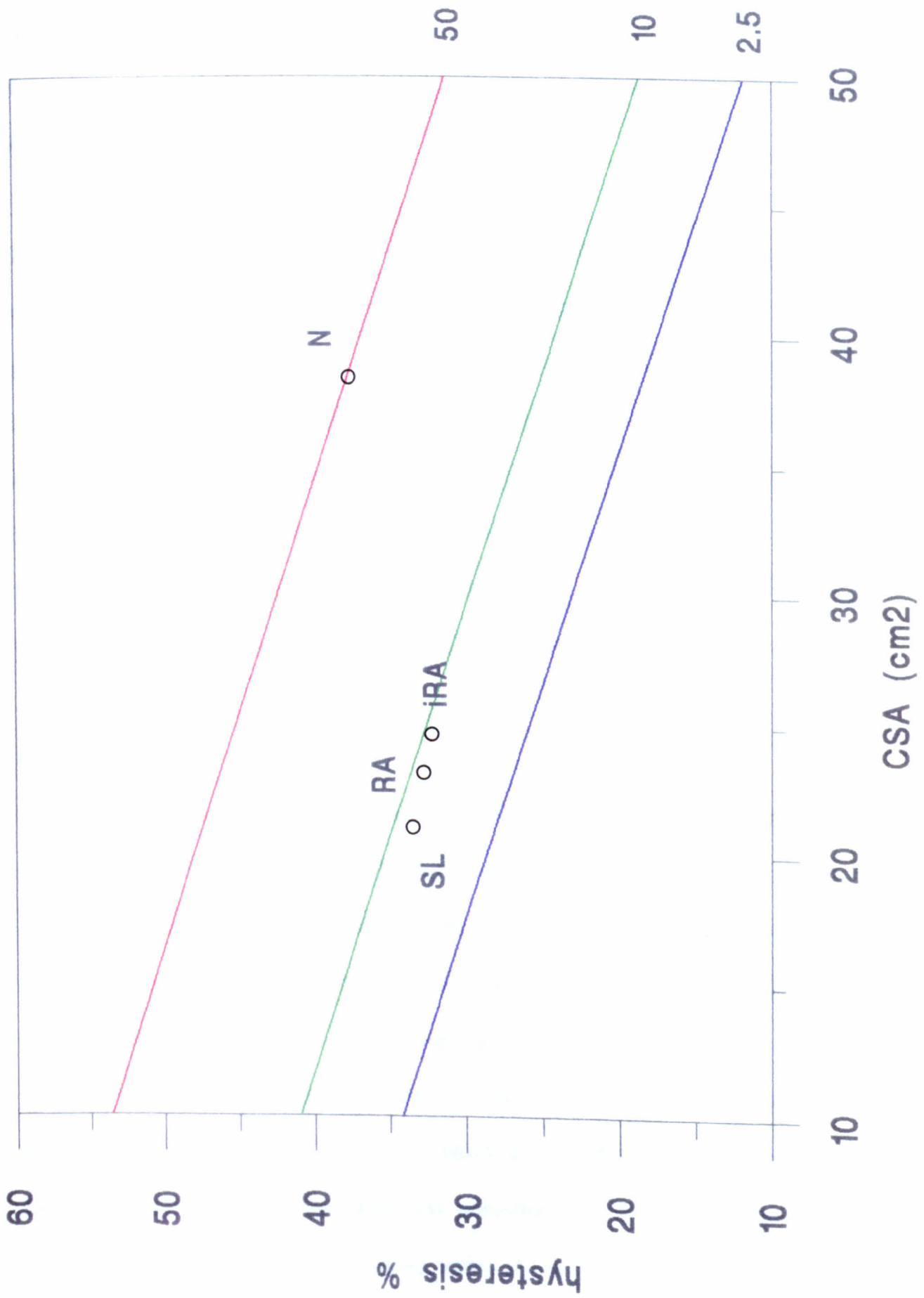SL = mean value for subluxed McP_3 joint (n = 32)

Figure 7.3a

Figure 7.3b

results, adjusted variables for mean slope and hysteresis were significantly different for rheumatoid arthritis collectively and all sub-groups, arthroplasty (n = 5) being the exception.

In Tables 7.5 and 7.6, the values for the standardised deviate, z, for each patient at each time point are presented for the control and experimental days and these are graphed in Figs. 7.4 and 7.5. A z value of above 1.645 is significant at the 5% level (one tailed) but few of the values exceed this level of significance. The changes apparent in mean slope are striking on the experimental day but are not sufficient to achieve statistical significance. It is clear from Table 7.6 and Fig. 7.5 that, despite the timing of the measurements, some spontaneous improvement in grip strength occurred on the control day - probably due to circadian variation.

Discussion

Although the variation in cross-sectional area explained by the variables in the equations of Chapter 5 is acceptable, some doubts must remain about the overall acceptability and applicability of this technique. Some of the problems encountered are exemplified by the distribution of data for cross-sectional area in the normal subjects studied in Chapter 5. The long 'tail' of this distribution influenced the predictive value of the regression equation so that when the equations were applied to the normal data, originally derived by Howe et al (1985), a rather high estimated forearm muscle cross-sectional area was obtained. To avoid this problem, only subjects with cross-sectional areas lying within the inter quartile range were used to derive the regression equation for this variable but the effect, although resulting in a less extreme prediction for CSA, was to reduce R^2 by a factor of 4.

Table 7.5

Equivalent z scores for mean slope values for each patient, at each time point, on control and experimental days. A score of >1.645 is significant at the 5% level.

PATIENT NUMBER	CONTROL DAY (time, h)					DRUG DAY (time, h)				
	0	1	2	4	6	0	1	2	4	6
16	0.89	0.89	0.34	-1.07	-1.07	1.40	-0.86	-0.14	-0.98	0.57
32	--	--	--	--	--	0.98	0.65	0.53	-1.02	-1.14
39	-0.81	-0.81	-0.56	1.04	1.14	0.09	-0.95	-0.02	-0.73	1.60
40	-0.39	-0.39	-1.22	1.31	0.69	-0.07	0.15	-1.48	1.33	0.07
67	-1.09	-1.09	0.92	0.63	0.63	1.72	-0.08	-0.77	-0.63	-0.22
118	-1.18	-0.14	0.68	0.66	1.30	0.21	0.73	-0.66	-1.35	1.08
121	0.85	-1.59	0.85	0.04	-1.63	-1.52	0.22	0.31	-0.24	1.22
129R	0.95	0.72	0.50	-1.08	-1.08	-0.78	-0.25	-0.78	0.17	1.64
129L	-1.21	1.08	0.92	-0.07	0.72	-0.45	1.79	-0.45	-0.45	-0.45
Mean S.D.	-0.25 0.98	-0.17 0.98	0.31 0.78	0.09 0.92	0.02 0.97	0.02 1.00	0.28 0.81	-0.41 0.66	-0.37 0.83	0.48 1.04

Table 7.6

Equivalent z scores for grip values for each patient, at each time point, on control and experimental days. A * is significant at the 5% level.

PATIENT NUMBER	CONTROL DAY (time, h)					DRUG DAY (time, h)				
	0	1	2	4	6	0	1	2	4	6
16	--	0.75	-1.13	0.38	--	-1.10	-0.87	0.00	1.23	0.73
32	--	-0.58	1.16	-0.58	--	-1.19	0.46	0.79	0.90	-0.97
39	0.51	-1.20	0.27	1.24	-0.83	-1.07	-0.78	1.46	0.29	0.10
40	-1.68*	0.22	0.22	1.03	0.22	-0.64	-0.59	-0.88	0.70	1.41
67	--	0.32	0.80	-1.12	--	-0.76	-0.58	-0.85	1.14	1.05
118	-1.77*	0.27	0.37	0.66	0.47	-1.58	-0.09	0.25	0.25	1.17
121	-0.70	-0.03	-0.78	-0.18	1.69*	-1.38	-0.50	1.25	0.50	0.13
129R	-0.66	-1.43	0.84	0.51	0.73	-1.73*	0.50	0.13	0.29	0.82
129L	-1.64	0.04	0.13	0.41	1.06	-1.29	-0.85	0.71	0.94	0.49
Mean S.D.	-0.99 0.89	-0.18 0.73	0.21 0.75	0.26 0.76	0.56 0.85	-1.19 0.35	-0.37 0.53	0.32 0.83	0.69 0.38	0.54 0.72

Figure 7.4

Mean slope.

z statistic as a function of time, on control and experimental (following oral ibuprofen 800mg) days.
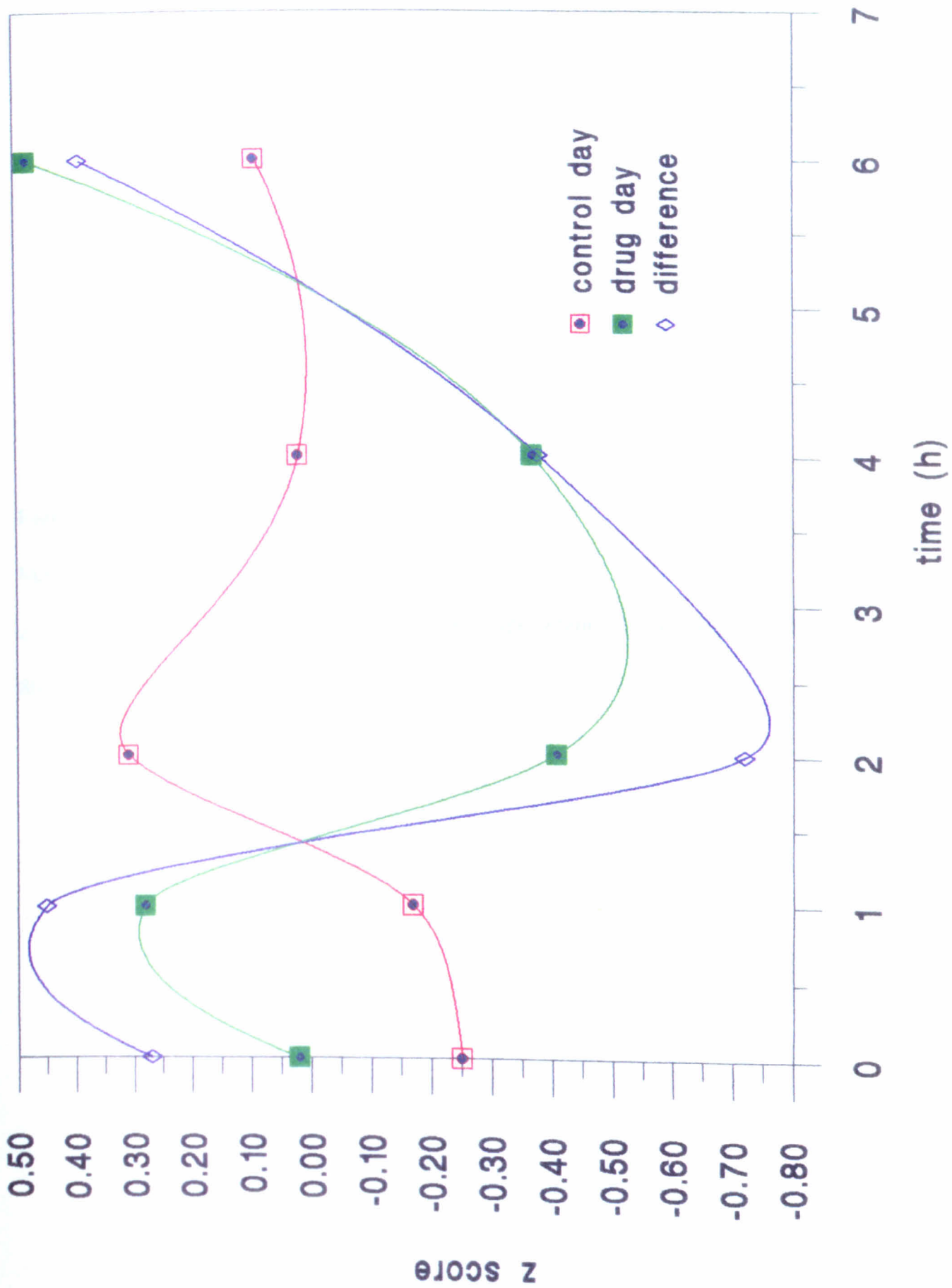
Figure 7.4

Figure 7.5

Maximum grip.

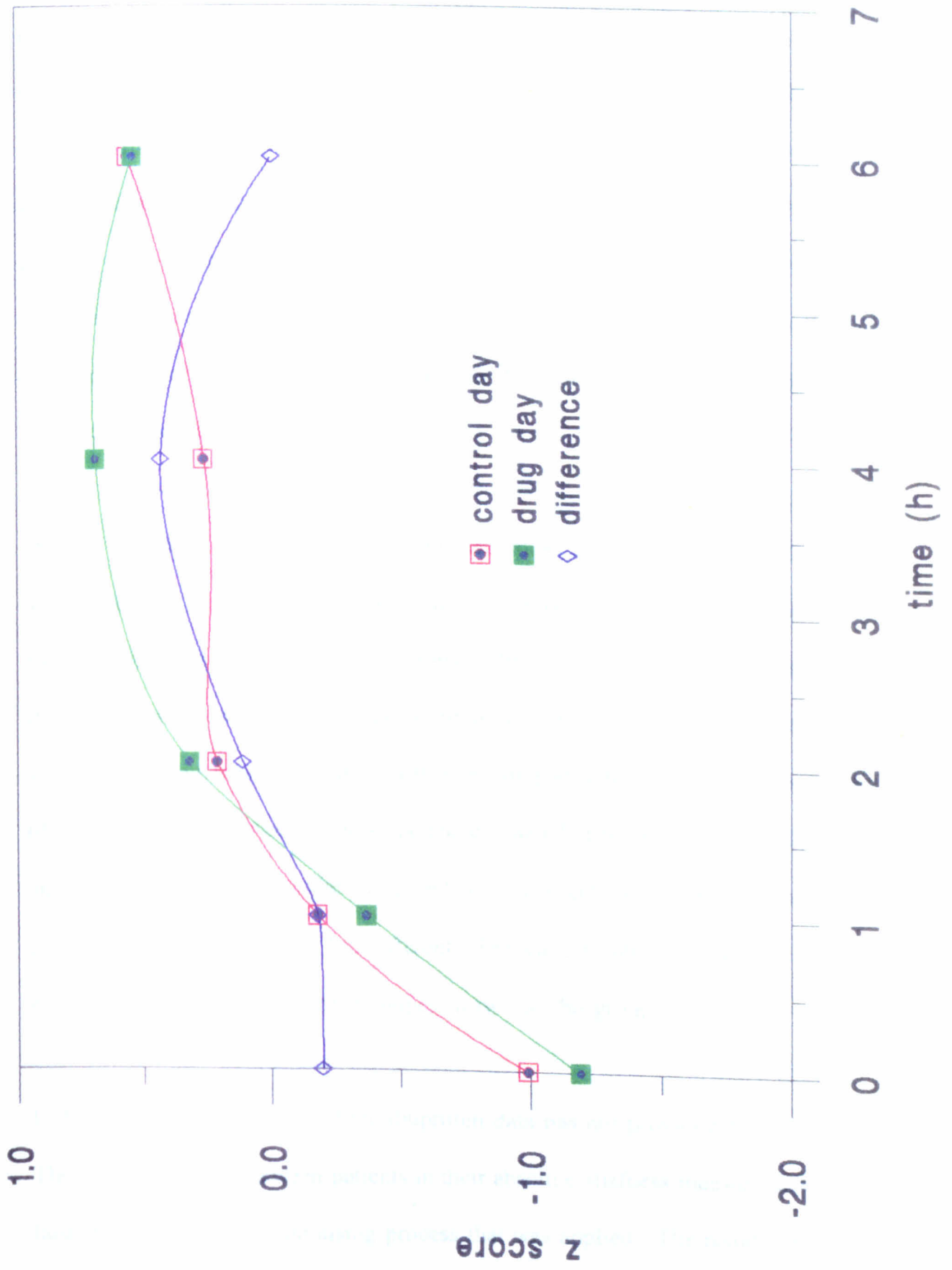z statistic as a function of time, on control and experimental (following oral ibuprofen 800mg) days.

Figure 7.5

Strictly speaking, the predictive power of these equations should be tested in an alternative sample of subjects in whom the actual cross-sectional area has been measured. However, this seems a futile exercise: the best alternative would be to measure arthrographic stiffness in a new group of subjects estimating forearm muscle cross-sectional area at the same time. It is, however, unclear whether the forearm muscle cross-sectional area would, in this case, be the only significant predictor variable of arthrographic stiffness. It should be recalled that the influence of sex and age on stiffness variables may not always be accounted for by differences in anthropometric data.

Despite the foregoing considerations, on theoretical grounds muscle cross-sectional area is likely to have a significant influence on passive articular stiffness and allowing for this variable in a re-analysis of previously obtained results shows that patients with rheumatoid arthritis are stiffer than normal in terms of both elastic and viscous stiffness, but primarily the former. It is interesting to note in Table 7.4 that the slope of the relationship between mean slope and estimated cross-sectional area for normals and rheumatoid arthritis is the same, but the intercepts, apart from the arthroplasty group, are highly significant, but different. The same result was found for hysteresis, even allowing for a difference in slopes in two of the groups.

Unfortunately, a re-analysis of the ibuprofen data has not provided any new insights. The wide variability between patients in their absolute stiffness measurements was too large to overcome any minimising process that was applied. The results, however, do not detract from the quite clear changes in stiffness and grip strength that occurred in the group as a whole on the experimental day, and these objective results were

accompanied by directionally appropriate changes in subjective variables in five out of the eight subjects. The results would have been more striking, although still unimpressive statistically, had the three unresponsive subjects been excluded from the analysis but it was felt that only a certain amount of manipulation of these results was acceptable.

The short term subjective changes that were found in this study are explicable in terms of the known pharmacokinetic profile of ibuprofen and its mode of action both peripherally and centrally (Willer et al, 1989). How could the ibuprofen be influencing the objective measures during this time period? The peak serum level of ibuprofen following oral administration is between one and two hours and the peak intra-synovial level occurs approximately two hours later. Any local affect of the ibuprofen on joint stiffness would therefore occur maximally between two and four hours following administration of ibuprofen, approximately what occurred in the present study. The only changes that could occur rapidly enough are movements of interstitial fluid, presumably from the tissues into the blood stream. Ibuprofen is unlikely to make any short term differences to the collagenous structures surrounding the joint; it is more likely to affect the matrix by promoting fluid absorption from the inflamed tissues.

How could these experiments be carried forward? Accepting the judgement of Huskisson (1976), perhaps only patients who are able to respond objectively and subjectively in these experimental paradigms should be studied. Experiments could be extended by performing dose/response curves using either ibuprofen or another rapidly absorbed anti-inflammatory drug. These experiments could be done 'blind' and if necessary with the addition of a placebo or analgesic. With this objective

measure, it might be possible to compare the strengths of different NSAID's, although it would appear that information on which preference is based may have less to do with strength and efficacy than the side effect profile (Cox & Doherty 1988).

Summary

Forearm muscle cross-section area has been estimated, using previously derived regression equations, in patients with rheumatoid arthritis and in normals. The predicted values in rheumatoid arthritis are of a similar magnitude to muscle CSA's previously obtained but the predicted values in the normal group are high.

Using the predicted forearm muscle cross-section area as a correction factor, patients with rheumatoid arthritis were significantly stiffer than the normal population.

Short-term changes in arthrographic stiffness can be seen in response to a single oral dose of an anti-inflammatory agent but the patients need to be selected for the characteristics of their response to these drugs.
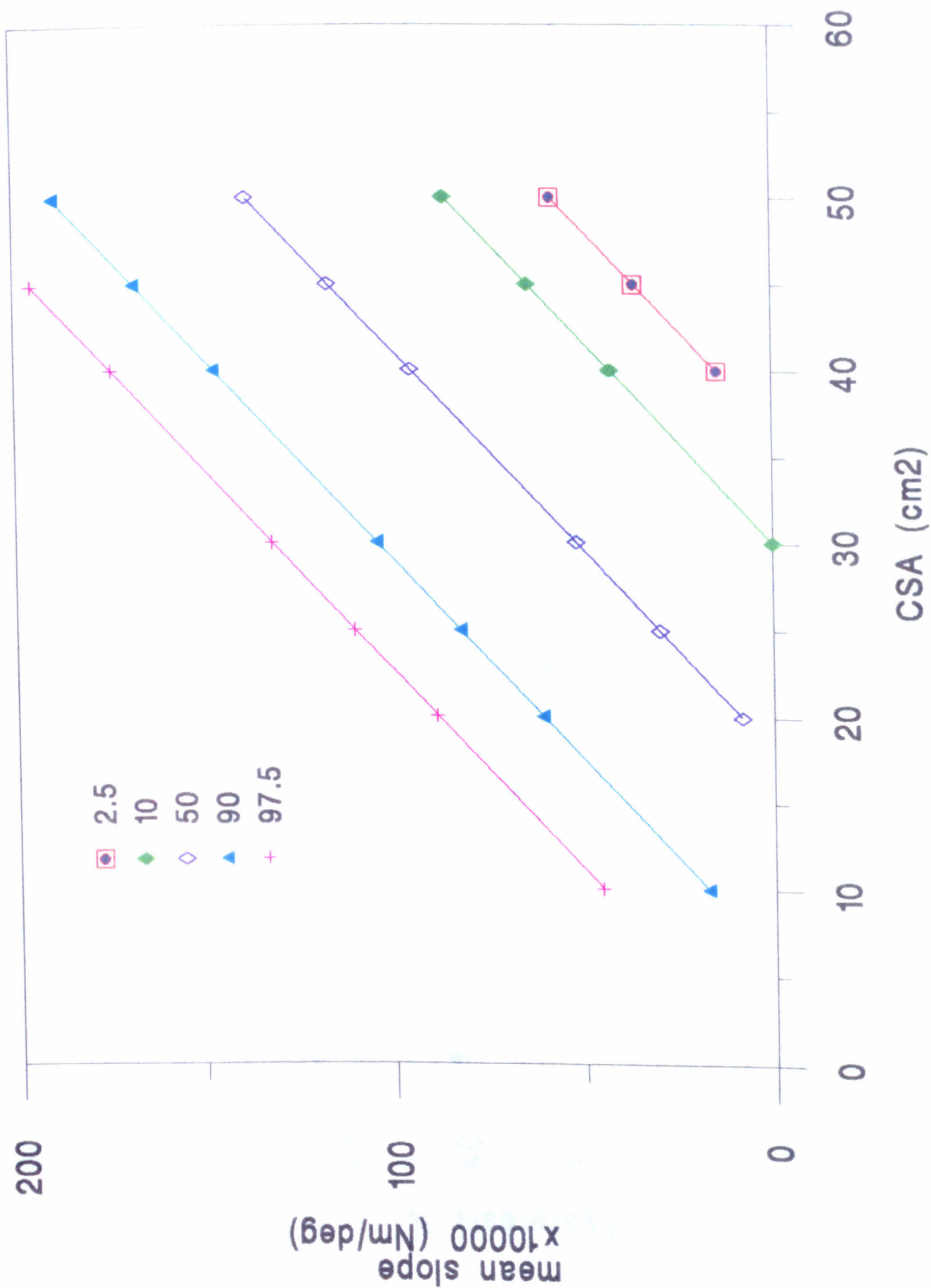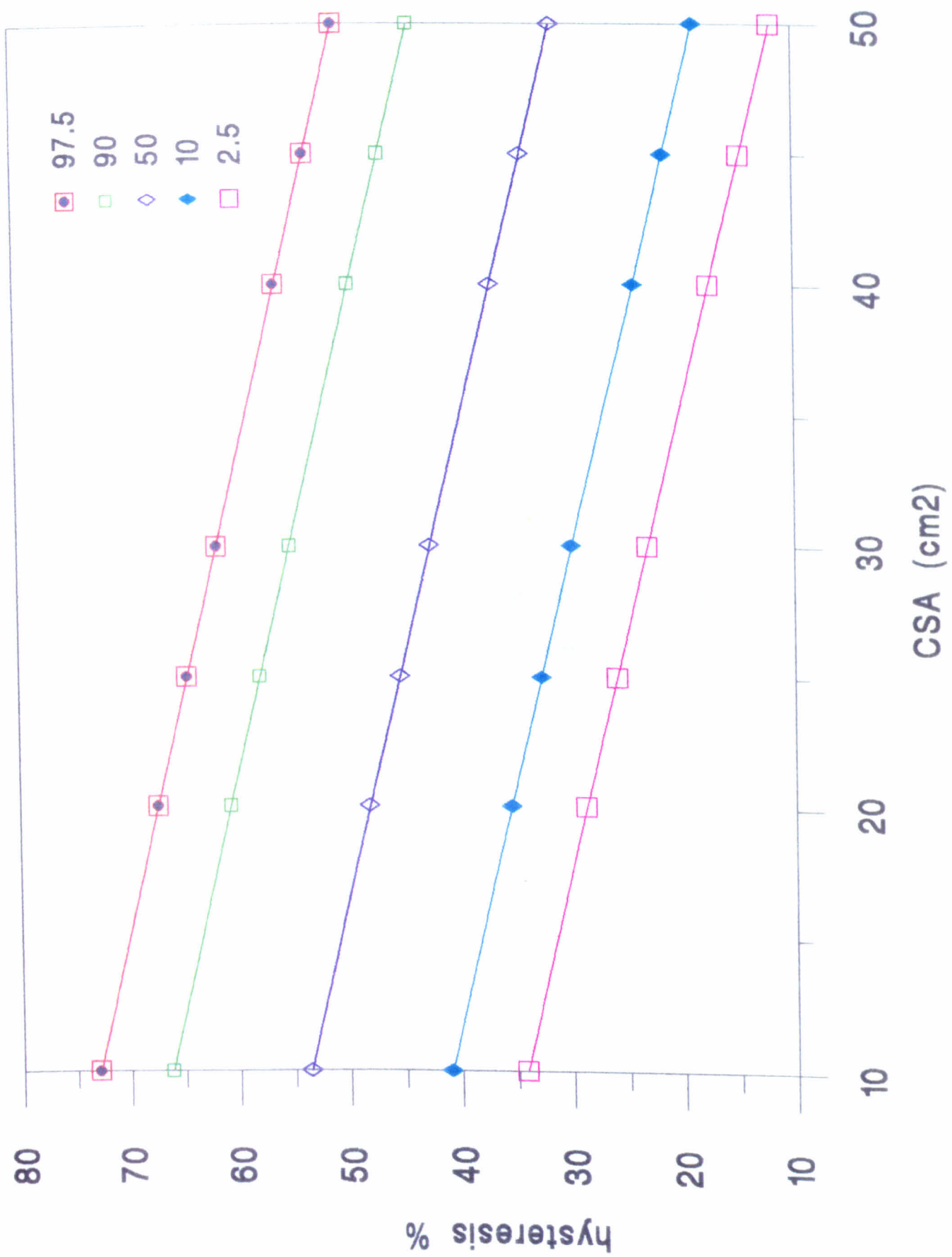
Figure 7.1a

Figure 7.1b

CHAPTER 8

SUMMARY, CONCLUSIONS AND SUGGESTIONS FOR FUTURE WORK

Introduction

Statement of hypothesis

Statement of thesis

Semeiology

Mechano-receptor thresholds

Muscle wasting

Muscle quality and corrected stiffness

Concluding Remarks

Has the arthrograph a future in clinical rheumatology?

Summary

Suggestions for future work

Introduction

As a starting point for this final chapter, I would like to quote from the abstract of my DM thesis: "Although symptomatic stiffness is a major feature of active rheumatoid arthritis, stiffness as defined in this study was not significantly increased. This discordance between subjective and objective stiffness was further demonstrated in a number of studies where subjective stiffness and pain were changing rapidly in response to several well established therapeutic interventions. Furthermore, circadian variation in stiffness could not be confirmed objectively. It is suggested that pain on movement of the joints is often misinterpreted as stiffness in active rheumatoid arthritis. Other possible explanations for the discordant results are presented, but little evidence is available to support these other hypotheses." In Chapter 1 of this thesis, these sentiments were recalled together with proposed explanations for this discordance. This final chapter will recall the evidence collected in exploring these explanations. Finally, the results will be discussed in the context of clinical rheumatology.

Statement of hypothesis

According the shorter Oxford English Dictionary, hypothesis means:

"A provisional supposition which accounts for known facts, and serves as a starting point for further investigation by which it may be proved or disproved."

The known facts as presented in Chapter 1 were that stiffness, although a prominent symptom in arthritic disease, had proved to be an elusive quantity, several studies failing to demonstrate an increase in physical stiffness of the joints in rheumatoid arthritis.

The provisional explanations, some of them complementary, included semeiology, abnormal proprioception, and quantitative and qualitative muscle abnormalities.

Statement of thesis

Semeiology

A questionnaire, based largely on descriptors used by patients to describe symptoms arising in their joints, was administered to both health professionals and different patient groups. The results showed that patients and health professionals share the same understanding of these descriptors, so that essentially a common language is spoken. Interestingly, as pointed out in Chapter 6, research scientists working in several different fields, (including neurology, rheumatology, bio-engineering, robotics and prosthetics), would, if questioned, probably differ as to their concept of stiffness. Considering the terms used, and their definition, reveals that patients are describing increased resistance to movement and limited range of movement. The former description remains the aim of all arthrographs and underlies the paradox of recent experimental studies. The latter description deserves further attention but remains a difficult descriptor to quantitate because inflamed joints hurt when pushed to the limit of their range.

An unexpected finding was the excellent discriminatory power of the questionnaire when comparing the responses of patients with rheumatoid arthritis, non-articular rheumatism and ankylosing spondylitis. The choice of different descriptors, both in quality and quantity, by these different patient groups is not a new finding but this does add an extra dimension to our knowledge of these diseases. For example, why are patients with non-articular rheumatism so aware of the frictional symptoms from

their joints. and why do they complain of a profound lack of energy? Another result of interest was the marked preference for the word 'stiff' in ankylosing spondylitis. The predominant use of the words 'tight' and 'tense' in ankylosing spondylitis suggest that perhaps we should be looking closer at muscular factors in this disorder. The clear difference in pain experience between rheumatoid arthritis and ankylosing spondylitis has been previously described and the confirmation of this result provides some credence to the validity of the results of the questionnaire.

Much work still needs to be done. however, before taking these results any further. Clearly, there are a lot of problems still to overcome with the questionnaire as developed. Many of the original words used in the semeiology questionnaire were derived from patients with rheumatoid arthritis, although the spectrum of words eventually chosen did seem to provide all the necessary descriptors needed by the four patient groups examined in this study. Perhaps, therefore, it is surprising that many of the significant odds ratios were greater than 1: if the words presented favoured rheumatoid arthritis then the significant ratios would predictably have been less than 1.

There is still the possibility that given a wider range of descriptors, patients could describe in more precise terms what their joints feel like. It is true, as pointed out by the philosopher Burge and by the Manchester Group studying arthritic symptoms in children. that we perhaps condition patients to provide us with expected and probably mechanistic descriptions of joint symptoms. The use of the term 'early morning stiffness' is an example: this is one of the first symptoms enquired of when patients attend rheumatology clinics so that. over the years, patients become conditioned and

ultimately present this symptom spontaneously, particularly during relapses. It may be better to ask patients if they have any early morning deterioration in their symptoms thus avoiding the use of the specific word 'stiffness' and encompassing other symptoms such as pain, or whatever symptoms are occurring in the joints.

It would be of interest to extend the study of joint symptomatology to other languages where, perhaps, the extent and range of descriptors available may be wider. The French, for example, have words which cover two of the three definitions of stiffness popular with the patients in this study: 'raide' (stiff joints), 'rigide' (fixed joints) and 'articulation ankylosèe' (fixed joint). A number of terms can be used to describe abnormal sensations from the joints in the Arabic language although this may reflect the large number of dialects rather than the spectrum of descriptors available (A Zakria, N Ruck, personal communications). It is possible that regional semeiological variations exist in England: the work of Prof. Stanley Ellis (personal communication) clearly shows the geographical influence of Nordic and Norman ancestry on our use of common words; for example, over a distance of 10 miles the word representing 'a narrow gap between two houses' can change from 'snicket' to 'ginnel'.

Mechanoreceptor thresholds

There is sufficient experimental evidence to suppose that receptor thresholds and synaptic activity are aberrant in arthritic disease. An over-riding influence is chronic nociceptor activity due to tissue inflammation, but other factors probably contribute such as capsular distension, distortion, ligamentous attrition and joint subluxation. In diseases where inflammation does not play a large part, such as osteoarthritis, the latter mechanisms may play a more important role in abnormal proprioception.

It is more difficult to know what contribution this abnormal neuro-physiological information makes to conscious perception of the articular state and whether, indeed, the magnitude is sufficient for stiffness to be a perceived rather than an actual state in rheumatoid arthritis. I would argue that the neuro-physiological abnormalities are not consciously perceived and do not contribute to the sensation of stiffness. Perhaps the strongest support for this argument are the results obtained in Chapters 6 and 7 of the thesis. However, there are two further pieces of evidence. Firstly, vibration perception thresholds measured at the finger tip in fingers where the PiP and McP joints were inflamed were not abnormal. Secondly, although accepting the results of Ferrel and Craske (1992) and Barrett et al (1990) concerning abnormalities in static joint position sense, it is difficult to know how much clinical relevance this finding has. If patients are obtaining incorrect information on joint stiffness and static joint position sense, surely they are also obtaining incorrect information on joint stability, not a common complaint about finger joints. It may be more relevant that incorrect stataesthetic and kinaesthetic information plays an important part in the loss of fine control of which patients complain. Clearly, other factors are also important (including joint deformity, pain and swelling) but hand dexterity tasks are consistently abnormal in this disease and correlate with other indices of disease activity and progression.

Some of the rehabilitative measures already used for arthritic joints are aimed at increasing proprioceptive information by augmenting mechanoreceptor responses, (for example, adding a firm bandage to the knee in osteoarthritis: Barrett et al, 1990) and it may be that similar approaches should be taken in hand rehabilitation. Measures could include adding cutaneous information to augment joint position sense and

planning programmes of rehabilitation designed to enhance proprioceptive functioning in the small joints of the hands. Such programmes may already exist but the aims of the programmes may be more directed towards joint protection and muscle wasting than specifically proprioceptive re-training.

Muscle wasting

A major finding of this thesis is the confirmation of muscle wasting in rheumatoid arthritis. The extent of muscle loss, however, was not quite as large as expected from grip strength reduction, but the results in Chapter 5 confirm that some of this extra variation can be accounted for by applying a correction for joint deformity and pain. The other variation may be explained by psychological factors and the systemic effect of a chronic inflammatory illness. In particular, both voluntary and involuntary inhibition of maximal grip strength is important: it must be remembered that we spend much of our time educating patients with rheumatoid arthritis that they should protect inflamed joints. The effect of a systemic illness might influence the maximum grip strength, particularly from a nutritional standpoint, and in this context it is worth recalling the findings of Haslock et al (1970) who felt that histologically their muscles looked cachectic. However, the findings of Chapter 6 suggest that the muscle itself is qualitatively normal and that the maximum isometric grip strength is inhibited voluntarily (or involuntarily) as a result of pain occasioned in the joints.

Muscle quality and corrected stiffness

The mean figure for dynamic angular stiffness of the wrist in patients with rheumatoid arthritis obtained in Chapter 6 fits nicely into the scale of mid-range angular stiffness in other joints tabulated in Table 2.2. The wrist would appear to be considerably stiffer than the elbow and it will be recalled that the same was true in the leg for the comparison between the ankle and the knee. Like the ankle, the wrist is a complex joint permitting movement in four planes but with the component bony structures constrained by tough interosseous ligaments. No attempt was made to grade patients according to the stage of their disease in the comparative study of dynamic angular stiffness described in Chapter 6, but it is worth noting that one patient had clear dorsal subluxation of the wrist with a resulting flaccid joint at rest and a dynamic angular stiffness of well below the mean for the group. Nevertheless, for the group as a whole patients with rheumatoid arthritis were significantly stiffer than normal once a correction had been made for forearm muscle wasting. Furthermore, the results depicted in Fig. 6.19 and 6.20 strongly suggest that, at least in terms of these experimental conditions, that the muscle in rheumatoid arthritis is qualitatively normal.

Vibration theory is acquiring increasing important in medical fields. The Edinburgh Group (Walsh et al 1989) have for some time been studying the resonant properties of the human wrist in order to obtain information about forearm muscle function and much of the work done in modelling and robotics, referred to in Chapter 6, relies on a comparison of the response of the muscle joint system to imposed vibrational stimuli. The transmission of vibration waves is also of interest and has been used to study shock absorption by the spinal column in normals and in ankylosing spondylitis (Helliwell et al, 1989). During the course of this thesis, the author considered

applying the technique of vibration transfer to the human arthritic MCP and PIP joints attempting to isolate the influence of the long flexor tendons as described by Barnett and Cobbold (1962). The projected experimental procedure involved applying a 100 Hz low amplitude stimulus to the tip of the finger and measuring the frequency response function with two accelerometers, one attached to the middle phalanx and the other to the proximal phalanx of the finger while keeping the MCP joint flexed to 90°. Although preliminary measurements were not made, it was felt (after some discussion) that the experimental arrangement would lead to amplification and wave propagation due to return of vibratory stimuli down the unconstrained finger, and that constraining the finger to prevent this would lead to erroneous results.

Concluding remarks

Although passive articular stiffness has been found to be increased in rheumatoid arthritis, the remarks made in Chapter 2 on the historical background of joint stiffness measurements remain valid. If passive articular stiffness is measured using an arthrograph then all measurements must be made in relationship to the equilibrium position of the joint and this study has added a further requirement, that a correction for muscle wasting should also be applied.

The work of Ingpen and Hume-Kendall, using the finger-drop technique, remains unique and it may be that these researchers by chance discovered the ideal constraint-free objective method of measuring stiffness (or its equivalent) in arthritis. One further comment, in addition to those made in Chapter 2, could be made on this experimental technique in the light of the present results. Following damage or injury to the knee, there is differential muscle wasting in the thigh, the quadriceps muscles

wasting more than the hamstring muscles. It is possible that with arthritic disease in the hand and wrist the forearm flexor muscles waste more that the extensor groups. In that case any increase in stiffness in the joints may be apparent in an experimental system that relies on the visco-elastic properties of the extensor muscles, as does the finger-drop technique.

Consider then, passive articular stiffness as comprising two components, contributions coming from articular tissue and muscle/tendon tissue. If the results of this thesis can be verified then previous comments on the pathological changes occurring in acutely arthritic joints need to be revised. Helliwell (1987) wrote "distension and distortion of collateral ligaments involved by inflammatory tissue, together with the severe muscle wasting which occurs in the early stages of the disease, are likely to produce decreased stiffness compared with normal joints." It must now be said that despite this attrition of peri-articular tissue, the increase in bulk of the soft tissues (so obvious clinically) results in an increase in passive resistance to movement and a decrease in the range of movement possible at the joint. As the disease progresses and the inflammation subsides, healing by fibrosis is likely to accentuate these changes. Articular subluxation, often a result of disrupted articular surfaces and attenuated collateral ligaments, results in a sharp decline in articular stiffness and is associated with equally dramatic reduction in functional ability.

Has the arthrograph a future in clinical rheumatology?

The author believes that important objective information on the joints can be obtained from these devices but would comment that in clinical practice physicians are loath to rely on anything else other than their intuitive judgement, patient symptomatology

and possibly the plasma viscosity (Kirwan et al, 1986). The objective clinical measures required in many investigative studies of pharmacological efficacy require a battery of time honoured assessments, few of which attempt to measure the mechanical integrity of the joint. The wide natural variation in disease activity seen in rheumatoid arthritis and the desire of patients to provide useful information, requires relevant and reproducible methods of assessment in order to test the efficacy of new therapies and, in the case of the individual patient, to assess the need for change of therapy. Where articular stiffness is the predominant symptom then it is assumed that this reflects the inflammatory state of the involved joints. If a quick and easy objective measure of this state were available then it would provide important additional information with which to assess the progress of the individual patient as well as providing an important measure for therapeutic trials.

I do not think, therefore, that the arthrograph should languish in the laboratory, although I do believe it still has an important role to play in a research environment because the devices such as this are able to continue to provide us with new knowledge on the biomechanics of affected joints, information which may be of use in designing, for example, prostheses and also in the field of physical rehabilitation (Schlapbach and Gerber 1991). There are other benefits of laboratory based bio-mechanical research which, although not extending creatively into the clinical field, may offer enlightenment and some degree of explanation of already recognised clinical phenomena. An example would be the confirmation of nocturnal ulna drift (Helliwell 1987) and the projection, from Chapter 4 in this thesis,, that proprioceptive training is important in rehabilitation of the rheumatoid hand.

Summary

Symptomatic stiffness in rheumatoid arthritis can be objectively assessed providing a correction for muscle wasting is made and, if an arthrograph is used to measure the stiffness, that measurements are made in relationship to the equilibrium position of the joint.

Health professionals and patients with arthritic disease share the same beliefs and concepts about the words used to describe the symptoms from arthritic joints. Patients with rheumatoid arthritis, non-articular rheumatism and ankylosing spondylitis can be separated on the basis of the diversity of descriptors selected to describe their joints. Patients with osteoarthritis are hard to distinguish from patients with rheumatoid arthritis on their choice of descriptors alone.

There are good theoretical, and some experimental, reasons to believe that mechano receptor signalling in rheumatoid arthritis is faulty but it seems unlikely that this contributes to the sensation of stiffness experienced in the joints. Movement perception threshold is difficult to measure because parallel information from cutaneous receptors cannot be easily excluded.

When patients complain of stiffness they imply increased resistance to movement in their joints and limited range of movement, a difficult quantity to measure in painful arthritic joints.

Suggestions for future work

a) Semeiology

Some modification of the questionnaire is required, particularly to exclude the words commonly not sorted (see Table 3.5). Future work with the questionnaire would not require patients to sort the words into different headings so completion could be made in the clinic or at the bedside. Some work has already started on presentation of the descriptors as individual visual analogue scales (Jamieson, 1993) and the discriminatory ability of this approach compared to simple word select could be explored. The ability of the questionnaire to discriminate between disease groups could be taken further with a new population of patients with arthritic diseases and this would permit the application of Bayes' theorem using receiver operating characteristic curves. An opportunity exists for comparing arthritic descriptors across cultures, particularly in a research unit where many overseas visitors are accommodated each year.

b) Mechanoreceptor thresholds.

A true measure of mechanoreceptor thresholds, particularly movement perception threshold, can only be obtained if cutaneous information at the point of attachment of the distal part of the joint can be eliminated. A close and tight fitting circumferential attachment might fulfil these requirements. The use of EMLA cream as described in Chapter 4, because of the time required for onset of anaesthesia, would seem impractical in a clinical setting but might be possible to use in a research environment. Extension of the work on vibration perception thresholds would require the measurement of the thresholds at the point overlying the inflamed joint and this would require the acquisition of a new set of normative data. An alternative device should be considered since the Biothesiometer has a flat calibration curve at its lower end

where changes in threshold are likely to be seen.

c) Objective measures of joint stiffness.

Although the exercise carried out in Chapter 7 provided interesting data, further arthrographic data should be collected on patients with rheumatoid arthritis and, at the same time, direct estimates of forearm cross-sectional area should be made.

Although short term changes in arthrographic stiffness as a result of physical rehabilitation have been observed (Helliwell, 1987) physiotherapy is essentially an ongoing process with occasional periods of intensive re-education. Longitudinal measurements of joint stiffness and forearm muscle cross-sectional area in response to such endeavours, perhaps different modalities, could provide interesting information on the effect of physical therapy on these important variables. If a reliable measure of mechanoreceptor threshold can be obtained, then this could provide an additional dimension with which to record the effect of therapies, particularly designed to improve hand function and manual dexterity.

Limited range of movement.

Although the arthrograph is an ideal instrument for measuring limited range of movement in arthritic joints the device cannot ethically be employed for this purpose in arthritis because of the pain produced as the joints reach the limits of movement. Unfortunately, unless the non-linear portion of the joint/displacement curve can be defined, information on total joint range cannot be obtained. The author has devised a technique whereby the joint range can be measured using the arthrograph: this relies on software monitoring the slope of the torque/displacement curve as stiffness is

measured over increasing amplitudes of displacement so that, as soon as a 10% change in slope occurs, the test is terminated. To overcome the problem of joint discomfort, the test could be carried out with a Biers block in place, perhaps in the following circumstances. Where several joints in a hand are inflamed and potentially responsive to intra-articular corticosteroid injections, it is possible to use a regional anaesthetic block and inject soluble corticosteroid into the devitalised arm. Measurements of limited movement could be made at this time without causing any discomfort to the patient and would add little to the complexity of the procedure.

Differential response to pharmacological agents.

Since it seems possible that the arthrograph is capable of measuring change in response to single doses of anti inflammatory drugs this work could be extended by measuring the response to anti inflammatory drugs of different strengths and duration of action, possibly compared to placebo tablets and certainly compared to analgesics. In this way the experiments of Ingpen (1968), who demonstrated that a pure analgesic had little effect in his measure of stiffness whereas an anti inflammatory agent produced measurable changes, could be repeated.

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Appendix 1

Units of measurement and conversion factors

Early arthrographs (Wright and Johns, 1961) quoted elastic stiffness in terms of kilograms centimetre per radian and viscous stiffness as kilogram centimetre per second per radian. Later papers have measured elastic stiffness in terms of Newton metres per radian (Kearney et al, 1991) or Newton metres per degree (Howe et al, 1985). Kearney et al (1985) used the units Newton metres per second per radian for viscosity whereas Howe et al (1985) preferred to use the dimensionless quantity of hysteresis to express viscosity. Although the 'correct' units of measurement - SI units - are those used by Kearney et al, this thesis has retained the units employed by Howe et al because degrees rather than radians are still commonly used in the clinical context. Where possible, for comparative purposes, quoted stiffness values have been converted into equivalent units. A list of conversion factors is given below.

Dimension	A	B	A to B (Multiply by factor)
Force	$g.cm.s^{-2}$ (dyne)	$Kg.m.s^{-2}$ (Newton)	10^{-5}
Angle	radian	degree	$180/\pi$
Stiffness	$Kg.cm.rad^{-1}$	$N.m. deg^{-1}$	1.71×10^{-3}
Stiffness	$N.m. rad^{-1}$	$N.m. deg^{-1}$	1.745×10^{-2}

Appendix 2

Please return to Dr P Helliwell

Please state your occupation ....

Below is a list of words, most of which have been used by patients with rheumatoid arthritis to describe their joint symptoms. Below these are group headings, which are mine. Please read through the list of words and, taking each word in turn, write that word under the most appropriate heading eg: "painful" is most suitable placed under the heading "PAIN". You may place the word in more than one group. In an emergency you may create an extra group. This is the first stage in the design of a questionnaire which I hope will help arthritis patients describe more accurately what they mean by joint 'stiffness'. Thank you for your help.

Painful, creaking, weak, cumbersome, tight, inert, unstretchable, rigid, inelastic, ache, stubborn, grating, solid, paralysed, limited, clumsy, cold, wooden, tense, compressed, unyielding, hurts, set, jammed, grinding, cramped, limp, dead, jerky, puffy, pulling, inflexible, sore, fixed, sluggish, restricted, all-thumbs, leaden, stiff, throbbing, seized, languid, taut, awkward, stuck, numb, squeezed, rusty, heavy, locked, squashed, lethargic, immovable, uncoordinated, won't go.

WEAKNESS   **FRICTION**   **LIMITED RANGE OF MOVEMENT**   **PAIN**   **SWELLING**

RESISTANCE   **NO FEELING**   **LACK OF MOVEMENT**   **DISABILITY**   ....
TO MOVEMENT

COMMENTS - continue overleaf if necessary

Appendix 3

Dear Patient,

As you may know at this hospital we do a lot of research into different types of arthritis. At the moment I am trying to find out just what patients mean when they say they are 'stiff'.

On the second page of this letter you will find the list of words which previous patients have suggested as describing their stiffness.

I would like you to read through the list of words and then do two things:

1.   Write each word in turn under one of the headings given underneath them. Tick each word off as you work along. For each word choose which you think is the most appropriate heading, for example, 'painful' is most suitably placed under the heading 'PAIN'.

2.   When you have worked through the list, consider which of the words best describes your joint symptoms, then underline these. You may underline as many words as you think appropriate.

Thank you for your co-operation.

Dr PS Helliwell.

Name.......................

Age................   Sex................

Diagnosis...................

These are the words

Painful, lethargic, creaking, limited, aches, puffy, stiff, solid, cold, fixed, weak, grating, restricted, stuck, hurts, stubborn, numb, jammed, grinding, sore, wooden, locked, rigid, set, tight, tense, heavy, inflexible.

These are the categories

WEAKNESS   FRICTION   LIMITED RANGE OF MOVEMENT

PAIN   SWELLING   RESISTANCE TO MOVEMENT

NO FEELING   LACK OF MOVEMENT

Appendix 4

Abbreviations

AS	Ankylosing spondylitis
CSA	Cross-sectional area
CT	Computed tomogram
HAQ	Health Assessment Questionnaire
McP3	Third metacarpophalangeal joint
MPT	Movement Perception Threshold
NAR	Non-articular rheumatism
NSAID	Non-steroidal anti-inflammatory drug
OA	Osteoarthritis
PiP	Proximal inter-phalangeal joint
RA	Rheumatoid arthritis
VPT	Vibration perception threshold

Acknowledgements