A PAIR MATCHED CASE CONTROL STUDY
OF THE CARPAL TUNNEL SYNDROME USING
MAGNETIC RESONANCE IMAGING

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Summary.

A system for collecting cross-sectional MRI images of the human wrist was developed, using the 0.15 Tesla resistive, whole body MRI system at the University of Surrey. A new patient position was designed. After experimentation and development using phantoms and pigs trotters, 58 normal human wrists were imaged. The carpal tunnel cross-sectional areas of the dominant and non-dominant sides were compared. Significant differences were found (p<0.05). Thus it was necessary to employ a pair matched case control study.

In a pair matched case control study, axial wrist images of cases and controls (patients/subjects with and without carpal tunnel syndrome) were collected. 13 cases and controls were matched by gender, age (±5 years) and gross hand dominance. The diagnosis of carpal tunnel syndrome was confirmed where possible using electrophysiological tests. Images were analysed on a graphics monitor and measures obtained of the wrist and carpal tunnel; width, depth and cross-sectional areas. The intra and inter observer reliability of the measuring technique was examined. No significant difference was found for intra-observer reliability (p>0.05), when an observer performed the identical analysis, either on the same day or on different days. Differences were found for the inter-observer reliability (p<0.025), indicating the need to provide adequate training for naïve observers performing analyses. One observer (the author) analysed all of the images throughout the case control study.

No significant differences were found between the cases and controls for any of the carpal tunnel measures. It was therefore not possible to identify differences between cases and controls using this method and equipment. This result confirms the latest findings where Computed Tomography was used to image the carpal tunnel.
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I dedicate this thesis to the memory of my father.
"And the smoke of their torment ascendeth up for ever and ever,
And they have no rest day nor night,
Who worship the beast and his image..." (Revelation XIV: 11)
Executive Summary.

A number of hypotheses regarding the aetiology of Carpal Tunnel Syndrome (CTS) were examined in this study. These hypotheses were related to the anatomical structures of the wrist. In vivo visualisation, through Magnetic Resonance Imaging (MRI) was used as a means of obtaining cross-sectional images of wrists at the carpal bones. This enabled the structure and dimensions of the carpal tunnel to be examined and measured.

CTS results from compression of the median nerve within the anatomical confines of the carpal tunnel. Increased pressure within the carpal tunnel compresses the median nerve, resulting in the symptoms of numbness and tingling in the median nerve sensory distribution and ultimately atrophy of the muscles supplied by the median nerve distal to the carpal tunnel. It is estimated that 70,000 individuals, in the 15-65 age group, annually consult their general practitioners with CTS in England and Wales (Turner 1989). It is likely that this is an underestimate of the total number of sufferers in England and Wales.

Commonly used imaging modalities such as Computed Tomography are designed to image bony structures and cannot easily collect information about the soft tissue boundaries of the carpal tunnel. MRI however, allows these soft tissue boundaries to be imaged non-invasively. Hence, MRI was used in this study to image the wrists of individuals and examine a number of hypotheses regarding the aetiology of CTS. In order to achieve this, some development of the MRI system was required, although it should be stressed that this thesis was not a MRI developmental study in itself.

Other authors have examined CTS using different imaging modalities, notably Computed Tomography. There are inconsistencies in the literature regarding the issue of carpal tunnel size. Some authors have observed significant differences between the carpal tunnel cross-sectional areas of cases and controls (Dekel et al. 1980; Bleecker et
al. 1985; Liang 1987), whilst others found no significant differences (Dekel and Coates 1979; Merhar et al. 1986; Schmitt et al. 1988). All of these studies employed an imaging modality that was not suited to imaging the soft tissue boundaries of the carpal tunnel, which are thought to be important in CTS. It is therefore unclear from the literature, whether the compression of the median nerve occurs as a result of a reduction in the size of the carpal tunnel, or an increase in the volume of the carpal tunnel contents. If the size of the tunnel was found to be an important factor in the development of CTS, it could be argued that individuals with smaller carpal tunnels are more at risk of developing CTS than those with larger carpal tunnels.

The aim of this study was to examine differences in carpal tunnel size, in particular the carpal tunnel cross-sectional area, of cases (with CTS) and controls (without CTS). The main hypothesis was that the carpal tunnel cross-sectional areas of cases would be smaller than those of pair matched controls.

A pilot study was undertaken to examine the carpal tunnels of 58 control wrists, with no evidence of CTS. Imaging methods, protocol and image analysis intra-observer reliability were tested. No significant differences between the carpal tunnel cross-sectional areas of the dominant and non-dominant sides were observed when normalised for overall wrist size. Repeat measures by the same observer were examined, no significant differences were found (the same observer analysed all of the images used in this thesis).

A pair matched case-control study was then undertaken. The cases and controls were matched for gender, age (± 5 years) and hand dominance, as these factors are known to be associated with CTS. The wrist images of 13 cases were compared with 13 controls.
No significant differences were found between the carpal tunnel cross-sectional areas of cases and controls. For these experiments the inter-observer reliability of the image analysis was examined. Significant differences were found when the measurements of naive observers were compared with those of an expert. Adequate training must be provided if images are to be examined by different observers. This is important not only in scientific studies, where inter-observer variation could bias results, but also in the clinical situation when inter-observer variation could influence the clinical diagnosis and ultimately treatment.

This study has shown therefore, that carpal tunnel cross-sectional area does not have an influence on the development of CTS and that there is no evidence that individuals with smaller carpal tunnels are more at risk of developing CTS, than those with larger carpal tunnels.
1 LITERATURE REVIEW
1 Introduction to the Thesis.

Carpal tunnel syndrome is a compression of the median nerve at the wrist. It affects the lives of many individuals, resulting in discomfort, absenteeism from work and often minor operations. There are a number of issues regarding the nature of the compression which require examination. The literature review contains a large body of published information about the carpal tunnel syndrome, the problems encountered during diagnosis and conflicting evidence regarding the importance of carpal tunnel size. This study aims to address these issues regarding compression of the median nerve by using an imaging system. Most of the publications which employed imaging systems to study the carpal tunnel, were poorly designed. Magnetic resonance imaging (MRI) was chosen in this study, because the internal anatomy of the wrist could be seen without risk to the patient. Issues regarding the carpal tunnel size were examined using MRI, the literature review highlights areas to be tested in the experimentation section.

Following the literature review is a pilot study, where some of the techniques to be used in the main study were tested. In particular, the instrumentation and more fundamentally the reliability of image analysis. If images were to be used, then intra and inter-observer reliability had to be tested. This had not been done in previous studies. The results of the pilot study gave important recommendations for the design of the main study.

The main study examined the differences between a group of carpal tunnel syndrome cases and a group of controls. Some of the issues raised in the literature review are also tested. The results of the main study are given in chapter 4 and the entire work is discussed in chapter 5.

The anatomy of the upper limb, elements of MRI and procedural details are given in the appendices.
1.1 What is Carpal Tunnel Syndrome?

Carpal tunnel syndrome or CTS is a common neurological disorder occurring at the carpal tunnel, causing sensory and motor impairment in the median nerve distribution. The first known reference to the condition, later to become known as CTS, was given by James Putnam in 1880. He described a condition involving paraesthesia in the median nerve distribution of 27 patient's hands. There was even a mention of how the symptoms could be relieved by "letting the arm hang out of bed or shaking it for some moments...". The implication that the symptoms occurred during the night (nocturnal exacerbation) and the reference to shaking the hand to relieve the symptoms (later known as the flick test), was later studied in detail by other authors (section 1.7.2).

The true cause of CTS was unknown until 1909 when James Ramsey Hunt of Columbia University attributed thenar atrophy to compression of the median nerve beneath the flexor retinaculum (Pfeffer et al. 1988). In 1913 Marie and Foix made the connection of thenar atrophy and releasing the flexor retinaculum surgically. They performed the first surgical release of the carpal tunnel resulting in relief of the thenar atrophy. However, the connection between the compression of the median nerve and sensory impairment was still to be made.

Brain et al. (1947) were first to report that median nerve compression at the carpal tunnel could result in motor and sensory impairment. This article preceded the surge of interest in CTS which later followed.

Today CTS is widely accepted and a commonly encountered condition throughout the medical and scientific world. Much interest has focused on CTS in order to establish the relative contribution of the many factors known to be associated with it. Although many of the publications have been predominantly case studies, some quality prospective case-control studies have been preformed, providing vital information about the prevention, diagnosis and treatment of CTS.
A definition of CTS, encompassing all of the risk factors contributing to it would not be feasible. The best definition to date was provided by Turner (1989);

"Carpal tunnel syndrome may be defined as a specified set of signs and symptoms indicative of focal median nerve dysfunction, within the anatomical confines of the carpal tunnel."

1.2 Signs and Symptoms of CTS.
A full description of the anatomy of the upper limb is given in appendix I. However, it is worth while elaborating on the anatomy of the carpal tunnel before describing the signs and symptoms of CTS.

By definition the median nerve dysfunction must occur within the confines of the carpal tunnel for a classification of CTS to be made. The boundaries of the carpal tunnel are formed on the lateral, dorsal and medial sides by the carpals bones (hence the name). The carpals bones provide a canal for the flexor tendons to run through, en route to the digits. Accompanying the flexor tendons is the median nerve, the most superficial structure on the palmar surface of the carpal tunnel. The palmar boundary of the carpal tunnel is provided by an inelastic ligament known as the flexor retinaculum, thus completing the carpal tunnel.

The median nerve distribution is described in detail in appendix I. Most of the symptoms occur in this area, comprised of the thumb and thenar eminence, the palm, the 2\textsuperscript{nd} and 3\textsuperscript{rd} and the lateral half of the 4\textsuperscript{th} digit. Also, the dorsal surfaces of the distal phalanx of the 1\textsuperscript{st}, 2\textsuperscript{nd} and 3\textsuperscript{rd} digits and the lateral half of the 4\textsuperscript{th} digit.

Most of the symptoms of CTS are confined to the areas of the median nerve
The symptoms may be classified into those involving sensory impairment and those involving motor impairment. In addition, some symptoms exist which fall into neither of these groups.

*Sensory Impairment*: Paraesthesia and "pins and needles" are the commonest symptoms of CTS reported in the literature. They are a result of the loss in sensory innervation to the areas of the median nerve distribution. Table 1.1 shows that paraesthesia occurs in as many as 99% of all CTS patients. The paraesthesia may not be consistent over the entire median nerve distribution, but may be restricted to merely the finger tips. Pain is another commonly reported symptom.

The sensory nerve fibres tend to be smaller and more susceptible to the effects of compression than the motor fibres. Thus the sensory symptoms tend to occur earlier than those of motor origin. Patients may discover that they have sensory impairment long before any evidence of motor impairment is noticed. Fig 1.1 shows the areas of the hand where the symptoms may occur (The median nerve sensory distribution.).
Fig 1.1 The Median Nerve Sensory Distribution.
Motor Impairment: Any motor impairment tends to occur after the sensory impairment. The most commonly reported motor impairment symptom is thenar atrophy. Some of the muscles of the thenar eminence are supplied exclusively by the median nerve. If the motor function of these muscles is reduced by the dysfunction of the median nerve at the carpal tunnel, wasting of the muscle will occur due to the inactivity.

Thenar atrophy was reported to occur in between 41 and 53% of patients with CTS (table 1.1).

Other symptoms: Other symptoms have been reported be various authors (table 1.1). Most noticeably nocturnal aggravation is common (27-95%), such patients reported being awoke by the symptoms. However, the reason for this nocturnal aggravation of the symptoms remains unclear and the mechanism has not yet been established.

Swelling of the palmar aspect of the wrist, proximal to the area of compression in the carpal tunnel was reported by Posch and Marcotte (1976) and Doyle and Carroll (1968), occurring in 10-20% of the cases. The compression in the carpal tunnel may have caused this swelling, although a comparison with a control population has not been carried out. The same can be said of the occurrences of dryness of skin and susceptibility to cold (2% for both conditions reported by Posch and Marcotte (1976)). In a smaller group Tanzer (1959) found 60% of patients suffered from susceptibility to cold due to vaso-motor imbalance.

The stiffness reported by Posch and Marcotte (1976) in 9% of cases may be attributed to arthritis, which occurred in 11% of the same population. Whether these were the same patients was not reported.

Other symptoms such as clumsiness may be a result of a combination of the sensory and motor impairment. Proprioceptive feedback may also be compromised by median nerve
dysfunction within the carpal tunnel.

CTS may also result in symptoms proximal to the carpal tunnel as Cherington (1974) pointed out. From a sample of 46 patients with proximal symptoms 94% had relief of these symptoms after surgical release of the flexor retinaculum. Although, these proximal symptoms may be present, it is worth noting that other disorders may also result in such symptoms. Care should be taken to eliminate the presence of these conditions before diagnosing CTS.
Table 1.1 Reported symptoms of carpal tunnel syndrome in the literature.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Paper</th>
<th>No. of subjects</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paresthesia, Hypesthesia and Numbness</td>
<td>Dekel et al. 1980</td>
<td>42</td>
<td>95%</td>
</tr>
<tr>
<td></td>
<td>Doyle and Carroll 1968</td>
<td>100</td>
<td>70%</td>
</tr>
<tr>
<td></td>
<td>Phalen 1966</td>
<td>654</td>
<td>79%</td>
</tr>
<tr>
<td></td>
<td>Posch &amp; Marcotte 1976</td>
<td>1201</td>
<td>67%</td>
</tr>
<tr>
<td></td>
<td>Tanzer 1959</td>
<td>34</td>
<td>97%</td>
</tr>
<tr>
<td></td>
<td>Yamaguchi et al. 1965</td>
<td>1215</td>
<td>99%</td>
</tr>
<tr>
<td>Pain</td>
<td>Dekel et al. 1980</td>
<td>42</td>
<td>57%</td>
</tr>
<tr>
<td></td>
<td>Posch &amp; Marcotte 1976</td>
<td>1201</td>
<td>63%</td>
</tr>
<tr>
<td>Tingling</td>
<td>Posch &amp; Marcotte 1976</td>
<td>1201</td>
<td>42%</td>
</tr>
<tr>
<td>Cold</td>
<td>Posch &amp; Marcotte 1976</td>
<td>1201</td>
<td>2%</td>
</tr>
<tr>
<td></td>
<td>Tanzer 1959</td>
<td>25</td>
<td>60%</td>
</tr>
<tr>
<td>Nocturnal aggravation</td>
<td>Dekel et al. 1980</td>
<td>42</td>
<td>95%</td>
</tr>
<tr>
<td></td>
<td>Posch &amp; Marcotte 1976</td>
<td>1201</td>
<td>27%</td>
</tr>
<tr>
<td></td>
<td>Ragi 1981</td>
<td>57</td>
<td>91%</td>
</tr>
<tr>
<td></td>
<td>Tanzer 1959</td>
<td>34</td>
<td>91%</td>
</tr>
<tr>
<td>Thenar atrophy</td>
<td>Dekel et al. 1980</td>
<td>28</td>
<td>43%</td>
</tr>
<tr>
<td></td>
<td>Doyle &amp; Carroll 1968</td>
<td>100</td>
<td>51%</td>
</tr>
<tr>
<td></td>
<td>Phalen 1966</td>
<td>654</td>
<td>41%</td>
</tr>
<tr>
<td></td>
<td>Ragi 1981</td>
<td>57</td>
<td>53%</td>
</tr>
<tr>
<td></td>
<td>Tanzer 1959</td>
<td>28</td>
<td>43%</td>
</tr>
<tr>
<td></td>
<td>Yamaguchi et al. 1965</td>
<td>1215</td>
<td>50%</td>
</tr>
<tr>
<td>Clumsiness</td>
<td>Dekel et al. 1980</td>
<td>42</td>
<td>55%</td>
</tr>
<tr>
<td>Swelling</td>
<td>Doyle &amp; Carroll 1968</td>
<td>100</td>
<td>10%</td>
</tr>
<tr>
<td></td>
<td>Posch &amp; Marcotte 1976</td>
<td>1201</td>
<td>20%</td>
</tr>
<tr>
<td>Stiffness</td>
<td>Posch &amp; Marcotte 1976</td>
<td>1201</td>
<td>9%</td>
</tr>
<tr>
<td>Dry skin</td>
<td>Posch &amp; Marcotte 1976</td>
<td>1201</td>
<td>2%</td>
</tr>
</tbody>
</table>
1.3 Disorders with Similar Symptoms to CTS.

It was mentioned earlier that other conditions may produce symptoms similar to those of CTS. Some of these conditions are shown in table 1.2.

Table 1.2 Conditions with symptoms similar to CTS.

1. Conditions resulting from localised damage to specific areas of:

   The Spinal Cord:
   - Spinal Cord Tumours
   - Syringomyelia

   The Cervical Root:
   - Cervical Disc Degeneration
   - Spondylosis

   The Brachial Plexus:
   - Cervical Rib Syndrome
   - Thoracic Outlet Syndrome
   - Lesions of the Brachial Plexus

   The Median Nerve:
   - Pronator Teres Syndrome
   - Entrapments under the Ligament of Struthers

   The Digital Nerves
   - Lesions of the Digital Nerves

2. Polyneuropathies

3. Conditions resulting from Anatomical Abnormalities.

   Ulnar nerve compression in Guyon's canal with Martin Gruber anastamosis

   (Turner 1989)

An examiner should be aware of these abnormalities and should be able to systematically eliminate the presence of these, if the true diagnosis of CTS is unclear. Since most of these conditions occur proximal to the wrist, the examiner should use a
battery of tests with which to identify where any neuropathy occurs. Only if this neuropathy occurs in the carpal tunnel CTS can be diagnosed. If the neuropathy occurs elsewhere then CTS may be eliminated as a possible diagnosis.
1.4 The Size of the Problem.

Due to the lack of epidemiological studies in the UK or abroad, there is very little information available about the incidence or prevalence rates of CTS. Ragi (1981) reported 59 patients presenting with confirmed CTS in the 529154 population of Copenhagen in 1979. This represents an annual incidence of 0.11 (per thousand at risk). However, this only gives the annual incidence of patients actually examined at the clinic, more cases may have existed in the population but were not identified.

More recently, information has become available from the Royal College of General Practitioners (RCGP 1986). The number of patients consulting with CTS to General Practitioners (GP) in selected clinics in England and Wales were reported, the results are given in table 1.3.

<table>
<thead>
<tr>
<th>Group</th>
<th>All Ages</th>
<th>15-24</th>
<th>25-44</th>
<th>45-64</th>
</tr>
</thead>
<tbody>
<tr>
<td>♂</td>
<td>0.6</td>
<td>0.4</td>
<td>0.9</td>
<td>0.8</td>
</tr>
<tr>
<td>♀</td>
<td>2.2</td>
<td>0.8</td>
<td>3.3</td>
<td>4.2</td>
</tr>
<tr>
<td>All</td>
<td>1.4</td>
<td>0.6</td>
<td>2.1</td>
<td>2.6</td>
</tr>
<tr>
<td>♂ : ♀</td>
<td>1:3.7</td>
<td>1:2.0</td>
<td>1:3.7</td>
<td>1:5.3</td>
</tr>
</tbody>
</table>

(Turner 1989)

These data relate to those individuals attending certain clinics in England and Wales. Turner (1989) used the population breakdown of England and Wales to produce the data given in table 1.4, showing the estimated numbers of patients consulting with CTS in the various groups.
It is estimated that about 70000 CTS sufferers consult their general practitioners each year in England and Wales. It is thought that these figures could be considerably underestimated for a number of reasons. Clearly some sufferers of CTS may not report to their GP about their CTS, particularly if the symptoms are mild or occur in conjunction with other conditions. GPs are not necessarily in a position to perform the types of test required to make a clear cut diagnosis of CTS. So General Practitioners may wrongly diagnose other conditions in those who indeed have CTS. It is less likely that a diagnosis of CTS would wrongly be made in those individuals who do not have CTS. The data in table 1.4 only represents those of the ages 15-64. It is likely that older individuals also suffer from CTS exist, thus increasing the numbers of referral even further.

Table 1.4 Estimated Numbers of Patients Consulting General Practitioner in England and Wales.

<table>
<thead>
<tr>
<th>Group</th>
<th>All Ages</th>
<th>15-24</th>
<th>25-44</th>
<th>45-64</th>
</tr>
</thead>
<tbody>
<tr>
<td>♂</td>
<td>14598</td>
<td>1658</td>
<td>6187</td>
<td>4337</td>
</tr>
<tr>
<td>♀</td>
<td>56306</td>
<td>3187</td>
<td>22375</td>
<td>23462</td>
</tr>
<tr>
<td>All</td>
<td>69893</td>
<td>4877</td>
<td>28674</td>
<td>28620</td>
</tr>
</tbody>
</table>

(Turner 1989)

It is not possible to provide a true figure for the annual incidence or prevalence of CTS in England and Wales. However, on the grounds of the data in table 1.4 the cost to industry per year must be worth considering, although this true cost is currently unavailable.
1.5 The Pathophysiology of CTS.

It has already been mentioned that the symptoms of CTS result from compression of the median nerve at the carpal tunnel. Although it is widely accepted that the symptoms arise from this compression, a number of questions regarding the reasons why the symptoms occur still require consideration;

i. Why does this long term compression of the median nerve result in these symptoms and neurophysiological changes?

ii. Is the compression of the median nerve the result of the anatomical confines of the carpal tunnel pushing into the carpal tunnel, or does the contents of the carpal tunnel increase in volume to such an extent, that the nerve becomes compressed?

Indeed Graham (1983) suggested that CTS must be attributed to one or more of the following;

1. An alteration in the osseous margins of the carpal tunnel.
2. A thickening of the flexor retinaculum.
3. An increase in the volume of the contents of the carpal tunnel.

In answer to the first question above, it would be useful to be able to measure the pressure on the median nerve in cases and controls. Gelberman et al. (1981) did just that, using a pressure transducer known as a wick catheter placed within the carpal tunnel of cases and controls during surgery. The pressure was measured when the wrist was placed in a flexed, neutral and extended position (table 1.5).
Table 1.5 Carpal tunnel pressures from Gelberman et al. (1981).

<table>
<thead>
<tr>
<th></th>
<th>Flexed</th>
<th>Neutral</th>
<th>Extended</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cases</strong></td>
<td>94 (20)</td>
<td>32 (4)</td>
<td>110 (22)</td>
</tr>
<tr>
<td><strong>Controls</strong></td>
<td>31 (3)</td>
<td>2.5 (0.6)</td>
<td>30 (4)</td>
</tr>
</tbody>
</table>

Significant differences between cases and controls for all measures \( p<0.001 \).

The carpal tunnel pressure of the cases was significantly greater than the controls. It is interesting to note that the pressure of the cases neutral position was similar to that of the controls measures when in the flexed and extended positions. Phalen (1966) observed that if a controls’ wrist where held in a flexed position for long enough the symptoms of CTS would be observed. Gelberman et al. (1981) showed that the conditions required to produce the symptoms of CTS (ie. pressure of 30 mmHg in the carpal tunnel) could be reproduced in the control subjects, supporting Phalens theory.

Evidence regarding the pressure inside the carpal tunnel is available from studies using wick catheters. How does this pressure cause the neurophysiological changes? It is thought that there are both mechanical and ischaemic factors contributing to the effects. Ochoa et al. (1972) demonstrated that localised compression of peripheral nerve resulted in demyelination of the nerves and invagination of the nodes of Ranvier. These effects were produced in baboons subjected to high pressures under a pneumatic cuff for several hours (1000 mmHg for 1-3 hours). It is thought that these changes could result in the characteristic slowing of the nerve conduction velocity. It is unlikely that such pressures would be encountered in the CTS, (Maximum pressures in the carpal tunnel in the Gelberman et al. (1981) study was 250 mmHg) but the results demonstrate the effect
of acute nerve compression.

Rydevik et al. (1981) monitored blood flow through rabbit tibial nerve under conditions of compression. At pressures of around 30 mmHg, the bloodflow though the venules was impaired. At higher pressures of around 65 mmHg there was almost complete arterial blockage. It is interesting to compare these results with those in table 1.5. Control subjects would only encounter the impairment of venule flow when in complete flexion or extension. Cases would experience permanent venule flow impairment and regularly complete arterial blockage. These blockages would compromise the supply of nutrient to the nerve and thus inhibit its function.

From the evidence available regarding the mechanical and ischaemic factors affecting the median nerve in the carpal tunnel, the critical carpal tunnel pressure would seem to be between 30 and 60 mmHg.

The second question regarding the issue of whether the compression is caused by the anatomical confines of the carpal tunnel pushing in, or the volume of the carpal tunnel increasing is more difficult to answer. It is worth considering both scenarios separately as CTS is without doubt caused by one, if not both.

i. Anatomical changes to the boundaries of the carpal tunnel do occur. Bony ossicles intruding into the carpal tunnel were observed by Yamaguchi et al. (1965). Abnormalities of other carpal bones have also been reported (Herndon et al. 1974) to result in CTS. Wrist fractures have regularly been reported to be associated with CTS (section 1.6.2). It is not clear whether the CTS is actually caused by changes in the bones following fracture or oedema and tenosynovitis resulting from the recovery processes of bone reformation.
Studies using computered tomography to image carpal tunnels has resulted in various inconsistencies in the literature. This issue is further elaborated in section 1.12.1. It is however, clear that in certain cases CTS may be caused by the infringement of bony ossicles into the carpal tunnel. Whether the carpal tunnel cross-sectional area is important remains unclear. It is hoped that this study will clarify the situation.

Thickening and tightness of the flexor retinaculum has been noted at surgery by various authors (Halter et al. 1981; and Yamaguchi et al. 1965). Thickening of the ligament may be as a result of the compression itself and not a direct cause of the compression. Lin et al. (1983) found no histological differences between cases flexor retinaculae and those from fresh autopsies.

**ii. Increases in the volume** of the carpal tunnel contents has also been widely reported. Yamaguchi et al. (1965) found tumours in three out of 204 hands operated on. Deposition of amyloid was reported in section 1.6.1. Callison et al. (1968) reported gross enlargement of the median nerve within the carpal tunnel. All of these would result in an increase in the volume of the carpal tunnel contents and thus compression of the median nerve.

Inflammation of the contents of the carpal tunnel, particularly the tendon sheaths (tenosynovitis), will lead to an increase in volume of the carpal tunnel contents and eventually to median nerve compression. Acute inflammation, present for only a few days may in the short term result in CTS. However, since the inflammation only persists for a few days, it is unlikely that a permanent state of CTS will result. Chronic inflammation is more serious. Oedema may develop when the inflammation persists, as plasma proteins pass through the capillaries. Fibrosis (the laying down of scar tissue) may develop as a result of persistent oedema, this may calcify over a longer period of time.
Tenosynovitis has been reported to be associated with CTS by various authors (section 1.6.2). Indeed, tenosynovitis is a prescribed industrial disease. CTS is only classified as a prescribed industrial disease when it occurs secondary to tenosynovitis. In 1981/2, 2282 cases of tendinitis and/or tenosynovitis of the hand or forearm were granted industrial injury benefit (HSE 1985). It is unclear how many of these sufferers also had the symptoms of CTS.

Oedema and the resultant deposition of scar tissue has been observed during surgery (Delmez 1982; Kenzora 1978 and Yamaguchi et al. 1965). This oedema may or may not occur as a result of inflammation; patients with CTS as a result of pregnancy have been noted to experience a high degree of oedema compared with asymptomatic pregnant women (Voitk et al. 1983).

A mechanism for median nerve compression as a result of the increase in volume of the carpal tunnel contents was hypothesised by Schuind et al. (1990). It was thought that after initial mechanical stress of the synovium of the flexor tendons, acute inflammation (tenosynovitis) occurs rapidly. A vicious cycle is then created: The mechanical stressess and the continuous tendon friction against the now inflamed tendon sheaths will eventually cause damage to those sheaths. Synovial cells are capable of rapid repair so the formation of scar-type synovial hypertrophy occurs rapidly. Now the cycle is completed as the synovial hypertrophy aggravated by oedema of the scar-type tissues enhances the tendon friction and mechanical stressess (Schuind et al. 1990).

The issue of carpal tunnel congestion is sometimes complicated by the presence of anatomical abnormalities which may increase the contents of the carpal tunnel. Details of these abnormalities are given in appendix I.
In summary, there now seems little doubt that an increase in the volume of the contents of the carpal tunnel, complicated by the presence of oedema, plays a major role in the CTS. The effect of carpal tunnel stenosis has still to be examined more thoroughly before agreement in the literature can be obtained. Sections 1.11 and 1.12 examine the use of imaging on this issue and the controversies which have developed as a result.
1.6 The Aetiology and Factors Associated with CTS.

The actual aetiology of the CTS is still not fully understood, due to the number of factors associated with the syndrome. Many factors have been reported to be associated with CTS. Most of these factors detailed in the following section influence the anatomical alterations mentioned by Graham (1983).

It is convenient to consider the systemic and local factors associated with CTS separately. Most of the information is obtained from studies of populations of patients with CTS, where the number of patients with the particular conditions are reported. In these studies there is a lack of control data with which to compare the results. Other studies have investigated populations of individuals with the particular condition of interest and the number of individuals with CTS calculated.

For some of the risk factors considered here there is strong evidence for an association between the risk factor and its influence on CTS. For other conditions the association may not be quite so apparent.
1.6.1 Systemic Factors Associated with CTS.

Acromegaly.

Acromegaly is an endocrine disorder involving the progressive enlargement of the head and face, hands, feet, and thorax. It is due to an excessive secretion of growth hormone, by the anterior lobe of the pituitary gland.

O'duffy et al. (1973) reported that 35% of 100 acromegalic patients also suffered from CTS bilaterally due to pituitary overactivity. Successful treatment of the pituitary disorder led to complete recovery from CTS.

Two studies on populations of CTS patients (Posch and Marcotte (1976) and Yamaguchi et al. (1965)) have reported the presence of acromegaly in the patient population. In both studies 0.5% of the patients suffering with CTS also suffered from acromegaly.

Amyloidosis.

Amyloidosis is a condition characterised by the accumulation of the protein amyloid in various organs and tissues of the body. Peri-collagenous amyloidosis is the particular type of amyloidosis found in blood vessels, the heart, respiratory tract, intestine, skin, joints and nervous system.

During a survey of individuals with primary amyloidosis, Mahloudji (1968) found 53 patients to be suffering from CTS. These data are of little use as no record of the total population was available.

Yamaguchi et al. (1965) found that in a population of 1215 CTS patients, only 1% also had evidence of amyloidosis.

Use of Oral Contraceptives.

Whether the use of oral contraceptives is associated with CTS is at present unclear.
Sabour and Fadel (1970) found that patients suffering from CTS could display marked improvement in their symptoms, when asked to stop taking oral contraceptives. A number of individuals resumed the use of the "pill", with the result of reoccurrence of the CTS. The cases in this study were taking the high dose type of contraceptive, which could manifest increased fluid retention and oedema. Cannon et al. (1981) found no significant difference between CTS patients and controls for the use of oral contraceptives in a case control study.

*Diabetes Mellitus.*

Diabetes mellitus is a metabolic condition involving reduced carbohydrate utilisation due to deficient insulin secretion. It has been reported to be present in between 3-8% of patients who present with CTS (Cannon et al. (1981) 3%; Doyle and Carroll (1968) 3%; Phalen (1966) 8%; Posch and Marcotte (1976) 5%; Yamaguchi et al. (1965) 5%).

Phalen (1970) suggested that the percentage was higher (16.5%). Further more, 27.2% of patients presenting with CTS either had diabetes mellitus or a family history of the condition.

*Hypothyroidism or Myxoedema.*

A condition caused by reduced secretion of the thyroid gland resulting in hard oedema of subcutaneous tissue, dryness and loss of hair and subnormal temperatures.

Yamaguchi et al. (1965) and Frymoyer and Bland (1973) reported that a proportion of their CTS patient also suffered from Myxoedema. Out of 49 CTS patients Frymoyer and Bland (1973) found a total of 10% myxoedemix, Yamaguchi et al. (1965) found 6% of the 1215 CTS patients studied, to be affected in this way.

The CTS symptoms tend to improve once the myxoedema has been treated successfully.
Literature Review

(Frymoyer and Bland 1973).

Myeloma.
A tumour composed of cells derived from haemopoetic tissues of the bone marrow. Phalen (1966) reported 4 cases suffering from myeloma out of 439 CTS sufferers (1%).

Hypertension.
Posch and Marcotte (1976) and Cannon reported between 7-10% of populations of patients presenting with CTS also suffered from hypertension (high arterial blood pressure), no account of their medication was reported.

Emara and Saadah (1988) reported three cases of hypertensive men, being treated with beta-blockers, and suffering from CTS. The symptoms of CTS were completely alleviated by withdrawal of the beta-blockers, suggesting drug induced CTS, although the mechanism of drug involvement was not fully understood.

Renal Failure.
Patients on renal dialysis have been reported to suffer from CTS by various authors, between 4 and 12% of renal dialysis patients had CTS in at least one hand (Gilbert et al. 1988; Kenzora et al. 1978; Delmez 1982; and Spertini et al. 1984).

There is wide variation in the prevalence of CTS in patients undergoing renal dialysis. Kenzora et al. (1978) and Delmez (1982) agreed that the prevalence rate was 40-50 per thousand at risk. This rate was found to be greater by Spertini et al. (1984) and Halter (1981) where the prevalence rate was 120 and 310 per thousand at risk respectively. The reason for this discrepancy is unclear. The studies reporting greater prevalence rates used smaller numbers of subjects.
Whatever the prevalence rate, there is general agreement that the presence of arterial fistulae contribute to the occurrence of the CTS in patients undergoing renal dialysis (Kenzora 1978; Delmez 1982).

_Haemophilia._

A disorder of the blood, characterised by the permanent tendency to hemorrhage, caused by the deficiency of factor VII (haemophilia A) or factor IX (haemophilia B).

Moneim and Gribble (1984) reported a case study of a factor IX deficient haemophiliac, who contracted CTS. Infusion of factor IX resulted in complete recovery from CTS. It was mentioned that CTS in haemophiliac patients could be completely resolved by replacement therapy and splinting. However, it was stated that if no response occurred within a few days, the median nerve should be examined surgically. Indeed, Moneim and Gribble (1984) reported the first carpal tunnel decompression operation in the English literature, on another haemophiliac.

_Gout._

This metabolic disorder is characterised by raised blood uric acid levels, resulting in acute and then chronic arthritis. Case studies of patients suffering from CTS caused by gout have been reported by Ogilvie and Kay (1988) and Grossman et al. (1961). In both cases the carpal tunnel was decompressed surgically and gouty deposits were discovered.

The number of CTS patients also suffering from gouty arthritis reported by Yamaguchi et al. (1965) was 6 (0.49%). Phalen (1966) reported 0.3% of the CTS population also suffered from gout.
Sex.

Females are more likely to develop CTS than males. Studies analysing CTS patients presenting at clinics, have found that females usually make up between 53-69% of the cases, with a mean of 63% and a standard deviation of 6.4 (Ragi 1981; Posch and Marcotte 1976; Phalen 1966; Graham 1983; Dekel et al. 1980; Yamaguchi et al. 1965; and Tountas et al. 1987). These figures only represent the proportion of females presenting at certain clinics. They by no means represent the true male : female ratio of CTS patients in the population.

In a study of patients consulting General Practitioners with CTS the male to female ratio was found to be 1 : 3.7 (RCGP 1986). The results are given in table 1.3. It is interesting to note that the ratio is less for the younger age group and higher than the mean in the old age group, this reflects the effect of the menopause on the syndrome. However, over the whole population the number of females with the condition seems to out number the number of males. Over 80% of sufferers are female according to the RCGP et al. (1986) report. There are 4 times as many female sufferers as males.

Menopause.

The termination of menstrual life. Posch and Marcotte (1976) reported that menopausal symptoms were present in 6% of the patients presenting with CTS, this was attributed to many of the patients being in the 40-50 years age group (28% of females). 85% of the CTS patients reviewed by Yamaguchi et al. (1965) were older than 45 years of age. It would be interesting to know the proportion of females in this age group, it was only reported that 65% of the total population were female.

Vitamin B6 deficiency.

Vitamin B6 deficiency has been reported to have been associated with CTS. However, Amadio (1987) stated that vitamin B6 was not likely to be a significant cause of CTS. This was confirmed later by (Turner 1989). There was no significant difference in the
vitamin B6 status of a pair match group of 34 cases and controls.

**Congestive Heart Failure.**

Mandawat (1985) reported a case study where fluid accumulation due to congestive heart failure was the cause of CTS. The symptoms were relieved by treatment of the congestive heart failure.

**Pregnancy.**

There is disagreement in the literature as to the extent at which pregnant women suffer from CTS. Ekman-Ordeberg et al. (1987) and Goni et al. (1987) both report about 2.5% of women developed CTS during pregnancy. Gould and Wissinger (1978) and Voitk et al. (1983) found the value to be ten times greater (about 25%).

There is agreement that the symptoms usually improve after delivery and so the treatment of the CTS tends to be conservative for pregnant women. The reason for the increased number of sufferers in this particular population is a result of the increased generalised oedema suffered by expectant mothers (Ekman-Ordeberg et al. 1987).
1.6.2 Local Conditions Associated with CTS.

Madlungs deformity.

Radio-ulnar subluxation due to curvature of the lower extremity of the radius.

A case study was reported by Luchetti et al. (1988) where a patient suffering from madlungs deformity also developed CTS. Release of the carpal tunnel was performed, but consideration had to be made for the bow stringing of the tendons afterwards.

Osteoid-Osteoma of the Capitate.

Herndon et al. (1974) reported a case study where osteoid-osteoma of the capitate was responsible for the CTS symptoms. This rare neoplasm, which decreased the volume available for the contents of the carpal tunnel to run through, was removed and the flexor retinaculum released, resulting in full relief from the symptoms of CTS.

Tenosynovitis.

Inflammation of the tendon and tendon sheath surrounding it commonly occurs in populations of patients with CTS. Various authors have reported that patients suffering from CTS also have evidence of tenosynovitis (Posch and Marcotte 1976 (15%); Phalen 1966 (22%); and Doyle and Carroll 1968 (37%)).

It has been stated that inflamed tendons and tendon sheaths in the carpal tunnel are prominent factors in the production of the symptoms of CTS (Doyle and Carroll 1968). It is interesting to note that CTS is not a prescribed disease. However, tenosynovitis is (HSE 1985) and may result in CTS.

The inflammation of the flexor tendon sheath will result in an increase in the volume of the contents of the carpal tunnel. This will result in pressure on the median nerve and
hence the symptoms of CTS.

Rheumatoid Arthritis.
This chronic systemic condition results in a thickening of the articular soft tissue, with the extension of synovial tissue over the articular cartilages. When the condition occurs at the wrist there is the possibility that compression of the median nerve may occur as a result of the thickening of the articular soft tissue.

Between 7 and 12% of patients presenting with CTS have been reported to suffer from rheumatoid arthritis as well (Doyle and Carroll 1968; Posch and Marcotte 1976; Phalen 1966 and Yamaguchi et al. 1965). It was also suggested by Phalen (1966) that rheumatic conditions affecting the wrist were more common in females and could account for the CTS occurring more frequently in females.

Wrist Trauma.
Local trauma to the wrist may take many forms. One of the most common injuries and most important in terms of compression or damage to the median nerve is the Colles fracture (fracture of the distal head of the radius, or fracture of the carpal bones.)

Local trauma to the wrist has been reported in between 5 and 16% of patients presenting with CTS (Doyle and Carroll 1968; Posch and Marcotte 1976; and Phalen 1966). Aro et al. (1988) reported that 8% of patients suffering from colles' fracture also suffered from CTS, this coincided with radial collapse in 85% of patients suffering from CTS after colles fracture.

Other authors have reported higher percentages of CTS patients also suffering from trauma to the wrist, Rietz and Onne (1967) reported 44% of 65 cases with CTS also had colles fracture. Immobilisation should be in the functional position after colles fracture.
in order to avoid later median nerve compression.

**Ganglionic Cysts.**
A cyst containing fluid within fibrous tissue attached to the tendon sheath of the hand, may result in an increase in the contents of the carpal tunnel leading to compression of the median nerve. Posch and Marcotte (1976); Doyle and Carroll (1968); and Yamaguchi et al. (1965) reported ganglionic cysts in 2-7.5% of patients with CTS. Ganglionic cysts have even been imaged using MRI in patients with CTS (Binkovitz et al. 1988).

**Lipoma of the flexor tendon sheath.**
Lipomas arise from adipose tumours comprised of mature fat cells. A case study of this rare condition was reported by Kremchek and Kremchek (1988). Compression of the median nerve was caused by a 4.5 x 2 x 3 cm tumour. This was excised from the flexor tendon sheath within the carpal tunnel, resulting in complete relief of the CTS symptoms.

**Hand sizes and dimensions.**
Various dimensions including hand length, palm width, and many wrist dimensions were compared between cases and controls by Armstrong and Chaffin (1979). Differences in hand dimensions were not found between cases and controls.

Other studies have examined the shape of the wrist in an attempt to categorise those individuals who are anatomically at risk to CTS. It was suggested by Gordon et al. (1988) that those with a wrist ratio (depth / width) of less than 0.7, were more likely to develop CTS. These results require confirmation before they should be used.
1.7 Diagnostic Tests.

Various diagnostic tests have been used in the diagnosis of CTS. The search for a test which can be used simply and easily by a GP, with a high degree of validity, has eluded physicians for many years. Some tests have been developed which may be carried out in the General Practitioners surgery (Phalen's test, Tinel's sign, and the Tourniquet test), others require a specialist to administer them (Thermography, Tests of Sensibility, Electrophysiological Tests).

The following section describes a method of evaluating the validity of these tests. Measures of how efficiently the tests can identify diseased and non-diseased individuals are described. The validity of each of the tests available to the physician are assessed on this basis, using the data available in the literature.

Information on the validity of these tests is available from two sources;

i. Retrospective studies: which have analysed a large population of patients with CTS, on whom the test in question was known to have been carried out and the results documented. These studies lack data from control individuals and in some cases confirmation of diagnosis by methods known to have the best validity.

ii. Case-controls studies: designed to examine the validity of the test. The test is administered to a group of diseased and non-diseased individuals (the cases and controls respectively) and the validity of the test assessed. This is considered to be the most definitive source of data for the validation of tests. It allows the investigator to assess how accurately the test can identify diseased individuals, as well as how effectively non-diseased individuals may be identified.
1.7.1 Assessment of Accuracy or Validity.

Sensitivity and specificity are measures of the accuracy of a test. They are usually determined by administering the test on a group of diseased and non-diseased individuals, and then comparing the results. Positive tests on diseased individuals are termed "true positives"; and non-diseased "false positives". Negative results from diseased individuals are termed "false negatives"; and non-disease "true negatives" as in table 1.6.

<table>
<thead>
<tr>
<th>Test</th>
<th>Disease</th>
<th>Non-Diseased</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>A (true positives)</td>
<td>B (false positives)</td>
</tr>
<tr>
<td>Negative</td>
<td>C (false negatives)</td>
<td>D (true negatives)</td>
</tr>
<tr>
<td>Totals</td>
<td>A + C</td>
<td>B + D</td>
</tr>
</tbody>
</table>

Sensitivity (%) = \( \frac{A}{A + C} \times 100 \) = true positive \times 100 (equation 1.1)

Specificity (%) = \( \frac{D}{B + D} \times 100 \) = true negatives \times 100 (equation 1.2)

(Lilienfield and Lilienfield 1980 p151)
By definition:

Sensitivity is expressed as a percentage of those who have the disease, and are so indicated by the test (equation 1.1).

Specificity is expressed as the percentage of those who do not have the disease and are so indicated by the test (equation 1.2).

The ideal test would have a sensitivity of 100% and specificity of 100%. In practice this very rarely occurs, there often has to be a compromise between either the sensitivity or the specificity of the test. Tests with high sensitivity are useful if the examiner wishes to identify diseased individuals (those who have a certain condition). Those tests with high specificity are useful if the examiner wishes to include only non-diseased individuals (those without the condition tested for). This dilemma is often encountered by physicians so a battery of tests is usually employed.
1.7.2 The Flick Test.

The flick test involves the examiner asking the patient presenting, "what exactly do you do with your hand(s) when the symptoms are at their worst?" (Pryse-Phillips 1984). If the patient reports that they shake their arm along side their body; then a positive flick test may be noted. Usually only levels of sensitivity can be investigated for the flick test, since non-diseased individuals would not report any symptoms and would therefore have no need to relieve the symptoms by shaking the hand. Subjects who reported being awakened by numbness and tingling in their hands, but were not found to be suffering from CTS were studied by DeKrom et al. (1990). A specificity value was calculated (table 1.7) on the basis of true negative results (those reporting negative flick test), divided by all those who had normal electrodiagnostic results, from the population reporting to be awakened by the numbness and tingling. However, the Dekrom et al. (1990) study phrased the questions differently to other studies. The patient was asked if flicking movements with the wrist and fingers eliminated the symptoms in the hand. This may have introduced bias into the study by suggesting a method of symptom relief. The original flick test was dependent on the subject recalling what they actually did when the symptoms were at their worst.

<table>
<thead>
<tr>
<th>Author</th>
<th>Sensitivity</th>
<th>No. cases</th>
<th>Specificity</th>
<th>No. controls</th>
<th>Diff</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pryse-Phillips 1984</td>
<td>93%</td>
<td>212</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Turner 1989</td>
<td>15%</td>
<td>34</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DeKrom et al. 1990</td>
<td>50%</td>
<td>44</td>
<td>61%</td>
<td>49</td>
<td>ns</td>
</tr>
</tbody>
</table>

A positive flick test has often been reported in the literature to occur in patients with
CTS (Ragi 1981; and Phalen 1966), although no levels of sensitivity were reported. In a study attempting to validate the flick test, Pryse-Phillips (1984) reported a 93% sensitivity for the test. The patients numbered 212 with confirmed CTS using electrophysiological tests (DML >4.5 ms). In contrast Turner (1989) found a sensitivity of only 15% in 34 patients, with electrophysiologically confirmed CTS (DML >5 ms).

DeKrom et al. (1990) also attempted to validate the flick test, a sensitivity of 50% was found for the 44 patients in the study. The lower sensitivity of the test found in the final two papers in table 1.7 casts serious doubt on the validity of the flick test. The specificity of 61% found by DeKrom et al. (1990) suggests serious problems with the test, almost half of the individuals without CTS were diagnosed as having it using this method. There was no significant difference between the results of the cases and controls, further fuelling doubts about the test.
1.7.3 Tinel’s Sign (The Percussion Test).

The examiner lightly taps the skin over the median nerve at the wrist. A positive sign is signified by the occurrence of "pins and needles" or small electric shocks in the median nerve distribution of the hand with each tap.

Although Jules Tinel has the honour of having his name associated with this test, he was not actually responsible for a test specifically for CTS. He did describe a phenomena which he called "fourmillement" after gentle tapping on a damaged nerve (Tinel 1915). The sensation literally translated meant the "swarming of ants", this was considered to be a sign of axon regeneration in peripheral nerves. Phalen (1966) reported it as a test for CTS. The nature of the test would suggest that a more appropriate name would be the percussion test, however it will be referred to here as the Tinel's sign.

Studies on large populations of CTS patients have tended to consider Tinel's sign as a useful indicator for CTS, but there is a wide range of sensitivity values, from 44–73% (Dekel et al. 1980 52%; Loong 1977 44%; Phalen 1966 73%; Stevens et al. 1988 55%; Szabo et al. 1984 61%; and Tanzer 1959 65%). These results are confounded by the low numbers of cases in some studies (Szabo et al. 1984 and Tanzer 1959); poor diagnostic criteria without the use of electrophysiological data (Phalen 1966; Tanzer 1959) and inconsistent application of the technique. The examiners would have used a different technique for the test, which may produce invalid results. The sensitivity of Tinel's sign reported by these studies on populations of CTS patients are higher than those of the case-control studies (mean 58 and 41.8% respectively; table 1.8). The case-control studies were better controlled than the retrospective studies mentioned earlier.

With the exception of Bowles et al. (1983) (who's number of cases were too small and will therefore not be considered in any further discussion) all of the case-control studies considered Tinel's sign to be of no diagnostic value. Mossman and Blau (1987)
commented that the failure of the Tinel's sign in detecting CTS may have been due to poor procedure by the examiner. They went further in suggesting that the best method of performing the test was by using a broad based Queen Square reflex hammer. Although this produced a sensitivity of 79%, it needs confirmation by other studies.

Table 1.8 Tinel's sign:- Sensitivity and Specificity in Case-Controls Studies.

<table>
<thead>
<tr>
<th>Author</th>
<th>Sensitivity</th>
<th>No. cases</th>
<th>Specificity</th>
<th>No. controls</th>
<th>Diff</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stewart and Eisen</td>
<td>45%</td>
<td>51</td>
<td>71%</td>
<td>52</td>
<td>ns</td>
</tr>
<tr>
<td>Gelmers</td>
<td>42%</td>
<td>47</td>
<td>75%</td>
<td>43</td>
<td>ns</td>
</tr>
<tr>
<td>Gellman et al.</td>
<td>44%</td>
<td>66</td>
<td>94%</td>
<td>50</td>
<td>ns</td>
</tr>
<tr>
<td>Golding et al.</td>
<td>25%</td>
<td>39</td>
<td>20%</td>
<td>71</td>
<td>ns</td>
</tr>
<tr>
<td>Seror</td>
<td>63%</td>
<td>100</td>
<td>55%</td>
<td>40</td>
<td>ns</td>
</tr>
<tr>
<td>Mossman and Blau</td>
<td>79%</td>
<td>33</td>
<td>84%</td>
<td>28</td>
<td>ns</td>
</tr>
<tr>
<td>#</td>
<td>49%</td>
<td>33</td>
<td>84%</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>DeKrom et al.</td>
<td>25%</td>
<td>44</td>
<td>59%</td>
<td>49</td>
<td>ns</td>
</tr>
<tr>
<td>Mean Values</td>
<td>41.8%</td>
<td></td>
<td>65.4%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(+ Using reflex hammer; # Using finger tapping.)

All of the case-control studies in table 1.8 used electrophysiological tests to confirm the diagnosis of CTS (all used a DML > 4.5 ms; except Seror (1987) who used a DML of > 4 ms). The lower DML threshold used by Seror (1987) could explain the higher sensitivity found compared with the other studies in table 1.9. The application of Tinel's sign was carefully controlled and standardised by the examiners. This careful application of the test would invalidate the Mossman and Blau (1987) claim that the test was applied incorrectly by some examiners. In a letter to the editor of the Journal of Hand Surgery, Clark (1988) suggested that this poor technique was the reason for the low sensitivity results by Seror (1987). In reply Seror confirmed that the technique was carried out by a variety of physicians. However, the very fact that there is confusion in
the literature about the method of application of Tinel's sign puts its validity in question. The low mean sensitivity (41.8%) confirms this apprehension. None of the studies found a significant difference between the cases and controls for a positive Tinel's sign.

The specificity ranged from 20-94% with a mean of 65.4% (table 1.8). The test was not specific enough to be of value as a diagnostic test. The mean specificity in the literature suggests that over one third of those tested without the disease would be identified as having the disease by the test. This is clearly an unacceptable figure, considering that the treatment often involves surgery.
1.7.4 Phalen's Test (Wrist Flexion Test).

A wrist flexion test was first reported by Phalen in 1951, a similar test was later reported by Cozen in 1963. Cozen performed the test with patient seated, elbows extended and the wrists forcibly flexed by the patient pressing down on the seat of the chair. This was held for a "few minutes" when the patient would invariably have reproduction of the symptoms of CTS. Phalen himself indicated in 1966, when actually reporting the results his own wrist flexion test, that the symptoms would be produced in a normal subject if held long enough. It is not surprising that Cozen (1963) managed to produce the symptoms of CTS "invariably", but no statistical evidence was reported to validate the test.

<table>
<thead>
<tr>
<th>Author</th>
<th>Sensitivity</th>
<th>No. cases</th>
<th>Specificity</th>
<th>No. controls</th>
<th>Diff</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dekel et al.</td>
<td>73%</td>
<td>42</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phalen</td>
<td>74%</td>
<td>515</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Szabo et al.</td>
<td>70%</td>
<td>23</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gellman et al.</td>
<td>71%</td>
<td>63</td>
<td>80%</td>
<td>50</td>
<td>ns</td>
</tr>
<tr>
<td>Golding et al.</td>
<td>10%</td>
<td>39</td>
<td>86%</td>
<td>71</td>
<td>ns</td>
</tr>
<tr>
<td>Mossman and Blau</td>
<td>33%</td>
<td>27</td>
<td>82%</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>DeKrom et al.</td>
<td>47%</td>
<td>44</td>
<td>53%</td>
<td>47</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Mean values</strong></td>
<td><strong>54%</strong></td>
<td></td>
<td><strong>75.25%</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Phalen (1966) described a more refined wrist flexion test as follows; "The patient is asked to hold the forearm vertically and to allow both hand to drop into complete flexion at the wrist for approximately one minute." (Phalen 1966). A positive result was recorded if the symptoms of CTS occurred within the duration of the test. The basis of the test was that the pressure on the median nerve in the carpal tunnel would be
increased during extreme wrist flexion. The test was designed to briefly increase the compression of the median nerve at the wrist. In subjects who already have an increased compression, as in CTS patients, the symptoms of median nerve compression would manifest themselves more readily than in normal subjects.

The sensitivity of Phalen's test reported from populations of individuals suffering from CTS suggests that the test has a sensitivity of between 70–74% (Phalen (1966); Dekel et al. (1980); and Szabo et al. (1984)). No record of specificity could be determined from these data, so the results are of limited use.

The case-control study data clarifies the situation. The case-control studies (the final four studies in table 1.9) used DML of >4.5 ms to diagnose CTS. Gellman et al. (1986) agreed with the sensitivity of the studies of Phalen (1966); Dekel et al. (1980) and Szabo et al. (1984), reporting a sensitivity of 71% (table 1.9). However, lower sensitivities were reported by Golding et al. (1986); Mossman and Blau (1987); and DeKrom et al. (1990), suggesting that the sensitivity of Phalen's test was lower than that reported earlier. The mean sensitivity of all of the studies was only 54%, although the later case-control studies suggest that the true figure could be still lower this.

The specificity of the test ranged from 53–86% in the case-control studies. A mean of 75% suggests that the test had a higher specificity than the Tinel's sign, but 25% of normal subject may have a positive Phalen's test. This is still quite a high percentage.
1.7.5 The Tourniquet Test.

A pneumatic blood pressure cuff is inflated around the arm, proximal to the elbow, to a pressure higher than the patient's systolic blood pressure. If the symptoms of numbness and tingling occur within a minute in the median nerve distribution, a positive result is recorded. Gilliatt and Wilson (1953) investigated this test on a group of normal individuals and on those suspected of suffering from CTS. No confirmation of the CTS diagnosis was available. The results were vague, subjective and the rather optimistic and should be treated with caution.

Table 1.10 Tourniquet Test: Sensitivity and Specificity.

<table>
<thead>
<tr>
<th>Author</th>
<th>Sensitivity</th>
<th>No. cases</th>
<th>Specificity</th>
<th>No. controls</th>
<th>Diff</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tanzer 1959</td>
<td>29%</td>
<td>20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dekel et al. 1980</td>
<td>50%</td>
<td>26</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Szabo et al. 1984</td>
<td>83%</td>
<td>23</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gellman et al. 1986</td>
<td>65%</td>
<td>65</td>
<td>60%</td>
<td>50</td>
<td>ns</td>
</tr>
<tr>
<td>Golding et al. 1986</td>
<td>21%</td>
<td>39</td>
<td>87%</td>
<td>71</td>
<td></td>
</tr>
<tr>
<td>DeKrom et al. 1990</td>
<td>82%</td>
<td>44</td>
<td>84%</td>
<td>47</td>
<td>ns</td>
</tr>
<tr>
<td>Mean values</td>
<td>52%</td>
<td></td>
<td>77%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The sensitivity measures for the tourniquet test on populations of CTS patients are poor (Dekel et al. (1980) 50%; Szabo et al. (1984) 70%; Tanzer (1957) 29%; table 1.10). These poor sensitivity measures could be a result of inadequate technique or recording of results (most of the studies were carried out retrospectively). However, the prospective case-control studies by Gellman et al. (1986); Golding et al. (1986); and DeKrom et al. (1990) have shown not only that the sensitivity of the test was poor (52%), but also the specificity as well. An average specificity of 77% was found in the case control studies. Almost 25% of individuals without the disease would be diagnosed as having CTS using
this test. The tourniquet test thus lacks the sensitivity or specificity to be a useful diagnostic sign.
1.7.6 Semmes-Weinstein Monofilament Test.

This pressure test for sensibility is performed on each of the digits using the Semmes-Weinstein monofilament. The monofilament is applied perpendicularly to the palmar digital surface and the pressure increased until the monofilament begins to bend. A positive response is recorded when the subject, with eyes closed, can verbally identify which digit was receiving the pressure. This pressure is then noted. The normal range corresponds to 0.0045 to 0.068 grams of force (Szabo et al. 1984).

There is agreement in the literature about the sensitivity of the Semmes-Weinstein monofilament test, Szabo et al. (1984); Gellman et al. (1986); and Koris et al. (1990) all found the sensitivity to be greater than 82% (average 85%; table 1.11). The former two papers used the standard test method mentioned earlier, but Koris et al. (1990) used a combination of the wrist flexion test and the Semmes-Weinstein monofilament test.

The specificity of the test was also good. Koris et al. (1990) found the specificity of the test to be better in combination with the wrist flexion, indeed the combination test had higher sensitivity and specificity than the wrist flexion test alone and more specific than the Semmes-Weinstein monofilament test alone.

The high sensitivity of the test meant that it was ideal for use as a screening tool, but should be combined with electrophysiological tests if used for diagnosis (Gellman et al. 1986).

1.7.7 Thermography.

Thermography involves the infrared imaging of subjects hands and then a subjective assessment of the images is made with respect to temperature differences on the skin surface. Abnormal thermograms were considered to be those which were 2.5 sd outside the normal range (So et al. 1989). This test has not been used solely for CTS. Clinicians
have attempted to adapt it for use with CTS.

Sensitivity values vary from 55 to 100% (So et al. (1989) and Herrick and Herrick (1987) respectively). The 100% sensitivity reported by Herrick and Herrick (1987) must be in doubt because of the inherent problems of thermographic studies, such as the subjective analysis of the images. There is more agreement on the specificity of the test (90 to 97% for So et al. (1989) and Herrick and Herrick (1987) respectively; table 1.11).

1.7.8 The Two Point Discrimination Test (2PD).

The 2PD test is a test of sensibility administered using a pair of callipers. The distance between the points of the callipers is set, they are then pressed against the skin and the patient asked how many points can be felt. If the minimum distance between the two points of the callipers, at which the patient can just perceive two points, is greater than 6 mm, the test is considered positive.

The test does not give high values of sensitivity 22 to 55% (Gellman et al. 1986; Szabo et al. 1984; and Rietz and Onne 1967). The only case-control study addressing 2PD test and CTS reported a specificity of 100% (Gellman et al. 1986). More work is required on this test to confirm the results.

1.7.9 Vibrometry.

Vibration frequencies of 8-500 Hz are applied at various amplitudes to the finger tips of subjects. The techniques of vibrometry testing vary and the positive test criteria may also vary from study to study. For example, some studies increase the amplitude of the vibration whereas others alter the vibration frequency. The different techniques are not
discussed any further here.

Considering the differences in test criteria Lundborg et al. (1986) and Szabo et al. (1984) reported surprisingly similar levels of sensitivity, 83 and 87% respectively (table 1.11). The specificity of the Lundborg et al. (1986) study on subjects not showing electrophysiological abnormalities were not as good (46%).
Table 1.11 Sensitivity and Specificity of the Semmes-Weinstein Monofilament, Two Point Discrimination tests, Thermography and Vibrometry.

### The Semmes-Weinstein Monofilament test.

<table>
<thead>
<tr>
<th>Author</th>
<th>Sensitivity</th>
<th>No. cases</th>
<th>Specificity</th>
<th>No. controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Szabo et al.</td>
<td>83%</td>
<td>23</td>
<td>80%</td>
<td>50</td>
</tr>
<tr>
<td>Gellman et al.</td>
<td>91%</td>
<td>67</td>
<td>86%</td>
<td>30</td>
</tr>
<tr>
<td>Koris et al.</td>
<td>82%</td>
<td>33</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean value</td>
<td>85.3%</td>
<td></td>
<td>83%</td>
<td></td>
</tr>
</tbody>
</table>

### Thermography.

<table>
<thead>
<tr>
<th>Author</th>
<th>Sensitivity</th>
<th>No. cases</th>
<th>Specificity</th>
<th>No. controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herrick &amp; Herrick</td>
<td>100%</td>
<td>55</td>
<td>97%</td>
<td>35</td>
</tr>
<tr>
<td>So et al.</td>
<td>55%</td>
<td>22</td>
<td>90%</td>
<td>20</td>
</tr>
<tr>
<td>Mean values</td>
<td>77.5%</td>
<td></td>
<td>93.5%</td>
<td></td>
</tr>
</tbody>
</table>

### Two Point Discrimination Test.

<table>
<thead>
<tr>
<th>Author</th>
<th>Sensitivity</th>
<th>No. cases</th>
<th>Specificity</th>
<th>No. controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rietz and Onne</td>
<td>55%</td>
<td>65</td>
<td>100%</td>
<td>50</td>
</tr>
<tr>
<td>Szabo et al.</td>
<td>22%</td>
<td>23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gellman et al.</td>
<td>33%</td>
<td>67</td>
<td>100%</td>
<td>50</td>
</tr>
<tr>
<td>Mean values</td>
<td>36.7%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Vibrometry.

<table>
<thead>
<tr>
<th>Author</th>
<th>Sensitivity</th>
<th>No. cases</th>
<th>Specificity</th>
<th>No. controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lundborg et al.</td>
<td>83%</td>
<td>53</td>
<td>46%</td>
<td>26</td>
</tr>
<tr>
<td>Szabo et al.</td>
<td>87%</td>
<td>23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean values</td>
<td>85%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
1.7.10 Other Tests of Sensibility.

Sensibility tests such as the 2PD test and the Semmes-Weinstein monofilament test do not directly relate to the functional aspects of tasks which are affected by a reduced sensibility. These tasks include tactile inspection of objects for protrusion or differences in the smoothness of surfaces in manufacturing industry, or indeed the ability to perform the day to day activities involving the tactile sense around the house. These are problems faced by many sufferers of CTS.

Radwin (1990) developed a test which did relate to these tactile qualities reported in the manufacturing industry. The equipment used was a Ridge Aesthesiometer, consisting of two rotating teflon discs. A ridge produced at the interface of the discs could be expanded or contracted during the test. The subject placed the distal phalangeal pad of the index finger against the rotating disc. A response was made when the ridge could just be perceived by the subject as rising. This rising threshold ridge size was then recorded and the ridge size reduced until the subject could no longer perceive the ridges presence. This ridge size was termed the falling threshold.

On a group of 13 normal subjects, the average ridge detection threshold was 0.09 mm (S.D. 0.07 mm), this was compared with a group of 12 CTS patients who had an average ridge threshold of 0.20 mm (S.D. 0.18 mm). There was a significant difference between the two groups for this ridge threshold (p<0.001). However, the standard deviations of both groups were high. This casts doubt on the validity of the test conclusion. The test needs examination to establish measures of sensitivity and specificity before it can be used further.
1.7.11 Electrophysiological Tests.

Electrophysiological tests can be divided into two groups. Those which test motor function of the nerve supply and those which test the sensory function. Normal ranges of these tests have been obtained from populations of control individuals. The important factor about electrophysiological testing, is that it can determine the point of neurological dysfunction. Other tests are not capable of this.

**Tests for Motor Function of the Median Nerve.**

The distal motor latency (DML) and nerve conduction velocity (NCV) may be measured by placing an active electrode over the belly of the abductor pollicis brevis muscle. This records the action potential in the muscle when stimulated by a nerve impulse. An inactive electrode is placed just proximal to the metacarpal joint. The nerve may be stimulated at a number of sites up the arm, Kimura (1983 p106) identified five such sites for the median nerve, although only two will be considered here.

i. For stimulation at the wrist the cathode is usually placed 3 cm proximal to the distal wrist crease on the volar surface. The anode is located 2 cm proximal to the cathode.

ii. At the elbow; stimulation is provided by the cathode placed in the cubital fossa, again the anode is 2 cm proximal to the cathode.

The latency is the time (usually measured in milliseconds) from the nerve stimulus to the response of the muscle monitored by the recording electrode. This latency consists of two components;

i. The nerve conduction from the stimulus point to the nerve terminal.

ii. The neuromuscular transmission time, including the time required for the muscle membrane to depolarise.

When measuring the DML (the latency from a point 3cm proximal to the distal wrist
crease) the measure stated includes both components of the latency measurement. It would not be possible to separate the two components when only one measure is recorded. However, if the latency at two points is measured, it is possible to remove the neuromuscular transmission part of the latency. Since the muscular component will exist in both measures, by subtracting one latency from another, the common element may be removed.

Dividing the length of nerve between the two points of stimulation, by the difference in latency, the NCV may be calculated (Kimura 1983 p89). Accurate determination of the NCV is important for useful results in tests of nerve function. The NCV allows the examiner to evaluate the nerve, in an area known to be free from compression. If the nerve in this region functions within the normal range, it is clear that any prolonged latency discovered at the wrist will be due to a neuropathy there and not a more general problem affecting other parts of the nervous system.

Thus two measures of motor function can be determined;

i. A measure at the wrist, including the nerve conduction time and the neuromuscular transmission time to test for areas of compression.

ii. The NCV to test the functioning of the nerve.

Tests for the Sensory Fibres.

When measuring the distal sensory latency (DSL) the stimulating electrode is still positioned 3cm proximal to the distal wrist crease. The distal potentials are recorded with ring electrodes, placed around the proximal and distal interphalangeal joints of either the second or third digit. The lateral side of the fourth digit may also be used. Errors may be incurred if the ulnar nerve is inadvertently stimulated by spreading of the current at the wrist.
Unlike the measurement of motor function, where a muscle action potential will be the same regardless of the site of stimulation, the amplitude of the sensory tests is significantly smaller with the proximal stimulation compared with the distal stimulation (Kimura 1983 p107). So the positioning of the electrodes is important. The amplitudes are also small compared with those of motor tests. There may also be partial extinguishing of the impulse by naturally occurring sensory impulses. Therefore averaging is often used to obtain a measurement of the DSL.

The ability to selectively stimulate the sensory fibres at exact points on the nerve, allowed Kimura (1979) to measure the DSL in steps of 1cm from a point proximal to the flexor retinaculum, to a point distal to the flexor retinaculum. The sensory latencies were measured at every 1cm along the length of the nerve. In normal subjects the latency increased linearly as the stimulus site was moved distally over the flexor retinaculum. However, in a patient with CTS there was an increase in latency in the area of the flexor retinaculum. The latencies at each point could be determined by the subtraction techniques mentioned in the previous section. This latency change was found to be four times greater in the region of the CT than in the adjoining proximal and distal regions. Thus the point of compression could be determined accurately in the patient.
The Normal Ranges for the Electrophysiological Tests.

The normal ranges for electrophysiological tests have been established by various authors (Thomas et al. 1967; Melvin et al. 1973; Felsenthal 1977; and Kimura 1983). The values in table 1.12 are those obtained by Kimura (1983 p.109) in a study of 122 median nerves of 61 patients, with no apparent neurological disease of the peripheral nerves. The median nerves tested were all stimulated at the wrist.

Table 1.12 Normal ranges for median nerves collected by Kimura (1983). Values are expressed as means ± standard deviation.

<table>
<thead>
<tr>
<th></th>
<th>Amplitude</th>
<th>Latency (ms)</th>
<th>Conduction Velocity (m/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor Fibres</td>
<td>7.0 ± 3.0 mV</td>
<td>3.49 ± 0.34 (4.2)</td>
<td>57.7 ± 4.9 (48)</td>
</tr>
<tr>
<td>Sensory Fibres</td>
<td>38.5 ± 15.6 μV</td>
<td>2.89 ± 0.34 (3.5)</td>
<td>56.2 ± 5.8 (44)</td>
</tr>
</tbody>
</table>

1 (Upper limits of the normals) calculated as mean + 2 standard deviations.
2 (Lower limits of the normals) calculated as mean - 2 standard deviations.

These normal ranges allow us to establish acceptable limits for normal median nerves. These are usually the mean + 2 standard deviations for the distal latencies and the mean - 2 standard deviations for conduction velocities. Therefore an abnormal DML would be >4.2 ms; and an abnormal DSL would be >3.5 ms, when stimulated at the wrist.

Once these normal ranges have been established measures of sensitivity and specificity may then be calculated. Melvin et al. (1973) did just this. The sensitivity and specificity
for 12 variables were calculated from a group of 24 normal volunteers and 17 patients suffering for CTS. The DSL was found to be the best measure for identifying those individuals with CTS. Table 1.13 gives the sensitivity and specificity for three of the variables under investigation, (These were the DML, DSL and the nerve conduction velocity.).

Table 1.13 Sensitivity and Specificity of the electrophysiological tests. (From Melvin et al. 1973)

<table>
<thead>
<tr>
<th>Test</th>
<th>No. of cases</th>
<th>Sensitivity</th>
<th>No of controls.</th>
<th>Specificity</th>
<th>Diff.</th>
</tr>
</thead>
<tbody>
<tr>
<td>DML</td>
<td>17</td>
<td>76%</td>
<td>24</td>
<td>100%</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>DSL</td>
<td>17</td>
<td>100%</td>
<td>24</td>
<td>92%</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>NCV</td>
<td>17</td>
<td>35%</td>
<td>24</td>
<td>100%</td>
<td>p&lt;0.05</td>
</tr>
</tbody>
</table>

Table 1.13 shows that there were significant differences between the cases and controls for the DML and NCV tests, when analysed using an analysis of variance. These tests give very high values (100%) for specificity and so are highly suited to identifying those individuals who do not have the disease in question. The high sensitivity of the DSL means that it is highly suited to identifying those individuals who do have the disease. Indeed, the combination of high sensitivity and specificity has made the DSL the most favoured test in the literature and medical institutions alike (Melvin et al. 1973; Loong 1978; Bhala and Toppil 1981; Di Benedetto et al. 1986; Johnson et al. 1987; and Albers 1990).

Even though these authors have found DSL to be the most useful diagnostic test there
are occasionally errors when using these tests. Indeed, the sensitivity values obtained by Melvin et al. (1973) were only from a small population. Other authors have found patients to have CTS and have treated the condition surgically, even with a normal electrophysiological test (Grundberg 1983). The explanation for this is unclear. The electrophysiological tests could have been carried out incorrectly or the temperature of the patients limbs was not carefully controlled. Another possibility is the presence of abnormalities in the nerve supply. Median-Ulnar nerve communications, such as Martin Gruber anastamoses have been reported in the literature as being responsible for incorrect electrophysiological tests (Iyer and Fenchell 1976; and Guttman 1977). Also the median nerve may have abnormal branches by-passing the carpal tunnel (Taleisnik 1978; and Lanz 1977).

However, it is now widely accepted the electrophysiological tests, particularly the DSL give the most accurate account of the condition, allowing the examiner to identify the exact area of compression. This is something which other methods do not allow.
In summary, there are many tests for CTS now available to the physician. The sensitivity and specificity of some of these tests are however inadequate for them to be used independently in the diagnosis of the condition. Suspicions of CTS derived by these simpler tests must be confirmed by electrophysiological testing before the final diagnosis is made. Indeed as mentioned earlier most physicians would use a battery of tests. Most hospitals have the apparatus to carry out the electrophysiological tests of sensory nerve function which are thought to be of most use. These facilities should be used when a compression neuropathy such as CTS is suspected.
1.8 The Bilaterality of CTS.

The bilaterality of the carpal tunnel syndrome has been studied directly by only a few authors (Bendler et al. 1977 and Reinstein 1981). Other studies have included information regarding the distribution of bilateral, right only and left only sufferers (The details of some of these studies are given in table 1.14). The mean percentage of carpal tunnel syndrome sufferers with bilateral involvement was 51%, this was higher than for those with right only or left only involvement (35% and 13% respectively). The results of studies reporting a higher bilateral involvement (Bendler et al. 1977; Reinstein 1981) may be explained by the fact that they actually assessed both sides with electrophysiological testing, because they were investigating the issue of bilaterality, and were thus more likely to find more bilateral involvement, than those studies who only tested the side which displayed the symptoms of carpal tunnel syndrome. Indeed Bendler et al. (1977) concluded that there was a need to test both extremities for carpal tunnel syndrome when carrying out electrophysiological testing studies, even for unilateral carpal tunnel syndrome.

It would also appear that those studies excluding subjects with systemic conditions known to be associated with carpal tunnel syndrome (section 1.6.1), reported lower percentages of bilaterality (Ragi 1981; Graham 1983). However, other studies which carefully controlled for systemic conditions (Turner 1989; Yamaguchi et al. 1965) reported a high bilateral involvement, although not to the same extent as the studies directly investigating the bilaterality issue.

The effect of removing the systemic factors on the distribution of bilaterality (and indeed handedness) remains unclear. It would be useful to investigate the distribution of bilateral carpal tunnel syndrome sufferers in those patients with the systemic conditions known to be associated with carpal tunnel syndrome. In those studies investigating pregnancy and CTS (Voitk et al. 1983 and Ekman-Ordeberg et al. 1987), where the subjects exclusively had a systemic condition and CTS, the percentage of bilateral carpal
tunnel syndrome was higher (78 and 79% respectively) than the percentages reported in those studies reported in table 1.14, which excluded subjects with systemic conditions. The diagnosis of carpal tunnel syndrome was not confirmed with electrophysiological testing. Some of the reported bilateral symptoms may not have been true bilateral CTS patients. However, the very fact that they had the symptoms does suggest that a problem was evident, although caution should be expressed when interpreting results.

<table>
<thead>
<tr>
<th>Author</th>
<th>Bilaterals (%)</th>
<th>Right Only (%)</th>
<th>Left Only (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yamaguchi et al. 1965</td>
<td>56</td>
<td>26</td>
<td>18</td>
</tr>
<tr>
<td>Phalen 1966</td>
<td>49</td>
<td>37</td>
<td>14</td>
</tr>
<tr>
<td>Posch and Marcotte 1976</td>
<td>35</td>
<td>46</td>
<td>19</td>
</tr>
<tr>
<td>Bendler et al. 1977</td>
<td>61</td>
<td>27</td>
<td>12</td>
</tr>
<tr>
<td>Ragi 1981</td>
<td>21</td>
<td>63</td>
<td>16</td>
</tr>
<tr>
<td>Reinstein 1981</td>
<td>76</td>
<td>18</td>
<td>6</td>
</tr>
<tr>
<td>Graham 1983 systemic</td>
<td>44.4</td>
<td>31.9</td>
<td></td>
</tr>
<tr>
<td>Graham 1983 without systemic</td>
<td>31.9</td>
<td>44.4</td>
<td></td>
</tr>
<tr>
<td>Turner 1989</td>
<td>59</td>
<td>29</td>
<td>12</td>
</tr>
<tr>
<td>Mean</td>
<td>51</td>
<td>35</td>
<td>13</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>18</td>
<td>15</td>
<td>4</td>
</tr>
</tbody>
</table>

O'duffy et al. (1973) investigated carpal tunnel syndrome in patients suffering from an other systemic condition, acromegaly. Out of 100 acromegalic patients included in the study, 35 were diagnosed to have carpal tunnel syndrome, on the basis of symptoms...
occurring in the median nerve distribution, only six of these patients displayed electrophysiological evidence. All of the carpal tunnel syndrome sufferers had bilateral involvement.

In a study investigating nerve entrapment syndromes in chronic hemodialysis patients, Delmez et al. (1982) found 83% of the patients (with electrophysiological testing confirmed carpal tunnel syndrome) to have a bilateral involvement.

It could be hypothesised from these observations that systemic conditions by their nature, affect the body on a more general level, than one would consider occupational factors to. These are confined more locally to the area involved. It would appear that where risk factors are applied at a general level a bilateral involvement is more likely to occur.

Referring back to table 1.18, it would seem that, the right side is more affected than the left, particularly when the systemic factors are removed. Unfortunately, only a few studies in the literature (Reinstein 1981; Turner 1989) give any indication of the hand dominance of the subjects. Reinstein (1981) took the issue a step further, when investigating the effect of hand dominance on carpal tunnel syndrome, by concluding that an increased daily activity with the dominant hand was a contributing factor in the development of carpal tunnel syndrome. This may also suggest that the higher work intensity of the dominant hand, could be responsible for the increase prevalence of carpal tunnel syndrome in the dominant hand compared to the non-dominant. However, Turner (1989) found that laterality of symptoms was independent of hand preference.

Hand preference was investigated further by Kucera and Robins (1989) by objectively calculating the degree of hand preference using the Edinburgh handedness inventory of Oldfield (1971) (section 1.9). The degree or strength of hand preference was greater in cases compared with the controls (p<0.01). This supported the hypothesis that strong
hand preference was a risk factor for occupational carpal tunnel syndrome.

When applying the hand preference questionnaire to a subject with a disorder, the subjects response could be affected by the presence of the disorder. In conditions of rapid onset and early detection this bias would not be strong. The subject could respond with an answer such as "If it wasn't for my condition I would use this hand". However, in conditions of slow and gradual onset the subjects behaviour may be changed by the condition, without the conscious knowledge of the subject or indeed the examiner. This would bias the results of hand preference questionnaires. Results should be treated very carefully.

Unfortunately, these results may provide evidence for those seeking to promote the philosophy of screening in industry for potential risk factors. But it was stressed by Kucera and Robins (1989) that considerations of hand preference, in particular with respect to job placement, screening would not nearly be as effective as considerations of job design. This could reduce the degree of high force and high repetitiveness identified by Silverstein et al. (1987) as being risk factors for carpal tunnel syndrome.

In summary, carpal tunnel syndrome sufferers with a systemic condition known to be associated with carpal tunnel syndrome would seem to be more likely to develop a bilateral involvement, than those without such conditions. These individuals would be more likely to develop carpal tunnel syndrome in the side which is exposed to the risk factors, namely highly repetitive and highly forceful tasks. This would usually be their dominant or preferred hand, hence the increased occurrence of carpal tunnel syndrome in the right hand. This observation awaits confirmation.
1.9 Hand Preference Questionnaires.

Section 1.8 identified hand preference as being an important factor in considering the occupational aspects of CTS. Indeed, Kucera and Robins (1989) identified a strong hand preference as a risk factor for CTS. Methods of assessing the hand preference objectively has been addressed by various authors (Crovitz and Zenner 1962; Annett 1970; Oldfield 1971; and Provens and Cunliffe 1972), the methods used by these authors were evaluated by Nichols (1982).

The Crovitz and Zenner (1962) test consisted of 14 items relating to everyday activities. The response was chosen from a choice of six (1. Always left hand; 2. Usually left; 3. Use both equally; 4. Usually right; 5. Always right; 6. Don’t know). The scores derived ranged from 14 (extremely right handed) to 70 (extremely left handed).

A major criticism of the Crovitz and Zenner (1962) inventory was the option to give a "Don't know" response to a question. If this null answer were given too often the results of the inventory could be invalidated.

The Annett (1970) hand preference questionnaire consisted of 12 items, six of which were termed primary (writing, throwing, holding a; racket, match, hammer and tooth brush). The remainder were termed secondary. Individuals were classified into three groups, right handed (who used the left hand for none of the activities); mixed handed (who stated mixtures of left and right preferences); and left handed (who used the right hand for none of the activities). Detail was lost as a consequence of a continuum of scores not being established. This was a major criticism as it was hoped that a degree of hand preference could be established for each of the subjects in the study.

This was not the case for the Oldfield (1971) Edinburgh handedness inventory. It consisted of ten items: writing, throwing, drawing, use of scissors, toothbrush, knife (without fork), spoon, broom, striking a match and opening a box lid (Appendix III).
The subjects were instructed to indicate their degree of hand preference for each of the items, by placing one or two ticks in the left or right columns (1 tick for "normally used that hand" and 2 ticks for "always use that hand"), or one tick in each of the columns if they were indifferent about them. The version shown in appendix III is a modified version for the main study, the principle of scoring the degree of hand preference was the same as the original. 2 ticks in the left column was now equal to OL, one tick in the left column equal to L, etc.

The laterality quotient is produced which has a range of -100 (totally left handed) to +100 (totally right handed), details are given in section 1.10. This method of calculating the degree of hand preference has been criticised (Nichols 1982), all of the items carried equal weighting, without empirical evidence for all of the items to be equally important. A scissors question was included, even though it is thought that scissors are designed for right handed individuals. Left handed individuals may be socialised into using scissors with their right hand, this would produce spurious results, biasing the answer in favour of right handed preference. For this reason the main study questionnaire included an extra question involving pliers, these were thought to be used by the preferred hand of individuals of either hand dominance, rather than a learned socialised habit.

The Oldfield (1971) handedness inventory, although it was not regarded as ideal by Nichols (1982), did provide a simple, quantitative measure of handedness, which could be beneficial in the assessment of large populations. The size of the inventory allowed it to be implemented in a few minutes unlike the Provens and Cunliffe (1972) inventory.

The Provens and Cunliffe (1972) inventory consisted of 31 items covering a wide range of activities and allowed 3 rating classifications; left, either and right for each one. The handedness characteristics was calculated by subtracting the number of questions
answered as left dominant, from those answered as right dominant. The result was then divided the total number of questions asked. A range of scores of between -1 (completely left handed) and +1 (completely right handed) could thus be derived. Although this inventory did allow for a range of scores for handedness, it included too many questions to be useful and was therefore thought to be too time consuming.

In a study evaluating the use of handedness inventories, including the ones mentioned here, Nichols (1982) found that problems occurred in using all of the questionnaires, but the Oldfield (1971) Edinburgh handedness inventory turned out to be the preferred one, although some of the instructions were ambiguous. Consequently, the Oldfield (1971) Edinburgh handedness inventory was selected for the main study, with some minor alterations in the information and answer sheet format.
1.10 Epidemiology and CTS.

Epidemiology, or the study of the occurrence and distribution of diseases and other health related conditions in populations (Kelsey et al. 1986), allows us to determine the effects of diseases in the population. It also allows us to identify the effect of risk factors on the development of a disease in a population. It is important to select the most applicable type of study so as to minimise the time and financial costs of the study. It would be undesirable if the wrong type of study were selected and years later on analysis, results were found to be meaningless. Hence, it is useful to examine the epidemiology of CTS.

Two measures of morbidity should be discussed before continuing with a description of how, epidemiological studies are selected and carried out. The relevance to CTS may then be examined.
1.10.1 Measurements of Morbidity.

The incidence rate is the rate at which new events occur in the population; or the rate at which non-diseased individuals become diseased over a specified period of time. It gives a measure of how many new cases develop a disease, in those individuals who are at risk over a specified period of time. This time is usually taken to be one year, hence the term annual incidence rate or annual incidence is often used. Rates are usually expressed as the rate per thousand at risk, as in equation 1.3.

\[
\text{Incidence rate per 1000} = \frac{\text{The number of new cases of a disease occurring in the population during a specified period of time}}{\text{The number of persons exposed to the risk of developing the disease during that time}} \times 1000
\]

Equation 1.3 Expression for the incidence rate (Lilienfeld and Lilienfeld 1980 p.138).

The incidence rate provides a measure of the rate at which new cases are occurring in the population over the specified period of time. Prevalence is the number of individuals who have a disease over a specified period of time. Several types of prevalence exist and are used by the epidemiologist;

i. Annual Prevalence: The total number of people with the disease over a year. (This is only occasionally used.)

ii. Lifetime Prevalence: The total number of people known to have had the disease in their lifetime.

iii. Period Prevalence: The total number of people known to have had the disease at any time during a specified period of time.

iv. Point Prevalence: The total number of people with a disease at a specified point in time.
When prevalence is used without qualification it usually refers to the point prevalence. The prevalence rate maybe determined by dividing the prevalence by the number of people at risk in the population. Rate is expressed as a rate per thousand at risk as in equation 1.4.

\[
\text{Prevalence rate per 1000} = \frac{\text{The number of cases of disease present in population at a specified time}}{\text{The number of people in the population at that specified time}} \times 1000
\]

Equation 1.4. Expression for the prevalence rate (Lilienfeld and Lilienfeld 1980 p. 139)

It should be noted that the incidence rate refers to those individuals who develop the disease over a period of time, i.e. new cases; whereas the prevalence rate refers to those individuals who have had the disease over the period of time, not necessarily new cases.
1.10.2 Identification of Risk Factors.

The identification of risk factors of diseases is complex, it involves the investigation of causal associations of an agent (the risk factor) and the disease. Table 1.15 outlines how the causal associations maybe identified and the effect of the risk factors analysed in detail.

Table 1.15 A common sequence in the discovery of a causal association between an agent and a disease. (Kelsey et al. 1986 p. 5).

1. Clinical observation of possible causal association between a factor and a disease.
2. Descriptive epidemiologic analysis establishing the association on a population level.
3. Analytical epidemiologic studies establishing the associations on an individual level.
4. Experimental reproduction of the disease by the risk factor and/or elucidation of the pathogenic mechanism of the factor in the disease.
5. Observation that the removal of the risk factor (or modification of the host response to it) decreases the incidence of the disease.

Clinical observation is the first step where associations are first suspected leading to descriptive epidemiologic studies of the disease. At this stage little is usually known about the epidemiology of the disease in question. Descriptive studies provides information about the occurrence of the disease according to such characteristics as age, sex, marital status, social class, occupation, geographical distribution and time of occurrence. Routinely collected data are usually used in the descriptive studies. These data may be collected from hospital records, analytical studies in other fields or Government statistics. Hypotheses may later be generated on the basis of these data and tested using analytical studies.

Experimental studies involving the reproduction of the disease by exposure of the risk
factor may be carried out to establish the exact nature of the causal association. However, in human subjects it is often unethical to reproduce the disease in individuals by exposure to a risk factor. The removal of the risk factor is feasible in certain circumstances, this may ascertain the causal association of the risk factor and the disease beyond the levels of doubt which other studies suffer.

When the causal associations has been identified with preliminary data and the population thought to be at risk identified, a hypothesis may be formulated and tested using an analytical study. There are three major types of analytical studies which shall be mentioned briefly; Cohort or incidence studies; Cross-sectional or prevalence studies; and Case-Control studies.
1.10.3 Cohort Studies.

Prospective cohort studies are thought to be the most definitive type of analytical study (Kelsey et al. 1986). The design of the prospective cohort study is simple. Two groups of individuals are selected on the basis that one will be exposed to the risk factor (the exposed group) and the other will not (the non-exposed group). All individuals must be free from the disease at the beginning of the investigation. The two groups are observed over a period of time (which may last for many years), at the end of which the incidence rate for the disease calculated, using the equation 1.3. The incidence rate for the exposed and non-exposed groups are compared, to test the hypothesis relating to the risk factor. The examiner can be precise with the diagnosis of the disease and the recording of when the onset of disease occurs, after exposure to the risk factor. Other types of study do not allow this degree of precision in either diagnosis or time of onset.

The long term structure of prospective cohort studies require the commitment of finance and man power over long periods of time. It is often difficult to muster such a commitment for long term prospective cohort studies. An alternative is to assemble a cohort study retrospectively. In this type of study the exposed and non-exposed groups are identified after exposure has occurred. The two groups are traced back in time to when the initial exposure occurred, the incidence of the disease is calculated up to the time of the study and sometimes beyond the beginning of the study.

Problems arise when the degree of exposure is unclear, so long after it has occurred. Also the retrospective analysis of the disease may suffer problems if records of the disease are unclear or incomplete. The onset of the disease would also be difficult to establish satisfactorily in some cases.

To date there have been no cohort studies reported in the literature investigating carpal tunnel syndrome and its risk factors.
1.10.4 Cross-sectional Studies.

In cross-sectional or prevalence studies the effect of exposure to a risk factor is examined at one point in time. There are two methods of grouping the individuals in the study;

i. Exposed and non-exposed groups are examined and the prevalence rate of the disease in each group compared. The risk of exposure to the risk factor may then be assessed.

ii. Diseased and non-diseased groups maybe examined and the relative exposure to the risk factors in each group compared.

The former type is the more usual method of grouping individuals. Problems arise when confusion occurs between the cause and effect of certain risk factors, since cases may have had the condition for a prolonged period of time. A proportion of cases may not be included, in conditions where subjects either recover quickly, or die quickly from the condition. However, with diseases with slow onset, where individuals do not seek medical attention until the disease has developed fully, the prevalence study is often the most practical approach.

There have been few cross-sectional studies investigating the prevalence of carpal tunnel syndrome and its associated risk factors. The detail of three such studies are given in table 1.16. All three cross-sectional studies used the first method of grouping individuals mentioned above; a group of individuals exposed to the risk factor were compared with a group of individuals not exposed to the risk factor.

The studies consisted of large numbers of subjects, Punnett et al. (1985) and Margolis and Kraus (1987) both selected the individuals from occupational groups known to be either exposed to the risk factor or not. Silverstein et al. (1987) used a different method, a large group of workers were selected and the 39 jobs represented were
graded for levels of relative risk (the degree of forcefulness and repetitiveness in the task). The prevalence of the carpal tunnel syndrome of workers in each of the categories was then calculated.

The diagnosis of carpal tunnel syndrome seems to be rather vague for all of these studies. No electrophysiological tests were performed and some data were collected using self administered questionnaires (Margolis and Kraus 1987). However, the subjective diagnostic criteria reported gives a good indication that the signs and symptoms of carpal tunnel syndrome were present, even without the electrophysiological test results. The findings of the studies were all in agreement, that exposure to highly repetitive and high force activities, increases the risk of carpal tunnel syndrome. Significant results were not found by Margolis and Kraus (1987) when nocturnal exacerbation was included in the selection criteria. This result increases the concern about the vague nature of the selection criteria in these studies.
<table>
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<tr>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Punnett et al. 1985</td>
<td>Exposed: 162 # Garment workers. Unexposed: 76 # Hospital workers.</td>
<td>Exposed. The garment workers were exposed to highly repetitive low force wrist and fine finger motions. References group was not exposed to repetitive tasks.</td>
<td>Symptoms of pain, numbness, tingling present at night or early morning; or two of the following: i. Weakness in pinching and gripping. ii. Alleviated by absence from work for ≥ 1 week. iii. Aggravated by house work or non-occupational tasks.</td>
<td>Higher prevalence of CTS in exposed group compared to the non-exposed. (Rate ratio 3 p&lt;0.025)</td>
</tr>
<tr>
<td>Silverstein et al. 1987</td>
<td>652 workers in 39 jobs from 7 industries.</td>
<td>Exposed. Grouped into jobs of equal force and repetitiveness.</td>
<td>All of the following; 1. Symptoms in the median nerve distribution. 2. Nocturnal exacerbation. 3. Symptoms occurring &gt; 20 times or lasting &gt; 1 week per year. 4. No acute traumatic onset of symptoms. 5. No rheumatoid arthritis. 6. Onset in current job. Also +ve Phalen's or Tinel's sign and rule out cervical root, thoracic outlet and pronator teres syndromes.</td>
<td>High force, high repetitive jobs had a higher prevalence of CTS than the low force, low repetitive jobs (Odds ratio 15 p&lt;0.001).</td>
</tr>
<tr>
<td>Margolis and Kraus 1987</td>
<td>Female supermarket checkout operators. 691 using a laser scanner. 291 not using the laser scanner.</td>
<td>Exposed. Those using the laser scanner. Not exposed. Those not using the laser scanner.</td>
<td>Postal Questionnaire. Self reported pain, numbness or tingling in hand or wrist, or nocturnal exacerbation.</td>
<td>Higher prevalence of CTS in worker using the laser scanner (Rate ratio 1.12 p&lt;0.05). When nocturnal exacerbation used no sig diff (Rate ratio 1.03 p&gt;0.05).</td>
</tr>
</tbody>
</table>
1.10.5 Case-Control Studies.

In case-control studies individuals with the disease (the cases) and those without the disease (the controls) are selected. The criteria for the selection of cases and controls will be discussed later. The individuals in the two groups may be matched and then the proportion of cases and controls with exposure to the risk factor of interest, may be compared and the odds ratio of the exposure calculated. The close matching nature of the case-control study allows the examiner to select fewer cases, thus reducing the time, financial and manpower requirements of the study. Case-control studies are generally less expensive than other studies such as cross-sectional or cohort studies, particularly when studying rare diseases.

Although case-control studies are more economical than other studies, there are concerns about this type of study which should be taken into consideration;

i. Information on potential risk factors and confounding variables may not be available, particularly if these rely on the patients memory.

ii. The cases may search for a cause of their diseases and are therefore more likely to report exposure than the controls (recall bias).

iii. It may be difficult to determine whether an agent caused the disease or if the occurrence of the disease caused the person to be exposed.

iv. Identifying the case group representative of all cases may be difficult.

v. Identifying the control group may be difficult.

These concerns about case-control studies often mean that the study may not provide a thorough enough answer to the problem posed to the examiner. It may be that the case-control study may only provide the leads for a cohort study to be carried out on.

There are two types of case-control study;

i. Incidence density:- Incident cases are sampled as they occur, controls are
sampled over the same time period. N.B. controls do not have the disease when
selected, but they may develop it later and become cases themselves.

ii. Cumulative incidence:- Cases are sampled over a defined period of time.
Controls are selected at the end of the time period and therefore have no chance
of becoming cases.

The Selection of Cases.
Cases are usually selected from those people seeking medical attention for the disease
under study. If possible new cases should be selected, as those with the disease for long
periods of time may find it difficult to distinguish exposure that preceded the onset of
the disease, from those that occurred after the disease had developed. This would make
the differentiation of cause and effect difficult. The time of onset of the disease may
not be known, so when identifying risk factors for the disease it is important to make
sure that the exposure at least preceded the onset of the symptoms. This ensures that
the person did not change his exposure status as a result of the disease.

The diagnostic criteria for the cases must be established carefully, various categories
may be established and analytical methods used to involve these multiple levels
employed later in the analysis.

The Selection of Controls.
There are four commonly used groups as controls;

i. Controls may be selected from the same group as the cases but had not
developed the disease. These may be selected on a probability basis, randomly
selecting cases in a geographical area.
ii. Persons seeking medical care at the same institution as the case, for a condition believed to be unrelated to the condition under study. Controls are usually selected with a variety of conditions, so that no one condition is too highly represented.

iii. Neighbourhood controls or persons living near to the case maybe selected, they are usually matched to the cases for variables such as age and gender.

iv. Friend controls are selected by asking the case to suggest a friend of the same gender and about the same age. This will increase the likelihood of the controls having similar social characteristics as the cases. However, over matching of certain characteristics, due to more exposure to the risk factor, than a less well matched group may take place, thus requiring a greater sample size for the same degree of power. Also, cases may not wish to expose their friends to the experiment. Problems may also arise if the case suggests a more sociable or extrovert person than would normally be selected from the general population, this may lead to bias if questionnaires are employed.

The risk factors should be carefully considered before selecting the control group. Certain groups may include more subjects who have been exposed to the risk factor than would be expected in the population. eg. Smokers or ex-smokers are common in hospitals because many conditions which result in hospitalisation have been associated with smoking, thus if smoking was a risk factor under consideration the selection of hospital controls should be reconsidered (Kelsey et al. 1986 p.160).

Recall bias may also be a problem in the case-control study. An individual who has recently had a disease, will remember any exposure to risk factors more readily than someone who's exposure occurred in the distant past.
When the choice of control group is in doubt the investigator should consider selecting more than one control group.

It is important that the cases and controls are interviewed in exactly the same manner. If possible the interviewer should not know whether the subject is a case or a control, this is not always possible. The interviewer at least should be unaware of the major hypotheses being tested, this will reduce the interviewer bias.

**Exclusions.**

The same exclusion criteria should be used for cases and controls where possible. If cases with certain medical conditions where excluded, then controls with the same condition should also be excluded. Cases and controls with no chance of being exposed to the risk factor should also be excluded; eg. males, if the contraceptive pill is to be tested as a risk factor.

**The Matching of Cases and Controls.**

Matching of the cases and controls allows the investigator to compare risk factors in the two groups, without the need to employ complex statistical techniques which remove the effects of confounding variables. Matching may be used to remove the effects of these variables.

Two type of matching is used in case-controls studies;

i. Individual matching involves selecting one or more controls for each of the cases. The matching criteria usually includes at least gender, and age and possibly race, however other variables may be used in the matching criteria. If
several variables are used it may be difficult to find a suitable control to match with a case. The matching criteria can be relaxed for variables such as age, thus matching may be based on the controls age being within five years of that of the case.

ii. Frequency or category matching involves first calculating the number (or expected number) of cases with each level of the confounding variables used for matching; eg. the number cases in each age range. The correct number of controls may then be selected from the control population.

The number of variables used for matching must be carefully controlled. Any variables should be strongly related to the disease and also related to exposure. If variables are used which are only related to the exposure and not the disease then the results could lead to a loss in precision (Kelsey et al. 1986 p173).

The matched design has a number of advantages over the unmatched;

i. Confounding variables must be controlled for, particularly those which are difficult to measure.

ii. The number of controls required is reduced; ie. less thus saving the project money.

iii. A non-hospitalised control group maybe selected which is valid, eg. from the neighbourhood of the case.

iv. Confounding by continuous variables can be difficult to adjust for in the analysis. Matching can eliminate these variables and make comparisons more valid.
v. The precision in estimating the odds ratio is increased from that using an unmatched design.

The details of six case-controls studies investigating CTS are given in table 1.17. It is noticeable that in most studies the numbers of subjects is lower than those in the cross-sectional studies given in table 1.16, although the number of cases identified were similar for both types of study. The studies by Armstrong and Chaffin (1979) and Cannon et al. (1981) use individuals matched for sex and working in the same factory. Armstrong and Chaffin (1979) included patients who had undergone a carpal tunnel release operation and found differences in grip strength in cases and controls. There have since been studies which cast doubt on the wisdom of including such individuals; Gartsman et al. (1986) found grip strength to decrease post-operatively as a consequence of carpal arch alterations. Gellman et al. (1989) found a similar result, where grip strength was only 28% of the pre-operative levels 3 weeks after operation. However, 6 months after the release, grip strength had increased to 116% of the preoperative levels.

Although these studies cast doubt on the selection of such individuals as cases in the Armstrong and Chaffin (1979) study, it was not reported how many such cases were selected or when the carpal tunnel release operation occurred. The differences in hand forces between the two groups should therefore be treated with caution.

The Cannon et al. (1981) study consisted of cases who had worker compensation claims for carpal tunnel syndrome in a particular plant. The diagnostic criteria for such claims is still even now in dispute and the details of such claims are not widely published. It is therefore difficult to assess the results of the study without more details of the subjects. If the results are expressed in context, ie. as those being representative of a group of workers making claims for CTS and not those fulfilling strict diagnostic criteria then they may be considered to be valid.
The other studies in table 1.20 (Dieck and Kelsey 1985; Vanwijck and Bouillenne 1986; Wieslander et al. 1989; and Turner 1989) all used cases who were attending hospital for carpal tunnel release or after referral to a consultant regarding the carpal tunnel syndrome (Turner 1989). The diagnostic criteria of the final three studies included electrophysiological examination of the median nerve. This increased the sensitivity of the selection of cases. Indeed, it is of some concern that some carpal tunnel release operations are now performed without electrophysiological confirmation as in the Dieck and Kelsey (1986) study. Other authors have expressed the need for electrophysiological testing to be performed to confirm the diagnosis of carpal tunnel syndrome, although the symptoms of CTS may exist even with negative electrophysiological results (Grundberg 1983). But, if other systemic neurological disorders are ruled out then a positive electrophysiological result would suggest CTS beyond any reasonable doubt.

The tightest selection criteria were reported by Turner (1989). Symptoms in the median nerve distribution were confirmed by electrophysiological testing, subjects with the other conditions reported in the literature to be associated with carpal tunnel syndrome were not included in the case group. Only carpal tunnel syndrome cases without systemic and local complications were included. Restrictions on age and duration of the condition completed the selection criteria.
<table>
<thead>
<tr>
<th>Author</th>
<th>Subjects</th>
<th>Matching</th>
<th>Diagnostic criteria</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vanwijck and Boullenne 1986</td>
<td>Cases: 90 females 15 males.</td>
<td>Controls living in the same area and same ethnic origin and sex as the cases.</td>
<td>Night pain or numbness in the median nerve distribution. + ve Tinel's and Phalen confirmed by EMG. Referred for carpal tunnel release operation.</td>
<td>No association between CTS and HL-A antigens.</td>
</tr>
<tr>
<td></td>
<td>Controls: 1814 females 116 males.</td>
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<tr>
<td>Wieslander et al. 1989</td>
<td>Cases: 38 males referred for CT release.</td>
<td>Sex, age ± 3 yrs. year of operation ± 3 yrs (hospital controls only)</td>
<td>CTS diagnosed by a hand surgeon and confirmed with EMG.</td>
<td>Use of hand vibrating tools (OR=3.3 p&lt;0.01) and repetitive movements of the wrist (OR=2.7 p&lt;0.01) more evident in the cases.</td>
</tr>
<tr>
<td></td>
<td>Controls: 38 male patients with gall bladder disease. 38 male patients with varicose veins. 76 males from the general population.</td>
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<tr>
<td>Armstrong and Cheffin 1979</td>
<td>Cases: 18 males</td>
<td>Matched for job.</td>
<td>Numbness or pain in the median nerve distribution or surgical decompression or +ve Phalen sign or thenar atrophy.</td>
<td>No difference in hand dimensions. Sig differences in hand forces and deviation from neutral position at work, cases greater than controls.</td>
</tr>
<tr>
<td></td>
<td>Controls: 18 males.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cannon et al. 1981</td>
<td>Cases: 3 male 27 female.</td>
<td>Sex and plant of work.</td>
<td>Cases receiving working compensation claims for CTS.</td>
<td>Risk factors := use of vibrating tools, gyni surgery and years on job (OR 7, 3.7, 0.7 p&lt;0.01)</td>
</tr>
<tr>
<td></td>
<td>Controls: 9 males 81 females.</td>
<td>No exclusions.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Author</td>
<td>Subjects</td>
<td>Matching</td>
<td>Diagnostic criteria</td>
<td>Findings</td>
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</tr>
<tr>
<td>Dieck and Kelsey 1985</td>
<td>Cases: 40 females referred for CT release.</td>
<td>Sex, ethnic origin and age.</td>
<td>Female who had CTS release at one of the five hospital in the study.</td>
<td>History of diabetes associated with CTS (OR 2.9 p&lt;0.025).</td>
</tr>
<tr>
<td></td>
<td>Controls: 1043 females on surgical wards in the same hospital.</td>
<td>Exclusions: Carcinomas of the breast, ovary or endometrium. None English speaking persons.</td>
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</tr>
<tr>
<td>Turner 1989</td>
<td>Cases: 11 males 23 females presenting at clinic for CTS.</td>
<td>Sex and age ± 3 yrs.</td>
<td>Symptoms in the median nerve distribution, with a DML of &gt;5ms.</td>
<td>No sig difference between cases and controls regarding vitamine B6 status.</td>
</tr>
<tr>
<td></td>
<td>Controls: 11 males 23 females attending physiotherapy dept. for fractures to the lower limb.</td>
<td>Exclusions: Those taking the following medication; Danazol, Disulphiram, Isoniazid, Penicillamine, Thalidomide and Vitamine B6 complex.</td>
<td>Had CTS for &gt;5 weeks and &lt; 5 yrs.</td>
<td>Repetitive manual work greater in cases than controls (OR 5.0 p&lt;0.025).</td>
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<tr>
<td></td>
<td></td>
<td>Those suffering from; Acromegaly, Amyloidosis, Diabetes mellitus, Hyperparathyroidism, Hypothyroidism or renal failure.</td>
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<tr>
<td></td>
<td></td>
<td>Any surgery to the hand, fractures to the wrist or pregnant females.</td>
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<tr>
<td></td>
<td></td>
<td>Those &lt;18 yrs and &gt; 65 yrs.</td>
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</table>
In summary, the cohort study is thought to be the most definitive type of epidemiological study that may be employed. The cost of such a study both in funds and man-power often make them unreasonable. The case-control study allows the investigator to carry out a well controlled study at a fraction of the cost of the cohort study.
1.11 Magnetic Resonance Imaging (MRI) of the Wrist.

MRI has been used by a limited number of authors to study the anatomy of the wrist and carpal tunnel (Hinshaw et al. 1977 and 1979; Weiss et al. 1986a and 1986b; Koenig et al. 1986; Baker et al. 1987; Middleton et al. 1987; Pittard 1987; Roger and Lavel-Jeantet 1987; Richman et al. 1987 and Mesgarzadeh et al. 1989 a and b). The early reports of the development of systems capable of imaging wrists (Hinshaw et al. 1977 and 1979) were followed by studies of; firstly the normal anatomy of the wrist; and then the clinical use of MRI. Wrists with disorders such as CTS were imaged and the observations reported. Many of the studies reporting images of CTS patients have involved only a few wrists and the interpretation of the images has been subjective. This subjectivity has been highlighted by the reports of more the rarely encountered causes of nerve entrapments at the wrists, such as ganglionic cysts in the carpal tunnel. The more common occurrence of this nerve compression, in the so called idiopathic CTS has rarely been addressed. No validation of the subjective measuring techniques has yet been reported.

The following sections give an account of the methods used for imaging wrists using MRI, including imaging planes and subject positioning. The results of some of the studies imaging patients with CTS are discussed.
1.11.1 Sequences used for Wrist Imaging.

High field commercial systems were used for all of the published studies using MRI to image wrists, except the early work carried out by Hinshaw et al. (1977 and 1979) which were developmental projects. Hence, the emphasis has been on clinical aspects of imaging, rather than in the development of new sequences. Indeed, apart from the work carried out by Hinshaw et al. (1977 and 1979), at the department of physics, University of Nottingham, all other work on wrists was carried out by medical practitioners, working in conjunction with the radiology departments of their hospitals. This is reflected in the limited variation in the types of sequences chosen to image wrists. The General Electric (GE) 1.5 T Signa system, used by Weiss et al. (1986a and 1986b); Baker et al. (1987); Middleton et al. (1987) and Richman et al. (1987), had resident software available for spin echo sequences. An image matrix of 256 x 256 pixels was available, but often only 128 x 256 pixel images could be captured due to time constraints. Mesgarzadeh et al. (1989 a and b) used a 512 x 512 image matrix. This increased the imaging time, as the greater the image matrix the longer the image would take to capture and the longer the subject would be in the apparatus, but also the higher the resolution of the images. The spin-echo sequences available allowed the use of various repetition times (TR) and time to the echo (TE) (T1 weighted image used Tr 600-1500 ms / TE 20-30 ms; Density sequences used Tr 2000-2500 ms / TE 20-30 ms; T2 weighted sequences used TR 2000-2500 ms / TE 60- 100 ms.)

Although Koenig et al. (1986); Roger and Lavel-Jeantet (1987); and Mesgarzadeh et al. (1989 a and b) used slightly lower field strengths (1, 0.5 0.3T respectively, now considered to be a mid-field strength), the sequences used were essentially the same as the GE systems, with TR ranging from 500-2000 ms and TE from 28-120 ms.

1.11.2 Coils.

The surface coils available with the modern commercial systems, all provide the resolution required to carry out an anatomical study of small areas such as the carpal
tunnel. All of the high field systems used surface coils of between 7.5 and 13 cm in diameter, depending on the size of the field of view required. In addition to the standard surface coils available, other types were utilised. Weiss et al. (1986a) used a prototype transmit receive surface coil, Middleton et al. (1987) used loop-gap resonator surface coils for receive only. Since the signal to noise ratio of these devices is so good, they are ideally suited to looking at small areas.

The slice thickness may be as thin as 0.3 cm in the high field systems. Some of the slightly lower field strength systems had to compromise their slice thickness, as their signal to noise ratio is not as good, although the 5 mm slice thickness used by Roger and Lavel-Jeantet (1987) was still acceptable.

1.11.3 Imaging Time and Subject Comfort.

The time taken to image the subjects ranged from 5 to 20 minutes. This time was dependent on the TR of the sequence, the number of pixels in the image matrix and the number of averages taken for each line of data in the image (table 1.18). The comfort of the subject had implications as to the optimum imaging time. The more averages taken the better the quality of the image, but also the longer the imaging time. The same applies for the number of pixels in the image matrix. Baker et al. (1987) reported that motion artifact introduced such a significant reduction in image quality, that a faster sequence had to be employed, reducing the imaging time.

The imaging times reported in most of the studies only represented the time when an images were being captured. A more important time consideration was provided by Weiss et al. (1986a), who included the time taken to position the subject and make the technical adjustments to the equipment. The imaging time of each wrist took in total 20–30 minutes, with total imaging time of one hour for each subject. With these lengths
of time in the system the subjects comfort would be of importance. If motion artifact is to be avoided, the subject position must be considered, to maximise the subject comfort and remove this source of error.

Table 1.18 Method for calculating total imaging time.

<table>
<thead>
<tr>
<th>No. of pixels in image matrix</th>
<th>512.0</th>
<th>128.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>TR in Seconds</td>
<td>2.0</td>
<td>0.5</td>
</tr>
<tr>
<td>No. of averages</td>
<td>1.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Total imaging time (sec)</td>
<td>1024.0</td>
<td>128.0</td>
</tr>
</tbody>
</table>

1.11.4 Subject Position.

The subject position favoured by the commercial systems involves the subject lying prone with the arm extended over the head. This position was adopted by Weiss et al. (1986 a and b), Baker et al. (1987), Middleton et al. (1987) and Roger and Lavel-Jeantet (1987). Experience suggests that the discomfort experienced with the arm in this position would be a problem, although it was only reported by one study (Weiss et al. 1986b). Subjects complained that the arm being imaged often 'fell- asleep' during the 20-30 minutes spent in the apparatus. Koenig et al. (1986) used a different subject position, the subject was supine with the arm extended over the head and bent at the elbow. The same criticism could be applied to this position. Mesgarzadeh et al. (1989) allowed the subject to lie either prone or supine, which ever was preferred.

1.11.5 Imaging Planes.

reported the use of coronal, sagittal and axial planes for wrist imaging. The coronal plane was considered best for observing the carpal bones and the course of the nerves and flexor tendons. The sagittal plane was considered to be of less use, except for imaging the digits. The best images of the carpal tunnel were taken in the axial plane. All workers in this area used the axial plane for studying and evaluating the carpal tunnel. Since the tendons have such a short T2 they could not be seen in the image. However, they could be observed by their absence, contrasting against the tendon sheaths surrounding them. The same was true of the flexor retinaculum, which could be observed as a dark band of low signal intensity on the palmer surface of the carpal tunnel. The tendons of the flexor digitorum superficialis and profundus muscles and the flexor pollicis longus muscle, could all be identified on the images. The median nerve was reported to have a intermediate intensity signal, lying adjacent and deep to the flexor retinaculum.
1.11.6 Imaging CTS Patients.

Few CTS patients have been imaged using MRI. Only 23 patients suffering from carpal tunnel syndrome have been imaged using MRI in all of the published studies to date (Weiss et al. 1986b; Koenig et al. 1986 and Middleton et al. 1987; Mesgarzadeh et al. 1989b). The only statistical comparisons with a control population were made in the Mesgarzadeh et al. (1989b) study. Thickening of the tendon sheath was reported in all studies. This was demonstrated using T2 weighted sequences (TR = 2500ms, TE = 100 ms).

Measurements of the calibre of the median nerve were made by Middleton et al. (1987), but validation and repeatability of the technique used was not reported. The windowing of the images had an affect on the size of the median nerve in the images.

Most of the studies of wrist imaging consisted of a description of the normal anatomy of the wrist, or reports of case studies of abnormalities including carpal tunnel syndrome (Weiss et al. 1986b; Koenig et al. 1986 and Middleton et al. 1987). Normal variation was reported by Middleton et al. (1987) only subjective comparisons were made, the lumbrical muscles could be seen to encroach into the carpal tunnel in two out of nine normal volunteers. This would have the effect of increasing the volume of material in the carpal tunnel. It was suggested that the wrist should be imaged in the neutral anatomical position.

Mesgarzadeh et al. (1989b) did carry out some statistical comparisons of a normal population (17 wrists) in a previous study, with a population of CTS afflicted wrists (8 wrists) the results are given in table 1.19. The CTS patients symptoms were supported by electrophysiological tests. (One of these subjects had a ganglionic cyst and should therefore have been excluded from the study, likewise another had symptoms only in the radial nerve distribution). Significant differences were found between the cases and controls, for variables such as swelling and flattening of the median nerve at the level
of the pisiform bone, as well as bowing of the flexor retinaculum. However, the small numbers of cases and the lack of validation of the results is of concern.

Table 1.19 Results from MR Imaging Studies Including Cases and Controls.

<table>
<thead>
<tr>
<th>Author</th>
<th>Cases</th>
<th>Controls</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesgarzadeh et al. 1989 a+b</td>
<td>6</td>
<td>17</td>
<td>Sig. diff (p&lt;0.005) found between cases and controls wrt swelling ratio at pisiform level. Sig. flattening (p&lt;0.025) of the nerve at the pisiform level. Sig. bowing ratio (p&lt;0.005) of flexor retinaculum. Validation: - Comparison with of images with cadaver sections.</td>
</tr>
<tr>
<td>Middleton et al. 1987</td>
<td>10</td>
<td>18</td>
<td>No objective statistics. Subjective observations of cases images were made but with no objective evidence. Validation: - Comparison with cadaver sections. No validation of the measuring technique.</td>
</tr>
</tbody>
</table>
1.11.7 Validation.

The only reported methods of validating the interpretation of the MR images, was by comparison with bone scintigraphy, radiography (Koenig et al. 1986) and with cadavers (Hinshaw et al. 1979; Weiss et al. 1986a; Baker et al. 1987; Middleton et al. 1987 and Richman et al. 1987). The bone scintigraphy and radiography failed to provide the adequate spatial resolution obtainable by MR imaging. The radiography could not provide information about the carpal tunnel. This would suggest that the validation of the Koenig et al. (1986) image interpretation is in doubt.

The use of cadavers for validation has been popular. Weiss et al. (1986a) imaged and sectioned cadaver wrists to demonstrate the normal anatomy of the hand and wrist. However, images of a cadaver may not represent images of a living wrist. The techniques used in preserving the cadaver and any histological and fluid changes which occur soon after death due to the method of preservation, would result in differences in the NMR parameters between cadavers and living tissue. This could explain why Koenig et al. (1986) compared cadaverous sections with the images of volunteers rather than with those of cadavers. Although this would remove the problem of changes in the NMR parameters occurring post-mortem, it still leaves the problem of comparing two different objects, when attempting to validate a system.

Richman et al. (1987) injected silicone into the carpal tunnels of cadavers after they had been imaged. The images underwent three-dimensional reconstruction to obtain a volume, which was then compared with the silicone injection. No significant difference was found between the volume of the injected moulds and the image volume dimensions. This only represents comparisons of the dimensions using MR imaging. Whether the true interpretation of the images were valid was not confirmed by silicone injection. Indeed, other authors using cadavers as a method of validation have compared images of volunteers with the cadaverous sections (Hinshaw et al. 1979; Baker et al. 1986 and Middleton et al. 1987). In addition to the comparison with cadavers made for
the normal anatomy, Middleton et al. (1987) used surgical reports to confirm the interpretation of the images of patients with pathological conditions.

Regardless of whether the authors comparisons of cadavers and volunteer images provides adequate validity, it is clear from the literature that there is wide agreement in the interpretation of the MR images of the wrist and in particular the carpal tunnel. Although this interpretation was been made on the basis of retrospective analysis of the images. Indeed, anyone wishing to identify the contents of an image would require a detailed knowledge of the anatomy of the wrist and carpal tunnel. Clearly an investigator would know what was expected to be found and would search the image for the contents that were known to be there, rather than identifying the contents that were actually visible. This investigator bias may invalidate this method. Some of the structures identified on the images in the literature (which are obviously the best quality available) could quite easily have been an artifact in the image.

Whether or not the structures were correctly identified, would be impossible to verify without sectioning each of the wrists images and comparing the true cross-section with the image. This would be unreasonable action especially when investigating normal wrists. There is therefore no option but to accept that some of the structures inside the carpal tunnel can be identified and are indeed obvious to the layman after being pointed out. However, claims that every structure within the wrist can be identified must be treated with caution.

Middleton and Lawson (1989; p83-121) provided an atlas of MR images along with the corresponding cadaverous section for wrists in all three planes. The cadaver preparations and the MR images corresponded adequately enough to justify their interpretations on the images. Caution should once more be stressed, as even these images of the highest quality, are still speculative in their interpretation, this doubt should be emphasised
Any validation of the measuring techniques used in studies reported in the literature are conspicuous by their absence. None of the studies reporting the use of direct measuring of the images (Middleton et al. 1987; and Mesgarzadeh et al. 1989 a and b) have addressed this problem. As with any new methodology, without evidence of validation, the results of any measurements must be treated with caution.

1.11.8 Pathological Disorders.

As well as the normal anatomy, pathological disorders in the hand and wrist have been investigated using MR imaging (Weiss et al. 1986b; Koenig et al. 1986 and Middleton et al. 1987; Mesgarzadeh et al. 1989b). The various disorders studied ranged from ganglionic cysts and bone tumours to arteriovenous malformations such as Raynauds' phenomenon and arthritis (Pittard 1987). No statistical data were available. All of the studies consisted of case studies with images interpreted using prior knowledge of the patients condition.
1.12 Other Imaging Techniques.

1.12.1 Computed Tomography (CT) Imaging.

Computed Tomography is another method of obtaining cross-sectional images through the body. X-rays are projected through the sample at various angles onto a detector, the computer reassembles the x-ray images into a cross-sectional image, using a method known as back projection. The sample must be placed perpendicular to the plane of the system's x-ray emitters and detectors to collect these cross-sectional images. Thus, whole body coronal and sagittal images are not possible. The use of x-rays in the imaging process means the technique has an element of risk to the subject, due to the exposure to radiation. The material that may be successfully imaged is limited to the more osseous structures such as bone and, to some extent, tendons. However, computed tomography has been used to image wrists by a number of authors in the past decade.

The slice thickness on wrist images in the literature ranges from 0.1cm (Schmitt et al. 1988) to 0.8cm (Zucker-Pinchoff et al. 1981). The subject imaging position has tended to be based on the needs of the imaging system, rather than those of the subject. Most studies reported the subject lying prone on the imaging bed, with both hands in the system out-stretched in front of them! (John et al. 1983; Liang 1987; Merhar et al. 1986; Quinn et al. 1989). Both wrists were usually imaged simultaneously. When the subject complained of restricted shoulder mobility, Liang (1987) changed the position to accommodate this. Each wrist was imaged separately with the subject lying on their side. Splints were used in both the Dekel et al. (1980) and the Liang (1987) studies to keep the fingers in a standard position during the imaging. They may also have removed any motion artifact, the resolution of the images would be reduced if movement occurred.

No mention was made in the literature of the comfort of the patient during the imaging process. It was only when the patient could not attain the required position, because of restricted shoulder movement, that Liang (1987) actually changed the imaging position.
Simultaneous imaging of both wrists has been employed where possible, at the cost of patient comfort. This may reflect the financial constraints of using high-tech imaging systems for the purposes of research.

1.12.2 CT Studies of the Anatomy of the Wrist.

The normal anatomy of the wrist has been investigated using computed tomography by various authors (Cone et al. 1983; Quinn et al. 1989; and Zucker-Pinchoff et al. 1981). There is general agreement that trans-axial imaging is the most useful for imaging the carpal tunnel. Sagittal and coronal images were possible, the manoeuvrability of the wrist allows orientation in the correct planes within the system. The carpal bones were clearly defined on the images, to such an extent that they could be identified by their shape and form. The osseous borders of the carpal tunnel were visible, but the tendons were not as clear although they were visible. Other soft tissue structures were less well defined.

Validation of the image interpretation was achieved by comparison with cadavers by Zucker-Pinchoff et al. (1981) and Cone et al. (1983). Images of the cadaver were obtained and the cadaver wrist was frozen and sliced. It was not disclosed in the literature whether the image interpretation was made before or after comparison with the cadaver slice. The latter is suspected, thus in terms of validation, a retrospective interpretation after comparison with the cadaver wrist is of no use. As mentioned in section 1.11.7 (with regard to MRI) the interpretation of complex images such as these may only be made by the most learned observers. Structures seen in the image slice may not be identifiable without prior knowledge of its position in the cadaver. The interpretation of the images of living subjects wrists would not have this comparison available, so identification of structures would be more vague.

Measurements of normal wrist interior dimensions are available from some studies.
Literature Review

(Zucker-Pinchoff et al. 1981; Cone et al. 1983; and Quinn et al. 1989), others have progressed to comparisons of the normal dimensions with those of cases (table 1.20). Distal carpal tunnel cross-sectional areas of normal wrists range from $1.46 \pm 0.07 \, \text{cm}^2$ for females to $2.54 \pm 0.078 \, \text{cm}^2$ for males (table 1.20). The variation in the studies is small, even considering the small number of subjects used in some. (3: Bleecker et al. 1985; and 4: Merhar et al. 1986).

Table 1.20 Carpal Tunnel Cross-sectional Areas (cm$^2$) and Standard Errors (SE) calculated from Computed Tomography Images.

<table>
<thead>
<tr>
<th>Author</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>No.</td>
</tr>
<tr>
<td>Dekel and Coates 1979</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>12</td>
</tr>
<tr>
<td>Dekel et al. 1980</td>
<td>26</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>19</td>
</tr>
<tr>
<td>Bleecker et al. 1985</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Merhar et al. 1986</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>9</td>
</tr>
<tr>
<td>Liang</td>
<td>15</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>62</td>
<td>50</td>
</tr>
<tr>
<td>Schmitt et al. 1988</td>
<td>5</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>31</td>
<td>19</td>
</tr>
</tbody>
</table>

(+ SE not reported)

Similar methods were used by all authors to obtain the measures of wrist cross-sectional areas. The images were displayed and then analysed using a digitiser. The carpal tunnel was mapped out using the cursor on the computer and the area calculated. The only way of accounting for the palmar surface of the carpal tunnel was to draw a line directly across from the hook of the hamate to the trapezium bone. This did not take
Literature Review

into account any bowing of the flexor retinaculum. This would have occurred when the
wrist became more congested, leading to compression of the median nerve. The
dimensions were only those of the osseous borders of the carpal tunnel and did not
involve and soft tissue, which may have encroached into the carpal tunnel.

Dekel et al. (1980) and Liang (1987) found that there were differences between the two
hands of their control subjects, but these differences were not significant. No study
gave details of the method of determining which hand was the dominant. Indeed, Liang
(1987) merely classified the sides as left and right, without any consideration of hand
dominance. Male carpal tunnels were consistently larger than those of females (table
1.20) the greatest difference was 0.679 cm² (Merhar et al. 1986).

Comparisons between cases and controls have been made but the results are conflicting.
All of the cases in the literature were diagnosed using electrophysiological tests, except
the Liang (1987) study where symptomatic diagnosis were made. Dekel et al. (1980);
Bleecker et al. (1985); and Liang (1987) found the cases' carpal tunnel cross-sectional
areas to be significantly smaller than the controls (table 1.20). Others found no
difference between the cases and controls (Dekel and Coates 1979; Merhar et al. 1986;
and Schmitt et al. 1988). The validity of the results of some of the studies is in doubt
because of the small numbers of subjects involved, although the standard errors of the
measures are very similar. The validity of the image analysis method was in question as
no validation of the methods was reported. There is clearly a need for further research
in this field to confirm the results already obtained.
1.12.3 Other disorders.

Computed tomography has been used to image other disorders of the wrist including scaphoid fractures (Bush et al. 1987) and a variety of other fractures of the carpus; paint in the soft tissue of the hands after a spray gun explosion; Neurofibroma and Giant cell tumours by (Quinn et al. 1989). These disorders are most commonly concerned with bony or structures opaque to x-rays, these are ideal for computed tomography imaging.
1.12.4 X-ray Imaging.

Conventional radiography using x-ray profiles of the carpal tunnel have been reported in the literature, even though its use is of limited value. The carpal tunnel may be imaged using conventional techniques, if the carpal bones of interest can be presented in a position where the radiologist can obtain a profile of the volar surface of the bones. This was achieved by Wilson (1954) by placing the wrist on the roentgenographic plate and holding the wrist in flexion of 60°. The central ray was directed along the longitudinal axis of the third metacarpal. The x-rays could penetrate the soft tissue of the hand and wrist, while a profile view of the volar aspect of the carpal bones could be seen. An alternative technique was employed by Templeton and Zim (1964) and Fodor et al. (1987), the palm of the hand was placed on the reontgenographic plate and the wrist held in hyperflexion of 90°. The x-ray tube was positioned at an angle of 50° to the plate. A profile view of the volar aspect of the carpal tunnel was obtained, showing the bony surfaces of the carpal tunnel.

Wilson (1954) reported some injuries that resulted in encroachment on the carpal tunnel. These were detected using conventional radiography. They were without exception of an osseous nature, comprising of; fractures or dislocations of the carpal bones; or in one case the presence of a separate ossicle of bony density inside the carpal tunnel. There have been no reports in the literature, of the detection of any soft tissue abnormalities resulting in carpal tunnel syndrome using conventional x-ray techniques. Indeed, Fodor et al. (1987) stated that routine radiography is unsatisfactory for the evaluation of soft tissues.

The are a small number of cases where bony abnormalities could be the underlying cause of the carpal tunnel syndrome. In these cases the x-ray profile view could be useful in diagnosis, although soft tissue abnormalities should be investigated first.
1.12.5 Ultra Sound Imaging.

Ultra sound was used to image peripheral nerves, including the median nerve, by Fornage (1988). The normal anatomy of the median and ulnar nerves in the forearm was demonstrated and lesions of the median nerve at the wrist were detected using ultra sound. The comparison of cadaver wrist, with the nerves injected with China ink, was performed to confirm the detection of the median nerve. The technique was of most value for the detection of nerve tumours. No quantitative data were available in the literature, perhaps as a result of the poor resolution of the images.
1.13 Summary of the Literature.

CTS is a commonly encountered median nerve compression syndrome at the carpal tunnel. It is recognised by a variety of signs and symptoms, all of which may be employed to aid the diagnosis of the condition. It is caused by compression of the median nerve within the anatomical confines of the carpal tunnel. There are various systemic and local factors which may contribute to this compression.

Many diagnostic tests are at the disposal of the physician when attempting to investigate possible CTS. Some are more useful than others. It is widely agreed that electrophysiological tests, particularly those of sensory function are the most sensitive tests available.

MRI has been used in the past to image wrists and the carpal tunnel. However, no studies have been reported which directly compare the carpal tunnels of cases and controls. Since MRI allows the imaging of soft tissue structures, which are so important in CTS, there is a need to examine differences between cases and controls using MRI.

Other imaging techniques have been employed to image the carpal tunnels of cases and controls. Early results from computed tomography imaging suggested that cases had smaller carpal tunnels than controls. More recent studies have contradicted those early studies. There is a need to examine the difference between the sizes of carpal tunnels of cases and controls in more detail.

Case controls studies offer the examiner a means of assessing differences between diseased and non-diseased individuals, both cheaply and efficiently.
1.14 The Aims of the Study.

In order to establish whether differences could be identified between the carpal tunnel dimensions of cases and controls (in particular the carpal tunnel cross-sectional areas). The following aims were set out.

i. Develop a system and imaging procedure to collect MRI axial wrist images from a group of cases and controls.

ii. Develop a method of analysing and obtaining spatial information from the images.

iii. Test the system and analysis reliability.

iv. Examine differences between control individuals, including their dominant and non-dominant sides.

v. Examine the differences between the carpal tunnel dimensions of cases and controls.

vi. Address the issue of compression of the median nerve; *vis-a-vis* the boundaries of the carpal tunnel pressing in on the contents and compressing the median nerve; or the contents of the carpal tunnel increasing in volume, thus increasing the pressure on the median nerve.
2 THE PILOT STUDY.
2.1 Introduction to the Pilot Study.

Appendix II describes the system developments which were made to enable wrist imaging to be successfully carried out. The development of a wrist coil and a comfortable wrist imaging position were the major components of this system development. Other minor changes are described in more detail in section 2.3.1. Before any research into wrist imaging could be embarked upon, the system had to be evaluated; this was done to check that a reliable methodology for imaging wrists and analysing the images was being employed. This evaluation involved confirming that:

i. The correct slice could be selected within the image set, once the subject had been correctly positioned in the system and the images captured.

ii. The images could be analysed using a reliable and reproducible technique.

iii. The system was capable of operating for a period long enough for a major study to be carried out, without excessive down time.

It was decided to evaluate these aspects of the system by imaging the wrists of a group of asymptomatic controls, ie. individuals who had none of the signs and symptoms of CTS mentioned in section 1.2. These control subjects were selected from staff and students of the University of Surrey. Once the reliability of the slice selection and image analysis techniques had been evaluated and the reliability of the technique confirmed, the data from the control images were analysed, to test for differences in the wrist and carpal tunnel dimensions. These data were required in the design of the main study, in which differences between cases (with the symptoms) of CTS and controls (without the symptoms of CTS) were to be investigated.

This chapter gives a detailed account of the aims and hypotheses of the pilot study, the methodology employed and presents the results of the reliability and anthropometric studies. The results of the image analysis, along with implications for the main study are discussed.
2.2 The Aims of the Pilot Study.

The overall aim of the pilot study was to prepare the methodology and analysing technique for the main study, which would compare the wrist images of cases and controls. To achieve this the following aims were set out;

2.2.1 To evaluate the imaging method; two aspects of the imaging system and method had to be tested:

   i. The ability to obtain the correct slice position.

   ii. Confirmation that a group of individuals could be successfully imaged, without undue discomfort to the subjects or excessive system down time.

2.2.2 To evaluate the Intra-observer reliability of the image analysis by testing the following null hypotheses;

   i. Repeated measures taken on the same occasion will exhibit no significant differences. Three measures were taken for each variable on each of the analysis occasions. These measures were analysed using an analysis of variance, to test for differences between the three measures.

   ii. Measures taken on two separate occasions will exhibit no significant differences. A selection of images were analysed on a later date in the same manner as the originals. The two sets of data were compared using an analysis of variance.

2.2.3 To examine the asymptomatic controls data and test the following null hypotheses relating to hand dominance.

   i. There will be no significant differences between the dominant and non-dominant linear wrist dimensions.

   ii. There will be no significant differences between the dominant and non-dominant linear carpal tunnel dimensions.

   iii. There will be no significant differences between the dominant and non-dominant wrist area dimensions.
iv. There will be no significant differences between the dominant and non-dominant carpal tunnel area dimensions.

v. There will be no significant differences between the dominant and non-dominant area dimensions when the carpal tunnel is expressed as a percentage of the wrist area.

(Note: Linear dimensions relate to the measurement (in cm) of 1 dimensional variables, eg. wrist width. The area measures refer to the cross-sectional area measures such as wrist cross-sectional area. The wrist measurements refer to the wrist outer boundaries as identified on the image, whereas the carpal tunnel measures refer to the internal measures of the carpal tunnel as defined in section 2.3.6. The dominant wrist was that considered to be dominant by the subject. No tests of hand dominance or hand preference were administered.)
2.3 The Pilot Study Method.

2.3.1 Equipment.

The Imaging System.

The MR imaging system used in the study was the 0.15 Tesla, whole body system in the Department of Physics at the University of Surrey (plate 2.1). A full explanation of the system is given in Appendix II.

The subject position was considered to be important, as any movement by the subject during the imaging session would result in reduced image quality. Other studies paid little attention to the comfort of the subject. Weiss et al. (1986b) noted that subjects suffered discomfort during the imaging session, the subject's arm often "fell asleep", where the arm was positioned above the subjects head within the coil (section 1.11.4).

It was thought that a more comfortable position could be assumed by positioning the coil and its mounting under the level of the bed. The subject's body was supported on foam blocks (plate 2.2). The edge of the block, in the angle of the elbow, was shaped to allow access to the coil by the smaller subjects.

The wrist being imaged was held firmly inside the coil by soft foam packing, the other arm was free to allow the attainment of a comfortable head position. Two pillows were arranged by the subject, with the help of the operator, until a comfortable position was attained.
Plate 2.1 The Imaging System at the University of Surrey.

Plate 2.2 The RF Coil and Perspex Mount.
The subject's arm was supported on the perspex plinth, which housed the RF coil, mounted on a set of sliding rails (plate 2.2). This allowed the alignment of the coil, so that the centre of the coil was aligned with the centre slice of the multi-slice sequence. The coil mount was secured to the bed with strips of Velcro, thus the coil could be removed easily for realignment when the opposite wrist was to be imaged. The base of one of the blocks was hollowed out to allow the braided radio frequency (RF) wire to pass under the blocks for connection to the RF system. The centre slice for each side was 90 mm from the centre of the bore.

The arrangement of the bed, shown in plate 2.1, was used to image the left wrist. When the other side was to be imaged, the coil and bed arrangement was changed to accommodate the subjects' other wrist. The blocks around the coil and the coil housing were removed from the bed. The coil and its mounting were rotated through 180° and repositioned on the bed. The blocks were repositioned to allow the subject's arm access to the coil and the blanket and pillows arranged for the subject to lie comfortably.

The sequences were selected on the basis of the work carried on phantoms, human volunteers and pigs trotters (see appendix II). The experiments included testing the different sequences, including saturation recovery, density and inversion recovery. The saturation recovery and density sequences were the most appropriate, given the best definition of the tissue surrounding the tendons.
The image consisted of a 128 x 128 matrix, with a slice thickness of 0.5 cm and inter-slice gap of 0.2 cm; the field of view measured 19.8 x 19.8 cm; spatial resolution within the plane was 0.15 cm.

A multi-slice sequence (TE 35 ms, TR 2500 ms) was used to obtain five images from each of the subjects wrist, thus 10 images were obtained from each subject. Section 1.11.1 gives the ranges of TR and TE used by other studies. The sequences used here were within these ranges. Two averages were taken, resulting in a total imaging time of just over 10 minutes (128 x 2 x 2500 ms) for each wrist. The subject spent an additional five minutes (on average) in the apparatus, in order to allow for tuning of the signal. A more complete description of the technical aspects of the imaging theory is given in the appendix II.
2.3.3 Subject Population and Selection Criteria.

The subjects were selected from the staff and students of the University of Surrey. In total 29 volunteers were selected, comprising of 14 males and 15 females with mean ages of 28.00 (sd 7.3) and 28.47 (sd 10.3) respectively. The subjects were all imaged between March and July 1988.

Exclusions.

Individuals who had experienced the signs and symptoms of CTS, as described in section 1.2, were excluded from the study, as were those with heart pacemakers fitted or any large metal implants.
2.3.4 Procedure.

The nature of the imaging system and the aims of the study were explained to all potential subjects before asking them to volunteer for the study. They were asked to attend the MRI Unit in the Physics Department, on an agreed date and time. All subjects were advised to wear loose fitting clothes.

Imaging.

The system was prepared prior to the subject arriving at the laboratory. The magnet was put on resonance and a test phantom imaged to check that the system was functioning correctly. Before entering the MRI laboratory each subject was again asked if they had been fitted with a heart pacemaker, metal implants or if they had any large metal objects or credit cards about their person. They then entered the MRI laboratory and were acquainted with the imaging equipment. Their clothing was checked for any magnetic materials, such as steel zips or clips as these would distort the field during the imaging session. The subject was asked to remove any such articles of clothing, if they were close to the wrist or abdomen. A dressing gown was available if articles of clothing had to be removed.

To aid the positioning of the wrist in the apparatus, the hand length of the subject was measured with a perspex ruler, from the distal wrist crease to the tip of the third digit. The coil orientation was altered to allow the appropriate wrist to be imaged and the patient bed and blankets were arranged to allow the subject to lie on the bed in comfort. When imaging the left wrist the coil was mounted on the right hand side of the bed, as shown in plate 2.1.

The subject was asked to lie face down on the bed, with their wrist in the coil situated underneath their abdomen. The wrist was positioned using the hand length and marks on the bed. By lining up the tip of the third digit on a marker corresponding to the hand length, the required part of the wrist could be positioned in the centre slice of
the multi-slice sequence. Some of the smaller subjects found it difficult to reach the required imaging position because their forearms were too short. By moving the shoulder down towards the foot of the bed all of the subjects managed to obtain the required position. The wrist was secured by packing foam in between the wrist and coil. The elbow was supported by a flat sheet of foam for comfort. After checking the position of the finger tips a final time, the subject was pushed into the bore of the magnet on the sliding bed and the coil connected to the apparatus.

When the subject was ready to be imaged and in position the signal "setup" programme was initiated, providing the operator with a trace of the signal on the oscilloscope and the Masscomp computer graphics monitor. The system preparation and "setup" programme are described in appendix II. It essentially produced a 90° and 180° pulse, along with the slice selection and frequency encoding gradients. The signal entering the Masscomp could be monitored on the oscilloscope, while the SCANTEST programme on the Masscomp provided a self scaling graphical representation and a one dimensional Fourier Transformation of the signal. This gave a one dimensional projection of the slice to be imaged. The coil was tuned on the signal and adjustments made to the attenuation of the RF pulses, to obtain the most optimum signal. Different subjects tended to load the coil in different ways so the coil was tuned for each individual. The multi-slice density sequence was then started.

During the imaging session the subject was asked to provide the operator with the following information; Height, weight, date of birth and dominant hand. The operator regularly checked the subject during the imaging session, not only to reassure the subject, but also to make sure that they did not move whilst the image was being captured.

On completion of the imaging sequence the subject was removed from the system and
the images described to them. The bed was rearranged to allow the other wrist to be imaged and the process repeated for the opposite wrist.

2.3.5 Image Storage.

The hard disc of the masscomp computer would only allow 10 images to be stored at any one time. It was laboratory policy to transfer all images to 5.25 inch floppy discs at the end of each imaging session, in order to alleviate this disc capacity problem. It had the added benefits of keeping the imaging directory tidy and also ensuring that data were stored immediately after collection, thus reducing the chance of data corruption or loss.

2.3.6 Image Analysis.

Images were analysed using the system Masscomp computer. The five images collected for each wrist were displayed on the graphics monitor, so that the slice position could be confirmed. The image for analysis was selected using the following criteria:

i. The most distal portion of the carpal tunnel had to be present in the image.

ii. The tendon of flexor carpi radialis was identified in the selected image. By comparison with the images either side of the selected one, the tendon path could be traced and its insertion found. The required image was just proximal to the insertion of flexor carpi radialis.

This image selection procedure was necessary because of errors in the automatic image labelling procedure on the computer. Normally the computer would suffix each of the image filenames with a number from one to five. The centre slice would be labelled number 1 and the other slices 2–5 according to the order of slice excitation order. Fig 2.1 shows how the images would be labelled normally.
Appendix II explains how the RF excitation and image data collection were controlled by separate computers. The Data General computer sent a "get data" signal to the masscomp computer, this informed the masscomp to start collecting data. It was believed that this signal sometimes failed to reach the masscomp because of a connection fault. Thus, the two computers would sometimes go out of sequence with each other. If this happened the image numbering sequence may have changed and the centre slice would no longer be suffixed with a number 1. Thus the image order had to be checked before selection, to avoid choosing the wrong image for analysis.

Once the correct image had been selected, the image was displayed using maximum magnification available with the computer software and graphics monitor (Double magnification). The computer mouse was used to position the graphics cursor in the required position; a single click on the left button allowed the position of the mouse to be recorded and a line was formed between that old cursor position and the new cursor position. The cursor was then moved to the next required position, where another click again recorded its position. The computer calculated the length of the line, between the
two points, using Pythagoras' theorem. This allowed linear measurements in pixels to be taken directly from the image data set.

Areas were calculated in a similar way. The mouse was used to move the cursor around the region of interest, clicking the left button of the mouse fixed the line in the position, where the next line would be produced from. Pressing the right and left mouse buttons together, completed the area by connecting the first and last recorded cursor positions. The computer calculated the area within the lines mapped out, the number of pixels inside the area was displayed. The average intensity of the pixels within the area was also displayed, these data could be used later for the calculation of the relaxation times of the sample.

Six variables were recorded from each of the images selected for analysis. The width and depth of the wrist and carpal tunnels were obtained using the linear measurement technique. Cross-sectional areas of both wrist and carpal tunnels were recorded using the area measuring technique.

The borders of the carpal tunnel were determined by noting the lateral, dorsal and ventral borders, which were well defined. The medial border was less obvious, but could be determined by tracing the position of the tendon of flexor carpi radialis. This was considered the lateral border of the carpal tunnel. Quality was an important factor in determining the borders of the tunnel. Some images were not as sharp as others, in these images the borders of the tunnel were not as clear.
Fig 2.2 The wrist measures taken from the images.

The linear measures taken from the images correspond to those in fig 2.2 and are described as follows;

Wrist depth (WRDP):— the maximum distance from the dorsal surface to the ventral surface of the wrist in the coronal plane.

Wrist width (WRWD):— the maximum distance between the lateral and medial surfaces of the wrist in the sagittal plane.

Carpal tunnel depth (CTDP):— the maximum distance from the dorsal to the ventral surface of the carpal tunnel in the coronal plane.

Carpal tunnel width (CTWD):— the maximum distance from the lateral to the medial borders of the carpal tunnel sagittal plane.
Three repeat measures of each of the variables were taken on the initial image analysis session. On a subsequent session one month later, the images of six subjects were re-analysed using the same method.

These data were analysed using an analysis of variance (Crowder 1988) in order to identify any differences between:

i. The three measures taken at each session.

ii. The measures taken one month apart.

iii. The differences between the dominant and non-dominant hands for all of the variables measured.
2.3.8 The Calculation of the 95% Confidence Intervals.

The data for the dominant and non dominant sides for both sexes were entered into the computer data base. An analysis of variance was run on the statistical Packages for the Social Sciences (SPSSx 1983) package which allowed the author to assess the 3 conditions mentioned in the previous section.

In addition the 95% confidence intervals were calculated on those data. The following formula was used in the calculation;

\[
\text{mean} \pm \left( t_{0.025,v} \cdot \frac{s}{\sqrt{n}} \right)
\]

Where \( t \) is the value from the \( t \)-tables at the 0.025 level (Two tail 95%) at \( v \) degrees of freedom (\( n-1 \)), \( s \) is the sample standard deviation and \( n \) the number of samples.

The confidence intervals calculated were later converted from pixel counts into cm measures for comparison with other studies and the main study data.
2.3.9 Pixel Conversion Factor.
The image measurements were determined from the images in pixel counts, these were either linear pixel counts or total number of pixels in a given area. They were converted into cm and cm$^2$ respectively by multiplying by their conversion factors. The conversion factors were calculated by measuring the pixel values of an object of known dimensions (Dekel et al. 1980), a bottle phantom in this case, then performing the following simple calculation to obtain the cm equivalent of a pixel and cm$^2$ equivalent of the pixel area.

The diameter of the bottle phantom was measured using a pair of engineering callipers, the internal diameter was obtained by subtracting twice the bottle wall thickness from the external bottle diameter. The area could then be calculated using $\pi r^2$. The image diameter and cross-sectional area were then measured from the screen and the conversion factor calculated as follows:

Linear measures:

\[
\begin{align*}
&\text{Bottle diameter} = 2.175 \text{ cm} \\
&\text{Image diameter} = 54 \text{ pixels} \\
\rightarrow &\quad 1 \text{ pixel} = \frac{2.175}{54} = 0.04 \text{ cm}.
\end{align*}
\]

Area measures:

\[
\begin{align*}
&\text{Bottle diameter} = 4.6 \text{ cm} \\
&\text{Bottle area} = \pi r^2 = 16.61 \text{ cm}^2. \\
&\text{Image area} = 866 \text{ pixels} \\
\rightarrow &\quad 1 \text{ square pixel} = \frac{16.61}{866} = 0.0192 \text{ cm}^2.
\end{align*}
\]
(Due to magnification, 1 area pixel was equal to 4 linear pixels See Appendix III)

(Note that the linear and area conversion factors for the pilot study were calculated separately, due to an error discovered after the system had been updated. The system
modifications for the main study also meant the conversion factors had to be recalculated. The main study conversion factors are given in section 3.2.2.)
2.4 Pilot Study Results.

2.4.1 Intra-Observer Reliability Results.

The images of 6 subjects were re-analysed one month after the original set of 29 subjects images. Three repeat measures (repeats 1 to 3) of each variable were taken on each of the two occasions (occ 1 and 2). These data were then examined to test the reliability of the image analysis technique, the results are shown in tables 2.1 and 2.2. The standard errors are not reported, as the data sets contained male and female, along with dominant and non-dominant hand measurements. It has been demonstrated previously by Dekel et al. (1980) that significant differences exist between the image dimensions of males and females. It would not be appropriate to include the standard errors with these data as data from 2 populations with known significant differences are reported. Therefore large standard errors would be expected. The data were analysed using a matched design to overcome this problem.

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Repeat 1</th>
<th>Repeat 2</th>
<th>Repeat 3</th>
<th>F-ratio</th>
<th>sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrist width</td>
<td>7.42</td>
<td>7.40</td>
<td>7.39</td>
<td>2.171</td>
<td>ns</td>
</tr>
<tr>
<td>Wrist depth</td>
<td>5.33</td>
<td>5.31</td>
<td>5.34</td>
<td>4.564</td>
<td>ns</td>
</tr>
<tr>
<td>Carpal tunnel width</td>
<td>2.43</td>
<td>2.41</td>
<td>2.41</td>
<td>0.424</td>
<td>ns</td>
</tr>
<tr>
<td>Carpal tunnel depth</td>
<td>1.16</td>
<td>1.19</td>
<td>1.19</td>
<td>4.452</td>
<td>ns</td>
</tr>
<tr>
<td>Wrist area</td>
<td>23.69</td>
<td>23.65</td>
<td>23.64</td>
<td>1.390</td>
<td>ns</td>
</tr>
<tr>
<td>Carpal tunnel area</td>
<td>1.99</td>
<td>2.00</td>
<td>2.01</td>
<td>0.817</td>
<td>ns</td>
</tr>
</tbody>
</table>

The results of the analysis of the repeat measurements (repeat 1, repeat 2 and repeat 3) are shown in table 2.1. Although there were some differences found between the three repeat measures, these were not significant for any of the variables tested. There were
no significant differences found between the three measures (repeat 1, repeat 2 and repeat 3), which the observer collected on each of the two occasions of the analysis. This supports null hypothesis 2.1 that there would be no difference between the three repeat measures.

Table 2.2 Means (cm and cm²), F-ratios and their levels of significance (F_{0.025 1,5}) of the different occasion reliability.

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Occ 1</th>
<th>Occ 2</th>
<th>F-ratio</th>
<th>sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrist width</td>
<td>7.39</td>
<td>7.41</td>
<td>1.504</td>
<td>ns</td>
</tr>
<tr>
<td>Wrist depth</td>
<td>5.32</td>
<td>5.33</td>
<td>0.173</td>
<td>ns</td>
</tr>
<tr>
<td>Carpal tunnel width</td>
<td>2.42</td>
<td>2.41</td>
<td>0.013</td>
<td>ns</td>
</tr>
<tr>
<td>Carpal tunnel depth</td>
<td>1.20</td>
<td>1.15</td>
<td>4.834</td>
<td>ns</td>
</tr>
<tr>
<td>Wrist area</td>
<td>23.61</td>
<td>23.71</td>
<td>0.903</td>
<td>ns</td>
</tr>
<tr>
<td>Carpal tunnel area</td>
<td>2.03</td>
<td>1.97</td>
<td>2.007</td>
<td>ns</td>
</tr>
</tbody>
</table>

There were differences between the measurements recorded on the first and second occasions (table 2.2). However, when tested using an analysis of variance, none of these differences were found to be significant. This supported the null hypothesis 2.2 that there would be no significant differences between the measurements taken on the two separate occasions.

Some differences (although not significant) occurred in the area measurements, where any errors would be expected to be the greatest. The method for obtaining the area measurements required more subjective decisions concerning the image interpretation than did the linear measurements. The mapping out of the areas with the cursor provided another source of error, which the linear measures escaped. So the differences
found between the measurements on the two occasions were anticipated to be greater than the differences between the repeat measures. This was confirmed by the results in tables 2.1 and 2.2. It should be noted that carpal tunnel depth seemed to be one of the least reliable measures. This may be again due to the difficulty in interpreting the exact edges of the carpal tunnel, particularly on the palmar border.

In conclusion, the results of the intra-observer reliability study confirmed that the image analysis technique was reliable. This means that an observer, could analyse a set of images reliably, with repeated measures on the same occasion and on separate occasions up to one month apart. This reliability was considered adequate for the image data to be examined for anthropometric differences between the dominant and non-dominant sides.
2.4.2 Image Anthropometric Findings.

The linear and area measurements of the image were converted from pixel counts to cm and cm$^2$ respectively, by multiplying by the conversion factors described in section 2.3.9. The data reported here represents cm and cm$^2$ for the linear and area dimensions respectively. Pixel values are not reported.

The Linear Measures.

The linear measures are direct distances from one point to another on the image. For example the wrist depth would be the maximum distance from the mid point on the dorsal surface of the wrist, to the mid point of the palmer surface of the wrist. Section 2.3.7 describes the strategy for determining the position of these points.

Table 2.3 Means (cm), standard deviation (SE) and F-ratios of the pilot study linear measurement image analysis.

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Sex</th>
<th>n</th>
<th>Dom</th>
<th>Non-dom</th>
<th>F-ratio</th>
<th>sig</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mean</td>
<td>SE</td>
<td>Mean</td>
<td>SE</td>
</tr>
<tr>
<td>Wrist width</td>
<td>σ</td>
<td>14</td>
<td>7.71</td>
<td>0.13</td>
<td>7.68</td>
<td>0.12</td>
</tr>
<tr>
<td></td>
<td>φ</td>
<td>15</td>
<td>7.00</td>
<td>0.14</td>
<td>6.92</td>
<td>0.13</td>
</tr>
<tr>
<td>Wrist depth</td>
<td>σ</td>
<td>14</td>
<td>5.49</td>
<td>0.12</td>
<td>5.67</td>
<td>0.08</td>
</tr>
<tr>
<td></td>
<td>φ</td>
<td>15</td>
<td>4.85</td>
<td>0.08</td>
<td>4.94</td>
<td>0.11</td>
</tr>
<tr>
<td>Carpal tunnel width</td>
<td>σ</td>
<td>14</td>
<td>2.17</td>
<td>0.05</td>
<td>2.23</td>
<td>0.06</td>
</tr>
<tr>
<td></td>
<td>φ</td>
<td>15</td>
<td>1.96</td>
<td>0.07</td>
<td>2.00</td>
<td>0.07</td>
</tr>
<tr>
<td>Carpal tunnel depth</td>
<td>σ</td>
<td>14</td>
<td>1.23</td>
<td>0.06</td>
<td>1.27</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>φ</td>
<td>15</td>
<td>1.10</td>
<td>0.05</td>
<td>1.23</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Table 2.3 contains linear measurements from the 29 subjects wrists in the pilot study. 58 wrists were analysed, these were divided into two groups, the dominant and the non-dominant wrists for each subject. A multi-factorial analysis of variance was used to test the hypotheses 3.1 and 3.2.
No significant differences were found between the dominant and non-dominant wrists for any of the linear measurements in table 2.3. These results support the two null hypotheses being tested; there were no significant differences between the dominant and the non-dominant sides with respect to the linear measurements. The F-ratios in the table were compared with the \( (F_{0.05, 1,13}) \) and \( (F_{0.05, 2,14}) \) values for males and females respectively. Figs 2.3–2.6 show that the differences between the males and females were for most measures significant at the 95% level. Only carpal tunnel depth showed any major overlap of the confidence intervals. Also, there was a trend for the non-dominant measures to be greater than those of the dominant, except for wrist width (see fig 2.3) where the opposite occurred.
Fig 2.3 Mean dominant and non-dominant wrist widths (cm) and 95% confidence intervals of the pilot study male (▲) and female (X) controls subjects.
Fig 2.4 Mean dominant and non-dominant wrist depths (cm) and 95% confidence intervals of the pilot study male (△) and female (X) controls subjects.
Fig 2.5 Mean dominant and non-dominant carpal tunnel widths (cm) and 95% confidence intervals of the pilot study male (▲) and female (X) controls subjects.
Fig 2.6 Mean dominant and non-dominant carpal tunnel depths (cm) and 95% confidence intervals of the pilot study male (▲) and female (X) controls subjects.
The area measurements are contained in table 2.4 along with the differences between the dominant and the non-dominant wrists. Like the linear dimensions a multi-factorial analysis of variance was employed to test the null hypotheses 3.3 and 3.4, stating that there would be no difference between the cross-sectional areas of the dominant and the non-dominant carpal tunnels and wrists.

Considering only the wrists cross-sectional areas first, on the basis of the analysis of variance, there was no significant difference between the dominant and non-dominant wrist cross-sectional areas. This would lead us to accept the null hypothesis 3.3 there was no significant difference between the dominant and the non-dominant wrist areas. However, fig 2.7 shows graphically, that there was a trend for the non-dominant wrists to be larger than the dominant. Although this may have occurred by chance, it should be noted that the non-dominant wrist cross-sectional areas did appear to be larger than those of the dominant.

Table 2.4 Means (cm²), standard errors (se) and F-ratio of the difference between dominant and non-dominant sides of the pilot study area measurement image analysis.

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Sex n</th>
<th>Dom Mean</th>
<th>Dom SE</th>
<th>Non-dom Mean</th>
<th>Non-dom SE</th>
<th>F-ratio</th>
<th>sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrist area</td>
<td>14</td>
<td>25.39</td>
<td>0.82</td>
<td>26.37</td>
<td>0.65</td>
<td>3.251</td>
<td>ns</td>
</tr>
<tr>
<td>15</td>
<td></td>
<td>20.74</td>
<td>0.61</td>
<td>20.84</td>
<td>0.72</td>
<td>0.025</td>
<td>ns</td>
</tr>
<tr>
<td>Carpal tunnel area</td>
<td>14</td>
<td>1.81</td>
<td>0.08</td>
<td>1.98</td>
<td>0.06</td>
<td>5.938</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>15</td>
<td></td>
<td>1.53</td>
<td>0.09</td>
<td>1.75</td>
<td>0.09</td>
<td>6.902</td>
<td>p&lt;0.025</td>
</tr>
<tr>
<td>Carpal Tunnel</td>
<td>14</td>
<td>7.13</td>
<td>0.21</td>
<td>7.51</td>
<td>0.16</td>
<td>3.030</td>
<td>ns</td>
</tr>
<tr>
<td>Wrist ratio</td>
<td>15</td>
<td>7.47</td>
<td>0.48</td>
<td>8.46</td>
<td>0.40</td>
<td>3.332</td>
<td>ns</td>
</tr>
</tbody>
</table>

On examining the carpal tunnel cross-sectional areas, the results in table 2.4 provide
The Pilot Study

evidence to reject the null hypothesis 3.4. There were significant differences between the dominant and the non-dominant carpal tunnel cross-sectional areas:— the non-dominant carpal tunnels being larger than the dominant (fig 2.8).

When the area measurements were corrected for wrist size, by dividing the carpal tunnel measurement by the wrist measurement and multiplying by 100, there was no significant difference between the dominant and non-dominant sides (table 2.4). Although the trend is still apparent (fig 2.9), we would accept the null hypothesis 3.5 that there was no significant difference between the carpal tunnel area measures, when expressed as a percentage of the wrist area.
Fig 2.7 Mean dominant and non-dominant wrist areas (cm²) and 95% confidence intervals of the pilot study male (♦) and female (X) controls subjects.
Fig 2.8 Mean dominant and non-dominant carpal tunnel areas (cm$^2$) and 95% confidence intervals of the pilot study male (▲) and female (X) controls subjects.
Fig 2.9 Mean dominant and non-dominant carpal tunnel area wrist area ratios and 95% confidence intervals of the pilot study male (●) and female (X) controls subjects. (Ratio calculated by dividing the carpal tunnel area by the wrist area and multiplying by 100.)
2.5 Pilot Study Discussion.

The ability to select the correct slice from the image set was accomplished satisfactorily, although the assessment of this was difficult when the image quality was not of the same standard as those reported in the recent literature (Middleton et al. 1987). It was only by the subjective assessment of the set of 5 images in the multi-slice image set, that the correct slice could be selected. A detailed knowledge of the anatomy of the wrist and carpal tunnel was required. When assessing the image set and the ability to trace the path of a tendon through the course of a set of images was necessary. So, although the initial positioning of the wrist in the apparatus was important, the assessment of the images during the image analysis session had to be carried out by a trained operator, using the criteria for image interpretation referred to in section 2.3.6. This ensured that the correct slice was selected from the image set and that the boundaries of the carpal tunnel were correctly identified.

Variations in image quality did occur, hampering the image assessment further. However, it was considered that the slice selection was sufficiently accurate to confidently select the distal portion of the carpal tunnel.

The MRI system stability was also tested throughout the pilot study. It had to continue functioning for the duration of the data collection period, which lasted some 5 months. This is a long time for an MRI system to last without a failure of some description. There were problems encountered due to the deposition of calcium scaling in the magnet cooling system. This meant that the magnet had a tendency to "trip out" when the temperature reach a critical point, this usually occurred on hot days when the cooling system became overloaded. Towards the end of the pilot study the ambient temperature steadily increased, thus increasing the frequency with which the magnet "tripped out". This fault was later corrected by descaling the cooling system, no further "tripping out" problems were encountered.
Apart from the tripping out of the magnet, the system lasted well with the minimum amount of maintenance required. Broken cables sometimes disrupted imaging, but on the whole the system was considered to be reliable enough to warrant continuation on to the main study.

Subject comfort is a problem encountered with all types of wrist imaging. Other authors have reported difficulties in this respect (Weiss et al. 1986b and Baker et al. 1987). The position of the subject and the total imaging time are both important factors when considering subject comfort, section 1.11.3 expands the issue of subject comfort. It was important to assess in the pilot study if a control subject could be imaged without undue pain and discomfort. This did prove to be the rule rather than the exception, although some complaints about discomfort were made. These were mostly confined to complaints about the excessive heat in the MRI laboratory or discomfort in the arm not being imaged. One subject was anxious that the size of the magnet bore was too small, it was soon discovered that she suffered from claustrophobia. However, after further careful explanation of the nature of the system and guarantees from the author that someone would talk with her throughout the imaging session, she agreed to be imaged and no further problems were encountered.

The majority of the control subjects found the imaging position comfortable. In many cases the subject fell asleep during the imaging session.

Thus the first aim of the pilot study was satisfied, the system was stable enough to complete a study lasting a number of months without any major faults occurring. The correct slice could be selected from the image set, if the observer had a background knowledge of the anatomy of the wrist and carpal tunnel and a knowledge of the basic principle of MRI and what the images represented.
2.5.1 Intra-Observer Reliability.

The image analysis technique was tested for intra-observer reliability by examining data from 3 repeated measures, on 2 separate occasions. The 2 occasions were one month apart. The null hypothesis 2.1 was supported by the results of the analysis of variance in table 2.1. There was no significant difference between any of the repeat measures on either of the 2 occasions (p>0.025). This indicated that after the initial image interpretation was made, the observer could reliably analyse the image and obtain the linear and cross-sectional areas.

This was the first stage in testing the reliability of the image analysis. It was crucial that the observer could reliably measure what he perceived to be a particular dimension and if necessary repeat those measures and obtain the same results. Thus, the first aim of the reliability study was achieved. The observer's ability to reliably measure a particular dimension on one occasion was considered to be satisfactory.

The reliability of the observer's interpretation of the image was tested by examining the data collected on 2 separate occasions, one month apart. Table 2.2 shows that there were no significant differences between the first and second occasion measures when tested using a multi-factorial analysis of variance.

Unlike the previous test of the observer's ability to reliably measure the same dimension on the same occasion, this test of reliability required the observer to make an interpretation of each image on both occasions. This had to be done before the image could be analysed. It was expected that the reliability of the repeated measures would be better than that comparing the two different occasions. Indeed, with the exception of the carpal tunnel width, which had very good reliability on both tests, the carpal tunnel dimensions were measured with less reliability between occasions (F-ratio 4.834 and 2.007) than between repeated measures (F-ratio 4.452 and 0.817). This result was expected because the identification of the boundaries of the carpal tunnel, in particular
the palmar surface, was difficult. This difficulty in identifying the palmar surface of
the carpal tunnel could explain the greater variation in the carpal tunnel depth
measures.

The wrist dimensions were slightly less reliable for the repeated measures test (F-ratio
2.171 4.564 1.390) than for the different occasion tests (F-ratio 1.504 0.173 0.903). The
reason for this result remains unclear. There is no doubt that the wrist dimensions
required less interpretation than the carpal tunnel measures, however the greatest
differences expressed as F-ratios was found in the wrist depth measurement (F-ratio
4.564 and 0.173 respectively). The other measures were not considered to differ greatly.

Accepting that some differences did occur in the measurements on different occasions
and with repeated measures, these differences were not significant. It was thus
considered that the image analysis technique to be a reliable one. The issue of reliability
has been overlooked in the literature where wrist imaging is concerned. No reference to
the reliability of the measuring technique has been made in any of the papers reporting
the analysis of the carpal tunnel dimensions, whether the method of imaging was CT or
indeed MRI.
2.5.2 Image Anthropometric Measurements.

The linear measurements of the dominant and non-dominant wrist and carpal tunnel were compared using a multi-factorial analysis of variance. No significant differences were found between the dominant and non-dominant wrist measurements. Figs 2.3 and 2.4 show that there was no obvious trend for either the dominant or non-dominant wrist dimension to be the greater. This suggests that the dominant and non-dominant wrists for the controls were very similar in linear dimensions.

There was no significant difference between the dominant and non-dominant carpal tunnel linear dimensions. There was a trend for the non-dominant measurements to be larger than those of the dominant side (figs 2.5 and 2.6). This trend was particularly obvious in the case of female carpal tunnel depth, fig 2.6 shows the female non-dominant carpal tunnel depth to be noticeably bigger than the dominant side. Fig 2.6 also shows a similar trend for the male dimension but not of the same magnitude as the female.

Although there were trends for the non-dominant side to be larger than the dominant, there were no significant differences found for any of the linear measurements. The null hypotheses 3.1 and 3.2, stating that there would be no significant difference between the dominant and non-dominant sides for the carpal tunnel or wrist dimensions, would thus be accepted.

The wrist area measurements showed a similar trend, the non-dominant wrists were larger than the dominant ones, this was particularly evident for the male measurements as shown in fig 2.7. When tested using an analysis of variance, there were no significant differences found between the dominant and non-dominant sides, thus the null hypothesis 3.3 was accepted. However, when the carpal tunnel areas were examined, there was a significant difference found; the non-dominant carpal tunnel area was larger than that of the dominant. The significant difference found was evident for both
the male and female controls, thus we would reject the null hypothesis 3.4. These results conflict with those of Dekel et al. (1980), where no significant differences between the dominant and non-dominant carpal tunnels were found and there was a trend for the dominant carpal tunnel to be larger than the non-dominant.

It is interesting to note that the carpal tunnel cross-sectional areas were smaller than those reported in the Computerised Tomography studies given in table 1.20, both for males and females. This is expected as soft tissue on the boundaries of the carpal tunnel poorly imaged with CT. Thus these CT measurements would result in larger measures of cross-sectional area than the MRI method.

When the carpal tunnel areas were expressed as a percentage of the wrist cross-sectional area no significant differences were found between the dominant and non-dominant sides (we would accept the null hypothesis 3.5). However, the trend was still apparent, suggesting that even after normalising for wrist size, there was still a relationship between the carpal tunnel areas of the dominant and non-dominant sides.

The reasons for this difference in carpal tunnel area are unclear. Since the dominant side is usually the largest, it might be expected that this would be the case for the carpal tunnel as well, as found by Dekel et al. (1980) (but with no significant differences). This may however mean over simplification of the situation.

It is known that the dominant side carries out more of the skilled manual work than the non-dominant; hence the preference. This manual work may result in thicker ligaments and bones to hold the structures in position. For external structures this "laying down of material" would result in larger external measurements. However, for a structure such as the carpal tunnel, which is enclosed by bones on three sides and a ligament on the other, any build up of material such as inter-carpal ligaments would result a reduction
in the size of the carpal tunnel. These structures would not be noticed on the CT imaging systems as used in the Dekel et al. (1980) study, thus explaining why similar results were not found. If only the bones were observed, as in the CT studies, then only minor changes in the bone structures would be likely to be seen. MRI has the ability to image soft structures, such as those laid down with increased manual work.

This seemingly contradictory result has been explained in a logical manner. A build up of material on the dominant side would result in a reducing the cross-sectional area of the carpal tunnel. This may partly explain why carpal tunnel syndrome occurs primarily on the dominant side (Phalen 1966). It should be noted that this explanation is only a speculative one, more research will have to be carried out to investigate this further.

The results of the pilot study has important implications for the design of the main study. It was originally thought that unilaterally affected CTS patients could have both wrists imaged, the unaffected wrist could then be used as the control with which to compare the affected one. This would not be possible after considering the results of the pilot study, as differences are now known to exist between the dominant and non-dominant sides. Even when the carpal tunnel size is expressed as a function of the wrist size, differences were still found, although they were not significant. It was therefore thought that it would not be possible to used the patients unaffected side as the controls for the affected one.
2.5.3 Conclusions and Implications for the Main Study.

The imaging system and subject positioning proved to be reliable enough for use in the main study. The intra-observer reliability was also adequate for use in the main study. Differences were identified between the dominant and non-dominant sides, the linear carpal tunnel and wrist measurements were not significant but the carpal tunnel cross-sectional areas were significant (p<0.05). These results imply that cases unafflicted wrists could not be used as controls against their afflicted ones, later in the main study.
3 MAIN STUDY METHODS.
3.1 Introduction.

The methods of the main study were based on those of the pilot study. Some system modifications had to be made, primarily as a result of system faults which had developed since the pilot study, but also to improve the quality of the images.

Both cases' and controls' wrists were to be examined. In addition to the images, other data were collected. Comparisons were made between the cases and controls on the basis of a matched pair design. The extra details of the methods to those employed in the pilot study are described in the following chapter.
3.2 Equipment and System Modifications.

The imaging equipment used in the main study was the same as that used in the pilot study. Some equipment modifications were necessary to correct some of the system faults which had developed since the pilot study, as well as to improve the quality of the images. The system faults resulted in a total down time of almost 12 months, this greatly hampered the developmental work on the system.

3.2.1 Shimming.

The system magnet had been installed around a decade ago, the field quality of this resistive type magnet was not equal to that of the more recent super conducting types of magnet. The inhomogeneity of the field was at best 110 parts per million (ppm) and in places 476 ppm, within 20 cm of the region of interest (Pomeroy 1989). This had to be improved if proposed work on chemical shift breast imaging was to be carried out. It was hoped that after a programme of passive shimming the field inhomogeneity could be improved from 110 ppm, to less than 3.3 ppm. This would represent 20 Hz at the field strength of 0.15 T, which was the separation of the resonance frequencies of fat and water. The new study would attempt to perform chemical shift imaging, which required the separation of these two frequencies and an improved field inhomogeneity.

In order to achieve this aim, the field was plotted to assess the inhomogeneity across the bore of the magnet. On the basis of these field plots, the size and position of the passive shims were calculated. The passive shims were installed and the field replotted to assess the effectiveness of the shims.

The passive shimming was achieved using steel wire taped to the bore of the magnet. The size, shape and orientation of the shims were calculated using the data from the field plots. The process of plotting the field was very time consuming. It required the positioning of a water filled glass phantom in the field, a 90° pulse at a repetition time of 1 second was then applied. The frequency of excitation was then varied by 50 Hz at
a time until the signal was considered to be on resonance. This frequency was recorded. This was repeated for each of the plot positions in the field. The system was inoperational for several months for the field plotting, but it was thought that the results justified the effort.

The field inhomogeneities before and after shimming are shown in table 3.1. The shimmed values for positions more than 5 cm from the centre slice position were not calculated, because the image slices were all within 5 cm of the centre slice. The inhomogeneity in the centre of the imaging plane at a radius of 10 cm, was improved from $110 \pm 16$ ppm to $16 \pm 16$ ppm. This did not achieve the required inhomogeneity of $3.3$ ppm as required for chemical shift imaging, although the field was improved. The chemical shift imaging project was thus abandoned until a field with less inhomogeneity became available.

<table>
<thead>
<tr>
<th>Z (cm)</th>
<th>Preshimming (ppm)</th>
<th>Shimmed (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-15</td>
<td>157</td>
<td></td>
</tr>
<tr>
<td>-10</td>
<td>86</td>
<td></td>
</tr>
<tr>
<td>-5</td>
<td>98</td>
<td>28</td>
</tr>
<tr>
<td>0</td>
<td>110</td>
<td>16</td>
</tr>
<tr>
<td>5</td>
<td>130</td>
<td>39</td>
</tr>
<tr>
<td>10</td>
<td>149</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>208</td>
<td></td>
</tr>
</tbody>
</table>
3.2.2 The Gradient Digital to Analogue Convertors (DAC).

A fault during the maintenance of the original DAC box resulted in the damage of the DAC chips. These could not be replaced so a new DAC box was constructed. It incorporated variable resistors, so the gradients could be altered quickly. The author had recorded the gradient outputs before the damage to the prototype DACs, so the output for the new DAC box just had to be matched to the old gradient strengths for imaging to continue. Fine tuning of the gradient strengths was then carried out using phantoms, to optimise the image quality under the new conditions.

A phantom of known dimensions was imaged. The Z gradient was set to achieve the same slice thickness as before. The frequency and phase encoding gradients were then altered, until an image of the correct size and shape was obtained. All values were then converted from pixels to cm for comparison with other studies.

The pixel correction factor was calculated in the same way as in the pilot study (section 2.3.9). A phantom of a known dimension was imaged and the correction factor calculated as follows:

Linear measures:

\[
\begin{align*}
\text{Bottle diameter} & = 5.6 \text{ cm} \\
\text{Image Diameter} & = 144.5 \text{ pixels} \\
\rightarrow 1 \text{ pixel} & = \frac{5.6}{144.5} = 0.039 \text{ cm}
\end{align*}
\]

Area measures:

\[
\begin{align*}
\text{Bottle diameter} & = 5.6 \text{ cm} \\
\text{Bottle area} & = \pi 2.9^2 = 24.53 \text{ cm}^2 \\
\text{Image area} & = 1059 \text{ pixels} \\
\rightarrow 1 \text{ square pixel} & = \frac{24.53}{1059} = 0.0232 \text{ cm}^2.
\end{align*}
\]

(Due to magnification, 1 area pixel was equal to 4 linear pixels See Appendix III)
3.2.3 The Centre Slice Position.

The centre slice was altered after the system faults had been rectified and the magnet had been shimmed. The advantages for changing the slice position follow;

i. The field strength of the centre slice was slightly changed by the shimming, so the resonance frequency of the centre slice also changed according to the larmor relationship (equation II.3).

ii. The shimming improvements explained in section 3.2.1 resulted in better homogeneity in the centre of the field. In order to make use of this improvement, the centre slice for the wrist imaging sequences repositioned in the area of the field with the lowest inhomogeneity.

iii. The subject had easier access to the coil once in position on the bed. The subjects did not have to push their arm quite as far into the coil as in the pilot study, thus access was be made easier, particularly for the smaller subjects (Appendix II).

In order to change the centre slice position the frequency of excitation had to be changed in the Data General sequence programmes. This meant changing the frequency codes in the fortran programmes used for imaging and then compiling the programme codes. The slice position then had to be checked by running an image of a thin phantom. Once the single slice code was established, the multi-slice codes were set up and the slice positions confirmed with the multi-slice sequence. The programmes used by the Data General to control the sequences and the gradients and described in appendix II.
3.2.4 Sequences.

Two sequences were used with different numbers of averages;

i. A saturation recovery sequence with one average was first used to assess the position of the subject's wrist. It consisted of TE 35 ms and TR 500 ms. Only one average was taken making the imaging time 64 s.

The saturation recovery sequence was used with TE 35 ms, TR 500 ms and five averages. The imaging time was 5 minutes 20 s.

ii. The multi-slice sequence was then used to obtain five images with TE 35 ms, TR 2000 ms. Three averages were taken resulting in a imaging time of 12 minutes and 48 s.

The total imaging time was 19 minutes. The total time the subject spent inside the magnet was approximately 25 minutes, as time was taken to tune the signal and run the imaging sequence programmes.
3.3 Subjects.

3.3.1 Cases.

*Population*: The cases were selected from two groups;

i. Patients referred for surgery for carpal tunnel syndrome, at the Orthopaedic department of the Royal Surrey County Hospital;

ii. Staff of the University of Surrey who had responded to advertisements, in the University press, for people suffering with CTS.

The case group consisted of 3 males and 7 females with mean age 47 (sd. 9.63).

*Case Selection Criteria.*

The cases had to satisfy the following case selection criteria before they were asked to partake in the study.

i. Age:- 18 to 65 years of age.

ii. Previous Medical History:- Cases were excluded if they had experienced the following; surgery to the wrist in question, cortisone injections in the wrist or fractures to the wrist.

iii. Electrophysiological tests:- a median nerve distal motor latency of greater than or equal to 4.5 ms. University cases did not have the nerve conduction velocities measured.

iv. Symptoms:- the signs and symptoms of the carpal tunnel syndrome at the time of the study, as described in section 1.2.
3.3.2 Controls.

Population: The controls were selected from the staff of the University of Surrey.

A with the case group the control group consisted of 3 male and 7 females with mean age 49.6 (sd. 8.51).

Control Selection Criteria.

The cases the controls had to satisfy the following selection criteria before they were asked to partake in the study.

i. Age:- 18 to 65 years of age.

ii. Previous Medical History:- subjects with a history of carpal tunnel syndrome, any surgery to the wrist or any wrist fractures were excluded.
3.3.3 Matching Criteria.

The cases and the controls were matched as follows:

i. By gender.

ii. By hand dominance: Gross hand dominance assessed by asking the subject which was their dominant hand.

iii. By age: The controls were matched with cases, to be within ± five years of the cases' age. It was not possible to match one of the cases with a control within the age band. The particular case was left-handed and the only left-handed control who volunteered for the study was 11 years older than the case.

3.3.4 Exclusions.

Subjects with heart pace makers or metal implants were excluded from the study.
3.4 Procedure.

3.4.1 Subject Identification.

Hospital Cases.

The hospital cases were identified from the waiting lists of the orthopaedic surgeons at the Royal Surrey County Hospital. Any suitable cases were contacted by post via Mr John Older (Orthopaedic Surgeon). Each letter was followed up shortly afterwards by telephone, when an appointment for the experimental work was made. A copy of the letter sent to the cases given in appendix III.

University Cases.

The cases from the University were selected by their response to various advertisements in the university press and on departmental notice boards. They were contacted and interviewed by the experimenter, suitable cases were identified and an appointment made.

Controls.

The controls were identified from members of the University staff who satisfied the selection criteria and who were appropriate under the matching criteria. They were approached in person and asked to volunteer for the study.

3.4.2 Preimaging Subject Interview.

Both the cases and controls from were interviewed in exactly the same manner once the appointment had been made. Each subject was sent a letter and a map of the University (appendix III). The letter contained background information about how long the session would last, the principles of MRI, the equipment to be used and a reminder of the restrictions on heart pacemakers, credit cards and large metal implants. The subjects were also reminded to wear lose fitting clothes with no metallic zips or fastenings for the imaging session.
3.4.3 Imaging.

The imaging procedure for the main study was the same as that of the pilot study, except for the following details.

Due to changes in the frequency of excitation the centre slice was nearer to the centre of the bore of the magnet. This made it more difficult for the subjects to enter the magnet with the coil under the abdomen, as in the pilot study. This resulted in more coil interaction with the body. It was decided that the coil should be moved to a position used before the pilot study. The coil was placed above the subjects head who could lie with the wrist in the coil positioned above their head. This reduced the interaction from the body and allowed easier access to the bore of the magnet. Subject comfort was compromised and the feeling of claustrophobia exacerbated. However, due to the size of some of the subjects and the interaction of the body with the coil, this was the only option.

A saturation recovery sequence was then run to check the slice position once again. If this was not satisfactory the subject was removed from the magnet and repositioned. The process was repeated until the correct slice position was obtained.

A multi-slice sequence (TE 35 ms TR 2000 ms with 3 averages) was then run followed by a saturation recovery sequence (TE 35 ms TR 500 ms with 5 averages).

While the subject was being imaged the examiner regularly checked to see if the subject was comfortable and content to complete the imaging session. If the subject preferred to sleep whilst being imaged, they were left to do so until the imaging sequence had finished. If not, the examiner asked the subject the questions on the questionnaires, beginning with the main questionnaire. The questions requiring the subject to shade in areas on the manikins were left until after the imaging session. Subjects who wanted to sleep during the imaging were asked the questions after the imaging session. The
occupational checklists were asked in a later session after the anthropometric measures were collected.

On completion of the imaging sequences, the subject was removed from the system and allowed to recover completely whilst viewing the images. The process was then repeated for the opposite wrist.
3.4.4 Questionnaire Application and Anthropometric Measurements.

The subjects were taken to another laboratory to be interviewed and measured after the imaging had been carried out.

Anthropometric Measurements.

Wrist breadth. Two wrist breadth measures were taken from each wrist:

i. Wrist Breadth styloid (Sliding callipers): Breadth taken across the styloid process (oblique to the long axis of the arm) with pressure to compress the tissues (Weiner and Lourie 1981).


Wrist depth (engineering callipers):- Maximum distance parallel to the wrist axis of radial-ulnar rotation over the distal wrist crease (Armstrong and Chaffin 1979).

Wrist circumference (steel tape measure):- With the tape passing just proximal to the styloid process of the ulnar, the minimum circumference was measured. (Weiner and Lourie 1981)

Hand length (steel tape measure):- Distance of long axis of the third digit, from the distal wrist crease to the distal end of the straight third digit. (Weiner and Lourie 1981)

Palm width (sliding callipers):- Maximum distance between the lateral surfaces of the second and fifth metacarpophalangeal joints (Armstrong and Chaffin 1979).

Forearm length (anthropometer):- Marked head of the radius to the tip of the radial styloid (Weiner and Lourie 1981).
The proximal interphalangeal (PIP) joint angle was then measured. The PIP joint of the second digit was fully flexed and the angle between the dorsal sides of the proximal and middle phalanx was measured with the custom built goniometer shown in plate 3.1. The maximum joint angle of the metacarpophalangeal (MCP) joint whilst maximally flexed without assistance, was measured in the same manner.

Plate 3.1 Goniometer for PIP and MCP measurements. Demonstration of the method of use.

The grip strength maximum voluntary contraction (MVC) was measured with the Robens Dynamometer. The subject stood supporting the dynamometer with the hand not being tested. After explaining the apparatus and the procedure to the subject, the examiner told the subject to provide an all out maximum effort after the count of three and held for a count of two (Randle 1988). The load cell in the dynamometer measured
the maximum force output in Kg. No feedback was given to the subject at any stage of the MVC tests.

The measures where then repeated for the right hand side. All of the results were recorded on the results sheet in appendix III.
Measurement of Nerve Conduction Velocity.

All nerve conduction velocities were carried out at the Neurology department of St Lukes Hospital Guildford. A full analysis was carried out by the neurologist including sensory latencies and potentials. Section 1.7.11 indicates that the sensory measures are considered the best diagnostic test for the CTS. Therefore the sensory latencies were also calculated. All of the cases DSL were greater than the thresholds given in table 1.12.

3.4.5 Questionnaires.

Three questionnaires were administered to all of the subjects in the study (Examples are contained in appendix III). The main questionnaire was a modified form of that previously used and validated by Turner (1989).

The hand preference questionnaire (appendix III) developed by Oldfield (1971) was used to assess hand preference. A check list to assess the occupational background of the subjects was also developed and administered. In addition to these, the cases were given the patient checklist. Section 1.11 explains more about the development of the questionnaires used.

An occupational checklist was also applied in the study (appendix III). This was used to gain more information about the subjects occupational background.

All questionnaires were administered by the author in person.
3.4.6 Image Analysis.

The images were assessed in a logical manner before they were analysed. All of the images of one wrist were displayed on the graphics monitor. A typical image is displayed on plate 3.2. The file names were entered onto the image assessment checklists (appendix III) and the check list followed. The examiner assessed the image recording whether to reject or accept the image for analysis, images totally blank or completely obscured by noise were rejected. These images were the end slices in the image sets. The examiner noted whether the image and carpal tunnel were sharp; whether the median nerve was visible and if the image contained any noise. Finally the slice position was noted.

All of the images in a set were assessed and then the image set check list was applied (Appendix III). The images not previously rejected were displayed and comments noted about each of the images in the set. The two images selected for analysis, consisting of the saturation recovery and density images, were noted in the check list. The next image set was then assessed.

This process was carried out for all of the images before any of the analysis was carried out. A back-up copy of all of the images selected was made and stored away from the central store of floppy discs, used to store the original data. This ensured that there were at least two copies of all of the images used for analysis.

The linear and cross-sectional area measures were obtained in the same manner to that of the pilot study (section 2.3.6 gives an account of the method). Two other measures; i. the signal intensity of the carpal tunnel and ii. the background noise were also taken.

The images of each wrist were examined and the centre slice of the multi-slice sequence and the saturation recovery image had signal intensities measured. The sharpest image was used for the anthropometric analysis.
Plate 3.2 A typical cross sectional MRI image of the wrist. Looking up the right arm towards the elbow.
3.4.7 Data Analysis.

Inter-observer Reliability.

To confirm the reliability when other observers performed the analysis the inter-observer reliability had to be tested. This was done by asking two trained observers to analyse five randomly selected images in a random order. These data were compared to identify correlation and differences using SPSSX paired t-test programme.

Observer training procedure.

Each observer attended a 1 hour training session on the day prior to the experimentation day. The equipment was explained to the observer and the measurement to be taken off the images pointed out.

A reminder of the cross-sectional anatomy of the wrist was given to the observer (Appendix I) with reference to Hamilton (1976 p.177). The position of the tendon of flexor carpi radialis was pointed out to each observer, this was considered to be outside the carpal tunnel. Both observers were well acquainted with the anatomy of the upper limb, they were both involved in major studies involving the physiological demands on the upper limb. The reminder of the anatomy of the upper limb was directed at the cross-sectional anatomy of the upper-limb, which is rarely encountered unless an individual had a specific interest in imaging.

The observer was then shown an image of a bottle phantom on the graphics monitor, double magnification. The method for measuring linear distances was explained as in section 2.3.6. The observer measured the diameter of the bottle until they, and the examiner were confident that they were measuring the true diameter. The observers measurements had to be equal to those of the authors measurement obtained earlier. The observer was then shown how to measure cross-sectional areas of the phantom. The observer started by mapping out random areas on the image to become accustomed to using the mouse. They then attempted to measure the cross-sectional area of the
phantom.

After two attempts, aided by the examiner, another phantom was displayed. The observer was asked to measure the width, depth and cross-sectional of the second phantom. On completion of these measurements, the observers were considered to be accustomed to the linear and area measuring techniques and the mouse movements.

An image of a wrist was displayed on the graphics monitor. The observer was asked to interpret the image for measurement according to the following criteria;

i. The perimeter of the wrist was identified. The outer edge of the wrist observed by checking to see if the perimeter was complete. In areas where the wrist perimeter was incomplete, the observer was asked to use the perimeter either side of the missing portion as a guide to completion of the perimeter. The wrist perimeter was incomplete for the following reasons;

i.1 Blood vessels on the surface of the skin appeared as areas of low signal intensity. This meant that portions on the dorsal surface of the hand could not be seen.

i.2 In areas where tendons were near to the surface of the skin, in particular the extensor tendons, would appear as areas of low intensity signal.

i.3 If the subject moved while the image was being captured an area of low intensity signal would result.

ii. The borders of the carpal tunnel were identified. First the tendon of flexor carpi radialis was identified. The position of the tendon was explained to the observer with reference to the text (Hamilton 1976 p.177), although it was known to both observers through their background in anatomy. The tendon of flexor carpi radialis was identified and was excluded from the carpal tunnel measurement. Thus, the lateral border of the carpal tunnel was identified. The other borders were identified as clearly defined by
areas of high intensity signal of the soft tissue, surrounding the areas of low intensity signal of the flexor tendons and tendon sheaths.

iii. Small regions of low intensity signal also appeared on the border of some of the carpal tunnels. The observer was told that these were the joints of the carpal bones which appeared as low intensity signals and should not be included as part of the carpal tunnel.

Once the wrist perimeter and carpal tunnel borders had been explained and identified, the observer was asked to take measures of the test image in the following order;

- Carpal tunnel width,
- Carpal tunnel depth,
- Wrist width,
- Wrist depth,

These measurements were recorded by the examiner on the record sheet (appendix III) in the same order. No feedback of the measurements was given.

The cross-sectional area of the carpal tunnel and the wrist were then recorded followed by the background noise intensity. The noise intensity was measured by mapping out a square of the image next to, but not including the wrist itself.

The observer was allowed to ask the examiner for advice about the image interpretation throughout the training session. The measures were repeated for the first test image and then a second image was displayed. The observer carried out two sets of measurements on the second image after interpretation. This completed the training procedure for the observer. The measuring session was carried out on the following day.
Main Study Methods

Image Analysis.

The observer was asked to analyse five images on the image analysis session. The observer was allowed to practice on one of the test images before starting on the main session. The observer was asked to use the same technique as they had been trained the previous day.

Image selection.

Five images for analysis were selected from the 40 images in the case control study on the following basis. Five, three figure random numbers were obtained from a calculator random number generator and each digit used for selection according to the following criteria;

i. The left digit in the number was used to select whether the right or left image was to be used from the image set, numbers less than 5 indicated the right wrist and those greater than or equal to five indicated the left wrist was to be used.

ii. The middle digit indicated whether a case or a control wrist was to be used. Numbers less than 5 indicated a case wrist and numbers greater than or equal to 5 indicated a control wrist.

iii. The right digit indicated which number of image should be used. The ten cases and controls were numbered, from one to ten, for identification purposes on the data base. So, the right digit in the random number made the selection of which subjects image was to be used.

The selected images were numbered 1–5 and then the order of analysis of the images was set by random number generator. The right digit was used. Random numbers were generated until a number from 1–5 appeared. This was recorded as the first image number to be analysed by observer 1. The process was repeated until all five images had been allocated to each observer.
3.4.8 Data Entry.

All of the data collected in the study was entered onto a data base package available on a personal computer. It was considered easier to handle the data using a data base management system with a "user friendly design", instead of the customary method of transferring data to coding sheets and data entry operators punching in the data. The "Reflex" data base management package was used.

The layout of the questionnaire or data sheet was entered into the data base, so that the data could be typed in on the same format as it appeared on the sheets. The data entry operator entered the data straight onto the data base from the sheet, without the need for any further coding.

The data could be checked against the original quickly as it appeared in that same format on the VDU as in the original. The order of the data could altered by the operator in an instant and graphs displayed to observe trends in the data set. When a more complex statistical analysis was required the data had to be transferred onto the main frame computer where SPSSX was available. It is hoped that a PC copy of SPSSX will shortly be purchased.
3.5 Experimental Design.

The experimental design was a pair matched case-control type as described in the literature review (section 1.10). Each case was matched with a control subject according to the matching criteria given in section 3.3.3. The continuous data were analysed using a paired T-test and correlation coefficients. Binomial data were analysed using MacNemars test.
4 RESULTS.
Results

The results of the main study are reported in the following chapter. The Intra-observer reliability was examined and discussed in the pilot study and is only briefly mentioned here. In the main study the inter-observer reliability was examined and the results of this are reported first.

The results of the case-control study were the examined. First the gross anthropometric measures, then the image measures. The main result to emerge from this part of the study was that, it was not possible to identify differences between the carpal tunnel cross sectional areas of cases' and controls' wrists.

Other results from the questionnaire and surgical observations are also reported.

Finally the results of the entire study are summarised in tables 4.17-20.
Results

4.1 Inter-Observer Reliability.

Five images were randomly selected from the 40 images in the main study data set. These images were analysed, using the image analysis technique described in section 2.3.6, firstly by the author (the main observer), and then by two naive observers. Both of the naive observers had a background knowledge of the anatomy of the wrist and carpal tunnel. They were given the same training procedure which is described in section 3.4. Six variables were measured from each of the images, the data were then entered on to the computer data base for analysis.

The data were analysed using the SPSSX paired t-test programme on the University's Prime main frame system. The t-test was used to test the null hypothesis; that there would be no difference between the observations of the main observer and the two naive observers. This test was applied to each of the variables obtained in the image analysis.

The images consisted of a mixture of dominant and non-dominant wrists from both sexes, this meant that the standard errors would be greater than if both wrists and sexes had been treated separately, as in the pilot study. The standard errors are reported here but they must be treated with caution if comparisons are made with other data.

The data collected by the two naive observers were compared with those of the main observer. This gave an indication of how the results of the naive observers, with only a limited training in image analysis, compared with the results of the main observer. The results of this analysis are contained in table 4.1, the means and standard errors of the five images are given for each of the observers; for each of the six variables measured from the images. The mean differences of the naive observers results from those of the main observer are also shown, along with the t values and their levels of significance derived from the $t_v=0.025$ ($v$ the number of degrees of freedom=4) value in the t-tables.
Table 4.1 Means (cm) and (Standard Errors) of the Inter-observer Reliability Results. Means differences of the naive observer results from the main observer, with the t-values (n=5).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Main observer</th>
<th>Naive observer 1</th>
<th>Naive observer 2</th>
<th>Mean diff. from main</th>
<th>t-value</th>
<th>sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrist width</td>
<td>6.21 (0.2)</td>
<td>6.06 (0.27)</td>
<td>6.05 (0.23)</td>
<td>0.16</td>
<td>3.16</td>
<td>p&lt;0.025</td>
</tr>
<tr>
<td>Wrist depth</td>
<td>4.34 (0.11)</td>
<td>4.36 (0.09)</td>
<td>4.31 (0.12)</td>
<td>-0.03</td>
<td>-0.56</td>
<td>ns</td>
</tr>
<tr>
<td>C.T. width</td>
<td>2.42 (0.10)</td>
<td>2.44 (0.20)</td>
<td>2.32 (0.15)</td>
<td>-0.02</td>
<td>-0.12</td>
<td>ns</td>
</tr>
<tr>
<td>C.T. depth</td>
<td>1.26 (0.23)</td>
<td>1.05 (0.11)</td>
<td>1.08 (0.13)</td>
<td>0.21</td>
<td>1.12</td>
<td>ns</td>
</tr>
<tr>
<td>Wrist area</td>
<td>21.24 (0.86)</td>
<td>20.57 (0.84)</td>
<td>21.02 (0.79)</td>
<td>0.67</td>
<td>7.05</td>
<td>p&lt;0.025</td>
</tr>
<tr>
<td>C.T. area</td>
<td>2.02 (0.29)</td>
<td>2.16 (0.34)</td>
<td>2.41 (0.35)</td>
<td>-0.15</td>
<td>-1.35</td>
<td>ns</td>
</tr>
</tbody>
</table>

Apart from the wrist width measurements, the naive observers' linear measurements were not significantly different from those of the main observer, in fact there was close agreement in most cases. There were however differences in the wrist width measures, both of the naive observers measured the wrist width smaller than the main observer.

The same was found for the wrist cross-sectional area. Both of the naive observers measured the wrist cross-sectional area smaller than the main observer, although only the measurements of naive observer 1 were significantly smaller (p<0.025) than the main observer. The opposite was found for the carpal tunnel cross-sectional areas. Both of the naive observers measured the carpal tunnel cross-sectional areas larger than the
main observer, although only the measurements of naive observer 2 were significant (p<0.025) in this case.

Table 4.2 Correlation coefficients (R) and their significance of the two naive observers results with those of the main observer (n=5).

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Naive Observer 1</th>
<th>Naive Observer 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R</td>
<td>sig</td>
</tr>
<tr>
<td>Wrist width</td>
<td>0.983</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Wrist depth</td>
<td>0.916</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Carpal tunnel width</td>
<td>0.252</td>
<td>ns</td>
</tr>
<tr>
<td>Carpal tunnel depth</td>
<td>0.619</td>
<td>ns</td>
</tr>
<tr>
<td>Wrist area</td>
<td>0.994</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Carpal tunnel area</td>
<td>0.949</td>
<td>p&lt;0.05</td>
</tr>
</tbody>
</table>

The correlation coefficients were calculated to test for correlations of the main observers' results with those of the naive observers (table 4.2). There were significant positive correlations for the majority of the variables tested, for both of the naive observers. However, there were two variables where the correlations were not significant (carpal tunnel width and carpal tunnel depth). On comparing these results with those in table 4.1, it should be noted that where the results did not show significant positive correlations, there was good agreement in the results of the main observer and the naive observers' (the t-values reported for carpal tunnel width were less than 0.6). There was such a small difference in the results of the two observers that correlation of the data became lost in the spread of the results. The variables where differences were identified displayed very strong correlations (p=0.001 for the wrist cross-sectional area measurements).
In summary there were significant differences found in the linear measurements. Those which were significant displayed a trend for the wrist measurements to be smaller in the naive observers compared with the main observer. The same trend was displayed in the wrist cross-sectional area results, although only one naive observer had a significant difference. The carpal tunnel cross-sectional areas showed the opposite trend, the naive observers measuring larger than the main observer. There were significant correlations between the results of the main observer and the naive observers, except for those variables where very strong associations occurred and a variation in the results was found.
4.2 Anthropometric Results.

Various anthropometric data were collected in the study, details are given in the methods section. The variables involving measurements of whole body status (Height, Weight and Laterality Quotient) were treated thus: Matched cases and controls were compared using paired t-tests and correlation coefficients. For the variables confined to a particular side of the body, each individual wrist/hand was treated separately (13 of the total 20 wrists in the case group were compared with the corresponding wrist in the control group). The variables were compared using a paired t-test and correlation coefficients.
Results

4.2.1 Whole Body Measurements.

The results of the height and weight comparisons are given in table 4.3. They show that there was no significant difference between the heights, or the weights of the cases and controls. This supports the hypothesis that there would be no difference between the cases and controls with respect to the height and weight variables. There were no significant correlations between the two groups for either variable.

Table 4.3 Heights, Weights and Laterality Quotient results.

Height (cm).

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>S. D.</th>
<th>Difference</th>
<th>t-value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>163</td>
<td>5.5</td>
<td>3.0</td>
<td>-0.92</td>
<td>p=0.380</td>
</tr>
<tr>
<td>Controls</td>
<td>166</td>
<td>10.6</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Correlation Coefficient 0.325 (p=0.360) n=10

Weight (Kg).

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>S. D.</th>
<th>Difference</th>
<th>t-value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>66.9</td>
<td>9.9</td>
<td>2.65</td>
<td>0.61</td>
<td>p=0.556</td>
</tr>
<tr>
<td>Controls</td>
<td>64.3</td>
<td>6.6</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Correlation Coefficient -0.359 (p=0.309) n=10

The height of the cases and controls were greater than the 50th percentile and less than the 95th percentile (Pheasant 1984).

The laterality quotient results are given in table 4.4. Although the cases and controls were matched for gross hand preference, it was thought that the degree of hand preference of the cases and controls should be compared. It was hypothesised that the
cases would have a stronger hand preference than the controls.

There was no significant difference between the laterality quotients of the cases and controls (p>0.05). There was also no significant correlation of the results of the two groups.

The hypothesis that the cases would have a stronger hand preference than the controls was rejected.

Table 4.4 Laterality Quotients.

<table>
<thead>
<tr>
<th>Laterality Quotient</th>
<th>Mean</th>
<th>S. D.</th>
<th>Difference</th>
<th>t-value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>77.6</td>
<td>22.0</td>
<td>-10.3</td>
<td>-1.23</td>
<td>p=0.249</td>
</tr>
<tr>
<td>Controls</td>
<td>87.9</td>
<td>9.0</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Correlation Coefficient -0.337 p=0.341 n=10
4.2.2 Measurements Confined to One Side of the Body.

Wrist dimensions.

Table 4.5 External Wrist Dimensions.

**Wrist Breadth:– Styloid process (cm).**

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>S. D.</th>
<th>Difference</th>
<th>t-value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>5.51</td>
<td>0.32</td>
<td>0.085</td>
<td>1.05</td>
<td>p=0.315</td>
</tr>
<tr>
<td>Controls</td>
<td>5.43</td>
<td>0.31</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Correlation Coefficient 0.581 (p=0.037) n=13

**Wrist Breadth:– Distal Wrist Crease (cm).**

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>S. D.</th>
<th>Difference</th>
<th>t-value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>5.37</td>
<td>0.31</td>
<td>0.32</td>
<td>4.74</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Controls</td>
<td>5.06</td>
<td>0.32</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Correlation Coefficient 0.717 (p=0.006) n=13

**Wrist Depth (cm).**

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>S. D.</th>
<th>Difference</th>
<th>t-value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>3.64</td>
<td>0.24</td>
<td>0.26</td>
<td>4.59</td>
<td>p=0.001</td>
</tr>
<tr>
<td>Controls</td>
<td>3.38</td>
<td>0.21</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Correlation Coefficient 0.583 (p=0.037) n=13

The wrist breadth was measured at 2 anatomical sites; at the styloid process and at the distal wrist crease. The results of the analysis are given in table 4.5. There was no significant difference between the cases and controls for the wrist breadth at the styloid process (p>0.05). This supports the hypothesis that there would be no difference
between the cases and controls with respect to the wrist breadth styloid process measurement.

There was a significant difference in the wrist breadth measurement at the distal wrist crease. The cases were significantly larger than the controls (p<0.05). The same was true for the wrist depth measurements. There was a significant difference (p<0.05) between the cases and controls wrist depth measurements, the cases being larger than the controls. Thus the hypotheses that there would be no difference between the cases and controls with respect to the external wrist dimensions was rejected.

The cases wrist dimensions were 9% larger than the controls for both width and depth measures.
Wrist Ratio Measures.

The results of the wrist ratio analysis are given in table 4.6. The wrist ratios were calculated by dividing the wrist depth measures by the wrist breadth measures, both at the distal wrist crease. The hypothesis that the wrist ratio for the cases would be smaller than the controls was tested (Johnson et al. 1983; and Gordon et al. 1988).

Table 4.6 Wrist ratio measures.

<table>
<thead>
<tr>
<th>Wrist Ratio</th>
<th>Mean</th>
<th>S. D.</th>
<th>Difference</th>
<th>t-value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>0.678</td>
<td>0.04</td>
<td>0.09</td>
<td>0.74</td>
<td>p=0.475</td>
</tr>
<tr>
<td>Controls</td>
<td>0.669</td>
<td>0.04</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Correlation Coefficient 0.364 (p=0.222) n=13

No significant difference between the cases and controls was found, the hypothesis was rejected. Johnson et al. (1983) stated that cases would have a wrist ratio of less than 0.7. This was true for only 7 of the cases and 9 of the controls. This suggests that the wrist ratio as a test for CTS was poor, with a sensitivity of 61% and specificity of 15%. All but 2 of the controls were wrongly identified as having CTS by the test.
Wrist Circumference.

The wrist circumference results are given in table 4.7. There was no significant difference between the cases and controls for wrist circumference. This supports the hypothesis that there would be no difference between the wrist circumference of the cases and controls. But there was still a trend for the cases wrists to be larger than those of the controls. There was a positive correlation ($p<0.05$) between the results of the two groups.

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>S. D.</th>
<th>Difference</th>
<th>t-value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>16.37</td>
<td>0.79</td>
<td>0.38</td>
<td>2.06</td>
<td>p=0.06</td>
</tr>
<tr>
<td>Controls</td>
<td>16.00</td>
<td>0.81</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Correlation Coefficient 0.661 ($p=0.014$) n=13
Palm Width and Hand Length.

The results of the palm width analysis are given in table 4.8. There was no significant difference between the palm widths of the cases and the palm widths of the controls. This supports the hypothesis that there would be no difference between the palm widths of the two groups.

Table 4.8 Palm width and hand length.

Palm Width (cm).

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>S. D.</th>
<th>Difference</th>
<th>t-value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>7.84</td>
<td>0.56</td>
<td>0.00</td>
<td>0.00</td>
<td>p=1.000</td>
</tr>
<tr>
<td>Controls</td>
<td>7.84</td>
<td>0.51</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Correlation Coefficient 0.734 (p=0.004) n=13

Hand Length (cm).

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>S. D.</th>
<th>Difference</th>
<th>t-value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>17.96</td>
<td>0.99</td>
<td>-0.6</td>
<td>-2.84</td>
<td>p=0.015</td>
</tr>
<tr>
<td>Controls</td>
<td>18.56</td>
<td>0.83</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Correlation Coefficient 0.662 (p=0.014) n=13

There was a significant difference between cases hand length and the controls hand length (p<0.05). The case's hand lengths were smaller than the controls. On the basis of this result the hypothesis that the cases and controls would have the same hand length was rejected.

Both the palm width and hand length measurements displayed significant positive
correlations (p<0.05) suggesting a relationship between either of the two variables and being a member of a particular group.

These measures were compared with the anthropometric data supplied by Pheasant (1984). Both hand breadth and length were greater than the 50th percentile and less than the 95th percentile female measurements.
Radius Length.

Table 4.9 gives the results of the radius length analysis. There was no significant difference between the radius lengths of the cases and controls. This supports the hypothesis that there would be no difference in radius length of the cases and controls. There was no significant correlation between the two groups.

Table 4.9 Radius length.

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>S. D.</th>
<th>Difference</th>
<th>t-value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>22.37</td>
<td>1.08</td>
<td>-0.68</td>
<td>-1.08</td>
<td>p=0.300</td>
</tr>
<tr>
<td>Controls</td>
<td>23.05</td>
<td>1.78</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Correlation Coefficient -0.224 (p=0.463) n=13
Results

Measures of Impaired Finger Joint Flexion.

The results of the finger joint flexion tests are given in table 4.10. The mean values given in table 4.10 are measures of the subjects ability to passively flex the particular joint from the neutral position, the greater the value in the table the greater the ability to perform the flexion manoeuvre. There was no significant difference between the PIP maximum joint flexion of the cases and the controls. The hypothesis that cases would have impaired PIP joint flexion was thus rejected.

Table 4.10 Tests of Impaired Finger Joint Flexion.

Proximal Inter-Phalangeal Joint Maximum Angle of Flexion. (degrees)

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>S. D.</th>
<th>Difference</th>
<th>t-value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>92.0</td>
<td>28.6</td>
<td>13.2</td>
<td>1.59</td>
<td>0.139</td>
</tr>
<tr>
<td>Controls</td>
<td>105.2</td>
<td>5.3</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Correlation Coefficient -0.171 (p=0.576) n=13

Metacarpo-Phalangeal Joint Maximum Angle of Flexion. (degrees)

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>S. D.</th>
<th>Difference</th>
<th>t-value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>55.2</td>
<td>18.6</td>
<td>11.6</td>
<td>2.34</td>
<td>0.037</td>
</tr>
<tr>
<td>Controls</td>
<td>66.8</td>
<td>12.6</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Correlation Coefficient 0.397 (p=0.179) n=13

There was a significant difference between the MCP joint flexion of the cases and the controls (p<0.05). The cases had a significantly impaired MCP joint flexion compared with the controls. This supports the hypothesis that the cases would demonstrate less flexibility than the controls with respect to the MCP joint.
Grip Strength.

Table 4.11 contains the results of the grip strength analysis. There was a significant difference in the grip strength of the cases compared to the controls ($p<0.05$). The cases had a significantly impaired grip strength compared with the controls.

This supports the hypothesis that the grip strength of the cases would be less than that of the control group. There was a significant positive correlation of the results.

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>S. D.</th>
<th>Difference</th>
<th>t-value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>26.97</td>
<td>11.2</td>
<td>-6.7</td>
<td>-2.57</td>
<td>p=0.025</td>
</tr>
<tr>
<td>Controls</td>
<td>33.67</td>
<td>8.3</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Correlation Coefficient 0.569 ($p=0.043$) n=13
4.3 Image Results.

The image dimensions of 13 wrists from the 10 matched case control pairs were compared using a paired t-test programme. Each of the cases afflicted wrists used in the study (13 in all) were compared with the corresponding wrist of their matched controls. Correlation coefficients were also calculated to assess the relationship of the variables being tested. It is expected that the variables would be independent of each other as they were measured from different individuals. The hypotheses to be tested for each of the variables are stated in the relevant sections. Plate 4.1 show a sequence of five images consecutively running down the arm, into the wrist and then the hand.
Plate 4.1 A sequence of five images. Showing consecutive images down the down starting from the forearm and running down into the hand. The third image would have been used in the analysis.
Results

4.3.1 Width Dimensions.

The carpal tunnel and wrist width measurement results are given in table 4.12. It was hypothesised that the carpal tunnel widths of the cases would be smaller than those of the controls. The results of the one tail t-test in table 4.12 show that there was no significant difference between the carpal tunnel widths of the cases and the controls, the hypothesis was thus rejected.

Table 4.12 Carpal Tunnel and Wrist Widths

Carpal Tunnel Width (cm).

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>S. D.</th>
<th>Difference</th>
<th>t-value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>2.26</td>
<td>0.42</td>
<td>0.18</td>
<td>1.28</td>
<td>0.224</td>
</tr>
<tr>
<td>Controls</td>
<td>2.08</td>
<td>0.43</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Correlation Coefficient 0.298 (p=0.323) n=13

Wrist Width (cm).

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>S. D.</th>
<th>Difference</th>
<th>t-value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>6.34</td>
<td>0.63</td>
<td>0.62</td>
<td>2.57</td>
<td>0.024</td>
</tr>
<tr>
<td>Controls</td>
<td>5.72</td>
<td>0.47</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Correlation Coefficient -0.226 (p=0.457) n=13

It was hypothesised that there would be no difference between the wrist width measurements of the cases and the controls. This hypothesis was tested using a two tail t-test. Table 4.12 shows that there was a significant difference (p<0.025) between the mean wrist width measures of the cases and the controls, with the cases wrists being larger than those of the controls. The hypothesis that cases and controls would have the same wrist width dimension was thus rejected.
As expected the correlation coefficients in table 4.12 show there to be no significant correlation between the variables being tested. The two groups were independent of each other.
4.3.2 Depth Dimensions.

The carpal tunnel and wrist depth measurement results are given in table 4.13. It was hypothesised that the carpal tunnel depths of the cases would be smaller than those of the controls. The results of the one tail t-test in table 4.13 shows that there was no significant difference between the carpal tunnel depths of the cases and the controls, the hypothesis was thus rejected.

It was hypothesised that there would be no difference between the wrist depth measurements of the cases and the controls. This hypothesis was tested using a two tail t-test. Table 4.13 shows that there was a significant difference (p<0.025) between the wrist depth measures of the cases and the controls, the cases wrists were larger than those of the controls. The hypothesis that cases and controls would be the same size was thus rejected.

Table 4.13 Carpal Tunnel and Wrist Depth Measures.

<table>
<thead>
<tr>
<th>Carpal Tunnel Depth. (cm)</th>
<th>Mean</th>
<th>S. D.</th>
<th>Difference</th>
<th>t-value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>1.10</td>
<td>0.23</td>
<td>0.02</td>
<td>0.23</td>
<td>p=0.823</td>
</tr>
<tr>
<td>Controls</td>
<td>1.08</td>
<td>0.22</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Correlation Coefficient 0.066 (p=0.830) n=13

<table>
<thead>
<tr>
<th>Wrist Depth. (cm)</th>
<th>Mean</th>
<th>S. D.</th>
<th>Difference</th>
<th>t-value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>4.64</td>
<td>0.42</td>
<td>0.43</td>
<td>3.67</td>
<td>p=0.003</td>
</tr>
<tr>
<td>Controls</td>
<td>4.21</td>
<td>0.15</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Correlation Coefficient 0.170 (p=0.579) n=13
Results

No significant correlations were found for the two groups, confirming that they were independent.

These results for image wrist depths and breadths reflect the same trends as those obtained for the external wrist measures given in table 4.5. The image measurements and external measurements cannot be directly compared as they were taken at slightly different point on the wrist. However, the general trend of the sizes of the cases and controls was consistent for the two types of measuring technique. The image depths and breadths of the cases wrists were 9% larger than the controls. The external measure in table 4.5 show that the cases wrists were around 9% larger than the controls. These results add validity to the measuring philosophy.
4.3.3 Cross-Sectional Area Measurements.

The carpal tunnel and wrist cross-sectional area measurement results are given in table 4.14. It was hypothesised that the carpal tunnel cross-sectional areas of the cases would be smaller than those of the controls. However, the results in table 4.14 show that there was no significant difference between the cross-sectional area measurements of the cases compared with the controls. There was also no significant correlation between the measurement of the two groups supporting the hypothesis that they were independent.

Table 4.14 Carpal Tunnel and Wrist Cross-Sectional Areas.

<table>
<thead>
<tr>
<th>Carpal Tunnel Cross-Sectional Area. (cm²)</th>
<th>Mean</th>
<th>S. D.</th>
<th>Difference</th>
<th>t-value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>1.91</td>
<td>0.41</td>
<td>0.28</td>
<td>1.78</td>
<td>p=0.101</td>
</tr>
<tr>
<td>Controls</td>
<td>1.63</td>
<td>0.29</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Correlation Coefficient -0.277 (p=0.360) n=13

<table>
<thead>
<tr>
<th>Wrist Cross-Sectional Area. (cm²)</th>
<th>Mean</th>
<th>S. D.</th>
<th>Difference</th>
<th>t-value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>22.97</td>
<td>4.36</td>
<td>3.47</td>
<td>3.30</td>
<td>p=0.006</td>
</tr>
<tr>
<td>Controls</td>
<td>19.50</td>
<td>2.10</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Correlation Coefficient 0.495 (p=0.085) n=13

In contrast, there was a significant difference (p<0.025) between the wrist cross-sectional areas of the cases and controls. The hypothesis that there would be no difference between the cases and controls was rejected. The cases had significantly larger wrist...
cross-sectional areas compared with the controls. Again there was no significant correlation between the two groups confirming that they were independent.
Normalising for subject size would be a logical development from the results in tables 4.12-4.14. Although there were no significant differences found for the internal carpal tunnel measures, there were differences identified in the wrist measures. The cases mostly had larger wrist dimensions than the controls. Table 4.15 gives the normalisation results, expressing the carpal tunnel measures as a percentage of the total wrist measurement.

### Table 4.15 Image dimensions expressed as a percentage of the wrist measure

#### Width Measures (Carpal Tunnel : Wrist).

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>S. D.</th>
<th>Difference</th>
<th>t-value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>35.74%</td>
<td>6.59</td>
<td>-0.50</td>
<td>-0.24</td>
<td>p=0.815</td>
</tr>
<tr>
<td>Controls</td>
<td>36.25%</td>
<td>6.31</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Correlation Coefficient 0.309 (p=0.304) n=13

#### Depth Measures (Carpal Tunnel : Wrist).

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>S. D.</th>
<th>Difference</th>
<th>t-value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>23.57%</td>
<td>4.21</td>
<td>-2.03</td>
<td>-1.24</td>
<td>p=0.240</td>
</tr>
<tr>
<td>Controls</td>
<td>25.60%</td>
<td>5.15</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Correlation Coefficient 0.211 (p=0.488) n=13

#### Cross-Sectional Measures (Carpal Tunnel : Wrist).

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>S. D.</th>
<th>Difference</th>
<th>t-value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>8.54%</td>
<td>2.26</td>
<td>0.18</td>
<td>0.25</td>
<td>p=0.810</td>
</tr>
<tr>
<td>Controls</td>
<td>8.36%</td>
<td>1.07</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Correlation Coefficient -0.206 (p=0.499) n=13
Results

After normalisation the cases width and depth measures were not significantly different from those of the controls. The hypothesis, that the carpal tunnel width and depth measures would be smaller than the controls, once expressed as a percentage of the total wrist measure, was rejected.

The same was true of the cross-sectional area measures. It was hypothesised that the carpal tunnel cross-sectional area would be smaller in the cases, compared with the controls, when the area was expressed as a percentage of the total wrist area. This hypothesis was rejected on the basis of the results given in table 4.15. There was no significant difference between the carpal tunnel cross-sectional areas of the cases compared with the controls, even when expressed as a percentage of the wrist area.

As with all of the other image variables tested, the correlation coefficients were not significant (p>0.05).
4.4 T1 Results.
It was proposed that the T1 of the carpal tunnel contents, including the median nerve, tendons and tendon sheaths, could be measured in the main study. This was to be done by using 2 types of spin-echo sequence. Saturation recovery and density sequences were used to obtain the two images for each wrist. The signal intensities M1 and M2 could be obtained from the respective images and the T1 calculated using equation II.18.

The carpal tunnels of the control wrists in the pilot study appeared as areas of very low signal intensity, only fractionally larger than the background noise (The signal to noise was only a factor of 5). The controls' tendons were assumed to be normal and free from any inflammation and oedema. This lack of signal in the carpal tunnel was attributed to the absence of water in the carpal tunnel. It was not possible to calculate the T1 in the pilot study. It was hypothesised that the carpal tunnels of the cases would contain more water/odema as a result of the CTS (Middleton et al. 1987), thus increasing the signal to noise ratio and making the calculation of T1 possible.

On this assumption, 2 sequences were used in the main study so that T1 could be calculated. Unfortunately, the carpal tunnels of the cases also had very little signal. They did not appear to be as oedematous as was first suspected, there was an absence of water in the carpal tunnel, resulting in a very poor signal to noise ratio. This made the calculation of T1 impossible. It was also thought that the tendons had a very short T2 further reducing the signal to noise ratio.

Although the lack of signal meant that the T1 could not be calculated, it did enhance the contrast between the carpal tunnel contents and the surrounding tissues.
4.5 Questionnaire Results.

4.5.1 Tests for CTS.

The Phalens test and the flick test were examined during the main study. They were both described in section 1.7 of the literature review. Phalens test was performed on all of the subjects, while the flick test was used for the cases only, for reasons given in the literature review. The sensitivity and specificity of the Phalens test and the sensitivity of the flick test were calculated. These results are given in table 4.16.

Table 4.16 Sensitivity and specificity of the Phalens and Flick Tests.

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phalens Test</td>
<td>90%</td>
<td>90%</td>
</tr>
<tr>
<td>Flick Test</td>
<td>50%</td>
<td></td>
</tr>
</tbody>
</table>

The results show that the Phalens test had high levels of sensitivity and specificity. These were greater than those obtained from the literature (table 1.9). On examining the raw data more closely it was evident that if the threshold time of the test was reduced from 60 seconds to 50 seconds the specificity would have been 100%. However this was at the expense of the sensitivity which would have fallen to 80%.

The results of the flick test agree with those DeKrom et al. (1990). The low sensitivity of the flick test appears to be reproducible suggesting that the test is inappropriate for CTS.
4.5.2 Tests for Prevalence of Pain and Discomfort.

It is worth noting that the case and control groups had similar prevalence of pain and discomfort in the areas of the body listed under section C of the main questionnaire. The responses of the cases and controls were compared using McNemars binomial test. No significant differences were recorded for any of the questions asked.

These results should be treated with caution. The small number of matched pairs in the study suggests that the results of this test would not be robust enough for any conclusions to be made about the differences between the two groups. However, by examining the two by two tables generated by the test it is clear that the cases and controls were very similar in their point and lifetime prevalence of pain and discomfort.

(Note: Due to the small numbers in the study the tables produced in the McNemars test are not reported.)
4.5.3 Other Questionnaire Observations.

Night Awakening. Night awakening was assessed in the main study. 90% (sensitivity) of the cases experienced awakening during the night by the symptoms of CTS. It is difficult to assess the usefulness of this test as specificity measures are unavailable. The physician could use it in the battery of tests which should be used in the assessment of CTS.

Family Connections. Subjects were asked if any of their family had experienced any of the symptoms of CTS. 20% of the cases reported direct blood relations who had experienced CTS.

Occupational Changes. The cases were asked if they had been forced to change their lives in any way as a result of their condition. 40% reported that they had been forced to change their job. It was not clear, in all cases, whether they had been forced to change job because it had contributed to the condition or because they could not perform the job as a result of the condition. The latter was almost certainly the case for 2 out of the 4 cases reporting job difficulties. On analysing the tasks done by these individuals it is unlikely that their job would have caused their condition. They were both employed in jobs which involved little force on the hands and wrists with low repetition rates.

The remaining 2 cases reporting job difficulties were performing tasks known to contain risk factors for CTS (Silverstein et al. 1987). One worked as a stacker for a supermarket, handling thousands of heavy cardboard boxes every day. At times the work rates were excessive, during deliveries work was carried out on a "flat out" basis, with few rest pauses. The other worked as a supermarket laser checkout operator. Again this involved highly repetitive movement of the hands and wrist. Both cases had to change their job.
Sports and Hobbies. 50% of the cases reported that the condition had resulted in a disruption of their pastimes.
4.6 Surgical Observations.

Four of the decompression operations were observed by the author. The flexor retinaculum was thickened and tight in all four cases, although it was not thought to be excessive in one case. The median nerve was hour glassed in all cases suggesting compression had occurred (Plate 4.2). This accounted for the nerve not being visible in the images.

The flexor tendon sheath of one of the patients appeared normal. All of the others had excessive thickening of the flexor tendons resulting in fibrous deposits in the carpal tunnel. This fibrous material was excised from the tendons to release the pressure on the median nerve (Plate 4.3).

There was no evidence of lipomas, ganglions or free fluid in any of the carpal tunnels.
Plate 4.2 Median nerve within the carpal tunnel. Note the hour glassing of the nerve.
Plate 4.3 Stripping the fibrous tissue from around the median nerve.
4.7 Summary of the Results of the Study.

Tables 4.17-4.20 contain a summary of the results of the entire study. Table 4.16 contains the results of the pilot study, note the differences in the controls dominant and non-dominant carpal tunnel cross-sectional areas.

---

Table 4.17 Pilot Study Controls Data: Dominant vs Non-dominant Measurements.

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Diff.</th>
<th>Direction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrist Width</td>
<td>ø</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>ν</td>
<td>ns</td>
</tr>
<tr>
<td>Wrist Depth</td>
<td>ø</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>ν</td>
<td>ns</td>
</tr>
<tr>
<td>Carpal Tunnel Width</td>
<td>ø</td>
<td>ns</td>
</tr>
<tr>
<td>Carpal Tunnel Depth</td>
<td>ø</td>
<td>ns</td>
</tr>
<tr>
<td>Wrist Area</td>
<td>ø</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>ν</td>
<td>ns</td>
</tr>
<tr>
<td>Carpal Tunnel Area</td>
<td>ø</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>ν</td>
<td>p&lt;0.025</td>
</tr>
<tr>
<td>Carpal Tunnel Wrist Ratio</td>
<td>ø</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>ν</td>
<td>ns</td>
</tr>
</tbody>
</table>
Tables 4.18 and 4.19 contain the results of the anthropometric measures.

Table 4.18 Main Study Whole Body Anthropometric Measures: Cases vs Controls.

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Diff.</th>
<th>Direction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Laterality Quotient</td>
<td>ns</td>
<td></td>
</tr>
</tbody>
</table>

Table 4.19 Main Study Uni-lateral Measures: Cases vs Controls.

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Diff.</th>
<th>Direction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrist Breadth (styloid process)</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Wrist Breadth (distal wrist crease)</td>
<td>p&lt;0.05</td>
<td>Cases &gt; Controls</td>
</tr>
<tr>
<td>Wrist Depth</td>
<td>p&lt;0.05</td>
<td>Cases &gt; Controls</td>
</tr>
<tr>
<td>Wrist Ratio</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Wrist Circumference</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Palm Width</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Hand Length</td>
<td>p&lt;0.05</td>
<td>Controls &gt; Cases</td>
</tr>
<tr>
<td>Radius Length</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>PIP Joint Flexion</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>MCP Joint Flexion</td>
<td>p&lt;0.05</td>
<td>Controls &gt; Cases</td>
</tr>
<tr>
<td>Grip Strength</td>
<td>p&lt;0.05</td>
<td>Controls &gt; Cases</td>
</tr>
</tbody>
</table>
Finally Table 4.20 contains the results of the image data. The main results of the study are reported here. There was no difference between the carpal tunnel cross-sectional areas of the case and the controls, even when the differences in wrist size were accounted for.

Table 4.20 Main Study Image Results: Cases vs Controls.

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Diff.</th>
<th>Direction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carpal Tunnel Width</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Wrist Width</td>
<td>p&lt;0.05</td>
<td>Cases &gt; Controls</td>
</tr>
<tr>
<td>Carpal Tunnel Depth</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Wrist Depth</td>
<td>p&lt;0.05</td>
<td>Cases &gt; Controls</td>
</tr>
<tr>
<td>Carpal Tunnel Area</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Wrist Area</td>
<td>p&lt;0.05</td>
<td>Cases &gt; Controls</td>
</tr>
<tr>
<td>Widths (Carpal Tunnel:Wrist)</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Depth (Carpal Tunnel:Wrist)</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Areas (Carpal Tunnel:Wrist)</td>
<td>ns</td>
<td></td>
</tr>
</tbody>
</table>
5 DISCUSSION.
5.1 Introduction to the Discussion.

The results of the case-control study and the system development are discussed in the following chapter. The results of the case-control study are discussed first, including sections on group characteristics and observer reliability. The image results are then discussed. The implications of the main result of the study, that there were no differences reported between the carpal tunnel cross sectional areas of cases compared with the controls, are explored.

Finally the system developments are discussed.
5.2 The Case-control Study.

5.2.1 Subject Selection and Study Delimitations.

The pair matched case control study was based on a group of cases selected from a local hospital waiting list and volunteers from the University of Surrey. Both groups had the symptoms of CTS at the time of the study (CTS was confirmed in the hospital cases using electrophysiological tests). Of the hospital cases all were operated on within a few months of the study. These cases were matched with controls selected from University volunteers, who did not have the symptoms of CTS and satisfied the matching criteria.

It was originally hoped that electrophysiological tests could have been performed on all of the cases and the controls; to confirm involvement of the median nerve in the university cases; and confirm healthy median nerves in the controls. However, ethical clearance was not permitted for tests on the university volunteers. This meant that four of the cases in the study did not have the most objective tests available for CTS performed on them (Kimura 1983). They did, however display the symptoms of CTS during the study, with no involvement at the neck or elbow. They had also had the diagnosis of CTS previously confirmed by their own general practitioner. It was therefore thought that the inclusion of these individuals in the study was valid. It was not possible to confirm that the median nerves of the control group were completely free from compression at the carpal tunnel. However, the fact that they had not experienced the symptoms of CTS satisfied the selection criteria. It was assumed that if any median nerve compression had been experienced, the volunteer would have been aware of this and informed the examiner.

The lack of electrophysiological evidence in some of the cases and the controls was not completely satisfactory, but the other selection criteria in the study were thought to be sufficient for confidence in the diagnosis.

Seven (70%) of the cases in the study were female. This was similar to the proportion of
females in other studies investigating CTS in large clinics (Yamaguchi et al. 1965; Ragi et al. 1981; and Graham 1983).

The number of subjects in the study was less than originally planned for the following reasons;

1. The number of patients expected to present with CTS, at the Royal Surrey County Hospital clinic, was over estimated by the consultants with whom liaison was made. It was originally thought that over 20 patients could have been collected over the six months experimentation period. Only six were eventually selected from the hospital.

2. The experimentation period was reduced by the decommissioning of the imaging system. This reduced the main experimentation period from six months to six weeks. It is impossible to estimate how many subjects could have been included if this limitation had not been imposed. It is however, a tribute to the running of the system, that it was able to collect enough information, in such a short period of time, for satisfactory results to be collected.

Since the numbers in the study were low, a comparison with those of other studies using this type of imaging technique would be useful. MRI studies are inherently small, due to the nature and expense of the systems. Table 1.19 gives the number of cases used in the only reported studies comparing cases and controls (Middleton et al. 1987; Mesgarsadeh et al. 1989 b). The total number of diseased wrists imaged in each study were 6 and 10 respectively. 13 diseased wrists were imaged in this study with 13 pair matched controls. 58 control wrists were imaged during the pilot study, providing a sound data base of image information from which to validate the study (Norman et al. 1989). In terms of numbers of wrists imaged, this study has more diseased wrists than

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1. Some four months were spent contacting subjects and organising electrophysiological tests for cases while the system was available for use.
other studies and a much greater number of control wrists. More wrists have been imaged using the more conventional imaging methods such as CT (Table 1.20). Even here this study compares well in terms of numbers.
Discussion

5.2.2 The Observer Reliability.

The results of this study would suggest that the observer reliability should be considered more often by other researchers. The reliability of measures obtained from images is of the utmost importance, if meaningful results are to be reported. There have been no other intra or inter-observer reliability studies (involving either CT or MRI imaging of the wrist) reported in the literature. The reason for this is unclear.

Possibly investigators were so confident in their measuring technique that it was (perhaps naively) not thought necessary to perform any reliability analysis. In the light of the results of this study, presumptions regarding the reliability of measuring techniques without analytical backup, are spurious.

The intra and inter-observer reliability were examined in this study.
The intra-observer reliability was discussed in section 2.5.1 of the pilot study. In summary, an expert observer could reliably analyse the images at two times on the same day and on separate days, one month apart. It was considered that the analysis technique was reliable enough to be used in the main study and that the results obtained could be reproduced on a separate occasion.

The variation in the measurements (which were not significant) obtained by the expert observer were not unexpected. The current opinion of psychologists on how the brain interprets information, suggests that noise would be expected in a situation such as this (Barber 1988 p18). The observer has to receive the information from the graphics screen and interpret the image. Decisions have to be made based on the observers previous knowledge of anatomy and experience with image interpretation. These decisions must then be implemented via mouse controlled cursor movement. The noise created by this information process is reflected in the variation of the intra-observer (same day) results, no significant variations were observed.
The *inter-observer* reliability study set out to establish whether different observers could reliably analyse the same images obtained in the study. The results of this study show that there was agreement between the main observer (the author) and the naive observers, for most of the variables measured.

Of the linear measurements (where the agreement was not as strong and significant differences were found) there did seem to be a trend in the results. For the external measures, such as the wrist width, the naive observers tended to under measure the dimension, compared with the main observer. This suggests that the naive observers found the identification of the outer most edge of the wrist difficult. On examining the area measures a similar trend was found to exist. The external wrist measures were recorded as smaller by the naive observers, compared with the main observer.

An explanation for this result is unclear, it was possible that the naive observers found identification of the boundary of the image difficult and allowed the cursor to encroach beyond the boundaries of the wrist during the analysis. This would also result in smaller wrist measures.

If this were the case, then one would expect that for the measurement of an internal dimension (eg. the carpal tunnel cross-sectional area) the naive observer would tend to measure larger than the main observer. Table 4.1 confirms this, the carpal tunnel cross-sectional area measurements of the naive observers were larger than those of the main observer. This suggests that the naive observers found the identification of the internal edge of the carpal tunnel difficult. The naive observers allowed the cursor to encroach into the image outside the boundaries of the carpal tunnel, thus finding larger carpal tunnel areas than the main observer.

Reasons for this behaviour are not obvious. It could be that the decision making processes of the naive observers could not cope with the amount of information
contained in the images. The naive observers could have been over cautious in their
cursor movement and positioning. These could all be as a result of insufficient training
of the observers.

These theories were not examined in this study and further work is required before a
full explanation of the inter-observer results can be presented. But these results
demonstrate that there was agreement in the results of the main observer and those of
the naive observers. However, there were some differences found in the results. It must
be stressed that caution should be expressed when analysing images of this nature, when
interpretation and measuring technique can both be sources of error. The limitations of
the information processing functions of observers is exacerbated, when the performance
of relatively naive observers is examined. It is particularly important when comparing
measurements with other studies or indeed with other observers, especially if a clinical
diagnosis is expected from the results of the analysis. Experience and training are
required before any measurements can be reliably obtained.

It should be stressed that the author performed all of the image analysis in the study.
Although the differences between observers were not encountered in this study the
inter-observer reliability study confirmed that the main observer was recording
satisfactory measures of the particular dimensions. Comparisons with other studies
reinforce this.
Discussion

5.2.3 Group Characteristics.

The comparisons of the heights and weights of the cases and controls suggests that the two groups were comparable with respect to self reported whole body measurements (No significant differences were found for height and weight).

The degree of hand preference of the cases and controls, assessed by the Oldfield (1971) Edinburgh handedness inventory, was compared. Kucera and Robins (1989) had previously reported a stronger hand preference in cases compared with controls. If this had been the case in this study, it would have been worth examining the correlation between the carpal tunnel sizes and hand preference. However, there was no significant difference between the two groups for laterality quotient (the measure of hand preference used in the Edinburgh handedness inventory). The claim made by Kucera and Robins (1989) was thus revoked. It was decided not to examine the image results with respect to the laterality quotient. It may be that the results of Kucera and Robins (1989) were biased by the subjects answers to the questionnaire. In chronic conditions such as CTS, the subject's use of the hands may be biased by the condition. The very fact that the subject had the condition may have stopped the subject using an afflicted hand for certain tasks. It could also have focussed the subjects attention on the afflicted side, further biasing the results.

Accepting these criticisms, it is useful to note that the use of handedness inventories give the examiner a more objective tool for assessing an issue, which is quite subjective. Asking the subject which is their dominant hand does not provide the examiner with information regarding the tasks performed by each hand, and the degree of hand preference. The use of handedness questionnaires is thus advocated, as long as the issue of cause and effect is accounted for.

The external wrist dimensions of the cases and controls were compared to assess the comparability of the two groups. Both wrist breadth and depth measures were found to
be different in the two groups. The cases had significantly larger wrist dimensions than the controls. The difference in the means was 9% for both the breadth and depth measures. A similar result was found for the wrist circumference measure. The cases wrist circumferences were 9.7% (p<0.05) larger than the controls. It is evident that the cases were larger than the controls, by a factor of 9% (consistent for all of the measurements). The implication of this 9% figure is discussed in the imaging section of the discussion.

Wrist ratios were also calculated to test the claims by Johnson et al. (1983); and Gordon et al. (1988), that the wrist ratio (the wrist depth divided by the breadth) would be smaller for cases compared with the controls. This claim was rejected as no significant difference was found between the two groups. The unsuitability of the test is demonstrated by examining the sensitivity and specificity of the test. 5 of the cases were identified as being above the 0.7 threshold for CTS. This results in a sensitivity of just 61%. 2 of the controls were identified as being in the risk group for CTS, if the threshold of a wrist ratio of 0.7 was used (Gordon et al. 1983). This results in a specificity of 15%. Since the sample size is small it is difficult to draw conclusions about the use of tests as diagnostic aids. But it is considered that the wrist ratio test is of little or no use for the diagnosis or screening for CTS. This requires further work to confirm this conclusion.

Other external upper limb dimensions were also measured and deserve only a brief mention here. Palm width and radius length were found not to differ between the two groups. Hand length was significantly greater in the controls. It was not thought that these results had an influence on the overall findings of the study.

The test for impaired joint flexion in the proximal inter-phalangeal (PIP) joint used by Turner (1989) was tested. The results here did not agree with those of Turner (1989)
where a significant difference was found between the cases and controls. In this study there was no difference found for the PIP test. Although there was a trend for the cases to have greater impairment than the controls (as suggested by Turner 1989). The reason for this still remains unclear. Whether the impairment of joint flexion is a result of increased joint stiffness, increased oedema or increased friction of the flexor tendons is still unknown.

Another test of finger mobility, at the metacarpophalangeal joint (the MCP test) was also performed. It is known that the action of flexing the index finger at the MCP joint, involves the use of the first lumbrical muscle of the hand. This muscle obtains its motor supply from the median nerve distal to the carpal tunnel. It was hypothesised that if any motor impairment had occurred, this would be reflected in the ability to perform the test. Indeed, there was a significant difference found between the cases and controls for the MCP test. Further work is required before any claims regarding the suitability of this test to CTS diagnosis can be made.

At this stage it is not possible to establish the sensitivity or specificity of these tests. Thresholds would have to be established to identify those with and without median nerve motor involvement. This would require a study with far greater numbers than this.

The grip strength of the cases was significantly smaller than the controls. Gellman et al. (1989) suggested that the grip strength would reach 116% of the preoperative level 6 months after surgery for CTS. Three weeks after surgery, grip strength was reduced to 28% of the preoperative level. These results express the need for patients to be given enough time to recover completely from surgery before returning to work. If the work involves the use of a power grip, particular care should be taken. If the occupation of the patient is suspected to be the cause of the CTS and return to work after surgery is anticipated, certain surgeons will not perform surgery (Louis 1990). The reduction in
grip strength postoperatively would surely exacerbate the occupational risk already suffered by the patient on return to work.
5.2.4 Image Data.

The images, once collected were analysed by the author. The widths and depths of the wrists and carpal tunnels were obtained. The wrist measures cannot be compared directly with the anthropometric data, as it could not be certain that the image slice was taken at the same position as the anthropometric measures. However, the ratio between the width and depths can be compared. As with the anthropometric measures both the width and depth measures for the cases were significantly larger than the controls. The difference between the two groups was 9%, as for the anthropometric measures. The differences in size of the two groups obtained by external measurement was thus reflected in the image data. No significant difference was found for the carpal tunnel width and depth measures.

As expected from the anthropometric data the wrist cross-sectional areas of the cases were significantly larger than those of the controls. The carpal tunnel cross-sectional areas were not. There was no significant difference between the carpal tunnel cross-sectional areas of the cases and controls. Clearly the anthropometric differences between the two groups may have biased the result obtained. By normalising the results for wrist size this source of bias may be removed (See Table 4.15).

After normalisation no significant differences were found between the cases and controls for any of the carpal tunnel measures. This result agrees with recently published data from CT studies on carpal tunnel cross-sectional areas, where no significant differences were found, although normalisation was not performed (Merhar et al. 1986; Schmitt et al. 1988).

All of the cases in the CT literature were diagnosed using electrophysiological tests, except the Liang (1987) study where symptomatic diagnosis were made. The results of the case-control studies are conflicting. Some authors (Dekel et al. 1980; Bleecker et al. 1985; and Liang 1987) found the case’s carpal tunnel cross-sectional areas to be
Discussion

significantly smaller than the controls. Others found no difference between the cases and controls (Dekel and Coates 1979; Merhar et al. 1986; and Schmitt et al. 1988). Winn and Habes (1990) reanalysed the results of Bleecker et al. (1980). Interestingly the opposite result was found when some of the confounding variables were controlled for. The case's carpal tunnel cross-sectional areas were found to be significantly larger than the controls. The validity of the results of some of the studies is in doubt because of the small numbers of subjects involved, although the standard errors of the measures are very similar. The validity of the image analysis method was in question as no validation of the methods was reported. The results of Winn and Habes (1990) seem at first to contradict the opinions of most of the authors in the area. However, looking at the other data in the literature (table 1.20), some of the female cases were reported to have larger cross-sectional areas than some of the male controls. There is clearly a need for further research in this field to confirm the results already obtained.

MRI has the advantage over CT imaging systems in that soft tissue imaging is possible. As the soft tissue is the main contributor to the compression of the median nerve in the carpal tunnel MRI is a more appropriate method for imaging the carpal tunnel, hence it's use in this study.

The consensus of the more recent studies, is that there is no evidence to suggest that cases have smaller carpal tunnels than controls (Merhar et al. 1986; Schmitt et al. 1988; and Winn and Habes 1990). This study supports this view.

A number of issues deserve comment in the light of these results;

i. It is now thought unlikely that the compression of the median nerve occurs as a result of a decrease in cross-sectional area of the carpal tunnel. It is therefore more likely that the volume of the contents of the carpal tunnel increases to such an extent that compression occurs.
ii. It follows that a predisposition to CTS, as a result of a small carpal tunnel is unlikely. It appears that cases and controls have similarly sized carpal tunnels. There is little evidence to suggest that those with small carpal tunnels, are at greater risk of contracting CTS, than those with larger carpal tunnels.

iii. Imaging of the median nerve in the area of compression would seem at first to be a reasonable course of action. However, surgical evidence suggests that the nerve is so compressed and flattened within the carpal tunnels of cases, that identification of the nerve from the surrounding tissue may be difficult, if not impossible, with current image resolution. This extreme flattening was confirmed during surgery where all of the median nerves were seen to be flattened.

iv. The use of MRI as a basis for diagnosing CTS seems inappropriate. MRI imaging is now very popular in the USA and patients are regularly sent for MRI diagnosis. Considering the disputes in the literature, regarding the difficulties in identifying differences between cases and controls, the reasoning behind imaging patients with CTS is unclear. The evidence suggests that investigators cannot identify objective differences between cases and controls. Problems of the inter-observer reliability only increases doubts as to the wisdom of this type of diagnostic aid.

MRI does have a place where the cause of a nerve compression at the wrist is thought to be a result of anatomical anomalies and abnormal structures. The images may help the physician decide on the best course of action.

v. The use of MRI as a pre-employment screening aid, could have been advocated by unscrupulous employers; if differences between cases and controls had been identified; or if individuals likely to develop CTS could be identified. There is no evidence to advocate the use of MRI for such a purpose.
These results are related to the resolution of the imaging system used in the study. This in no way negates the work carried out here. It is logical to assume that as resolution of imaging systems increases, the confidence intervals of the results obtained from images will reduce. This provides more chance of significant results being obtained. In the field of MRI where progress over the past decade has been so great, it would be foolish to attempt to make absolute conclusions from even the most up to date equipment. The image quality and resolution has developed in just 12 years from almost indistinguishable wrist images reported by Hinshaw et al. (1979), to images of high quality from Healy et al. (1990). Three dimensional wrist imaging is now a reality (Richman et al. 1987). The rate of progress must not be ignored and this progress must be put to good use in the development of our scientific understanding of conditions such as CTS.
5.2.5 The T1 Calculations.

The decision to attempt to measure the T1 of the cases carpal tunnels was based on the assumption that a diseased wrist would experience an increase in water content. If this did occur the sequences used would be expected to identify these areas of increased water content. This increase in water content may indeed occur in the acute state, where the condition is in its early stages, particularly when occupationally induced. Schuind et al. (1990) hypothesised that mechanical stresses caused irritation of the synovium by friction. This would result in acute oedema and eventually the formation of scar-type synovial hypertrophy. Indeed, this synovial hypertrophy was observed during the surgical observation of the cases' release operation (section 4.6).

The scar-type synovial tissue would not be expected to contain any more water than the tendons themselves, they appeared as areas of low signal intensity. So, although oedematous formations may initially occur as a result of the initial stages of the condition, they will be replaced with the scar-type synovial hypertrophy. This will appear as a similar signal intensity as the tendons themselves. Thus once the scar-type synovial hypertrophy had been laid down, the carpal tunnel will appear on the images as similar to those of the controls.

It is more likely that the change from oedematous tissue to scar-type synovial hypertrophy occurred too rapidly to be encountered in a study of this nature. The cases were imaged at least one month after they were identified. It is likely that the condition had developed many months before the patients had even reach the stage of appearing on the consultants waiting list. Indeed, the condition probably developed long before this, as the patient under went the procedure of attending the general practitioner clinic and then eventually being referred to the consultant.

It is not clear whether an early diagnosis of CTS and immediate imaging would result in any increased signal within the carpal tunnel. This is an area for further study where
strict time constraints would have to be applied.

Other methods could be employed to image the tendons in the carpal tunnel. Sequences used to image solids can be employed. Tendons have short relaxation rates and would be more suited to alternative imaging sequences which allow for this. Hardware changes would be necessary for this type of imaging.

Another method of investigating the relaxation times of the carpal tunnel would be to increase the field strength to increase the signal to noise ratio. This again would require hardware alterations. These changes would only be worth considering if further investigation of the carpal tunnel were envisaged. The theory and implications of such a study will not be discussed here.
The tests for CTS (Phalens test and the flick test) were both carried out during the subject interviews. The sensitivity and specificity were both 90%. This was higher than those figures quoted in the literature (mean sensitivity and specificity of 54% and 75.25% respectively: tables 1.9 of the literature review). Although these sensitivity and specificity values of Phalens test are high, it is easy to see how susceptible the test is to errors in timing. By reducing the test time to 50 seconds, the specificity was increased to 100% at the cost of the sensitivity (falling to 80%). It was not possible to predict the effect of increasing the test time by 10 seconds, but clearly the almost arbitrary 60 second test time chosen by Phalen for the test requires thorough validation.

The flick test performed less well in the study. A sensitivity of only 50% was found. This compares well with the results of DeKrom et al. (1990) who also found a sensitivity of 50%. Half of those with the condition were not identified as having it by this test. There is clearly variation in the literature as to the sensitivity of this test (table 1.8). More work is required.
Since the subject numbers were so small the other questionnaire details collected will be discussed only briefly.

_Night awakening_ was found to be a test with high sensitivity, 90% of the cases reported this symptom. Other studies have reported this symptom to be associated with CTS (Tanzer 1959; Posch and Marcotte 1976; and Ragi 1981).

_Occupational changes_ were found to have occurred in 40% of the cases. Half of these changes were almost certainly as a result of having CTS. It was not possible, due to lack of evidence, to attribute the onset of CTS to any occupational factors in any of the cases. However, out of those cases who reported job difficulties and actually changed job, two were found to be performing tasks known to be risk factors for CTS (Silverstein et al. 1987). Both were carrying out highly repetitive and forceful manoeuvres throughout the working day, often on a "flat out" basis.
5.3 The System Development.

Although the MRI system at the University of Surrey had the facility to image wrists, improvements to the image quality had to be made for the purposes of this study. This was the first aspect to be investigated. A solenoid coil had been previously developed, but alterations had to be made.

i. Excessive noise in the system meant that the coaxial cabling had to be further shielded using copper braiding. Although this did solve some of the noise problems, it also changed the tuning properties of the coil, by altering the capacitance of the cable. This resulted in problems when attempting to tune the coil on the vector impedance meter. The tuning box in the system did not have the range of capacitance, on one of the variable capacitors, to tune the coil. By reducing the length of the cable from the tuning box to the coil, the tuning capacitor eventually came within range and the coil could once more be tuned.

This was a lengthy piece of experimentation, the coil had to be tuned on a meter whilst it was connected to the system. The magnet had to be switched off, as the field interfered with the meter dial.

ii. The correct slice position had to be calculated by imaging phantoms of a known shape and comparing the images with the positions of the phantoms. The centre slice of the multi-slice sequence was then marked on the coil mount. A scale was also fixed to the bed which corresponded to distances from the centre slice to the scale. These scales were later used to align the subjects distal wrist crease with the centre slice. This depended on the bed being in the correct position during the imaging session. It became clear that the bed position had to be checked each time a subject was imaged.

iii. The coil had to be tested on volunteers to establish whether a subject could be imaged successfully. Problems have previously been encountered with the subject position, this was discussed in the literature review. Subjects arms regularly became
ischaemic during the imaging session. It was decided to change this position to a more comfortable one, positioning the arm under the abdomen.

Although the subjects comfort was improved and no complaints about ischaemic arms were reported, loading of the coil was encountered. The subjects body was too close to the coil during the imaging, thus changing its tuning properties. In an attempt to solve this problem the coil was positioned further away from the body, by raising the bed and lowering the coil. Foam packing between the body and the coil ensured that the subjects body was not too close to the coil. It was also found that tuning the coil while the subject was in position improved the signal.

In conjunction with the improvements in the coil, it was hoped that surface coils could be developed. Surface coils are used extensively in MRI to increase the signal to noise ratio (Middleton et al. 1987). The solenoid coil was used to transmit the RF signal and the surface coil used to receive the signal. Various designs were tested on phantoms and volunteers. These tests proved unsuccessful. The signal to noise ratio was improved close to the region of the surface coil, but in the region of the carpal tunnels of volunteer’s wrists, the signal to noise ratio was greatly reduced. The signal drop off was so great, that the back of the wrist was not visible. The same was true of the phantom experiments.

It was thought that if the whole body coil was used as the transmit coil the signal could be improved. An attempt was made to tune the whole body coil in the system. Interaction of the whole body coil with the gradient coils made this impossible. There was no further attempt made to use either surface coils or the whole body coil in the study.

It was clear from published material (Middleton et al. 1987; and Mesgarzadeh et al.
1989a and b) that imaging of the tendons would be difficult. It was thought that this deserved further investigation. An alternative supply of tendons was required, as subjects could not be persuaded to lie in the system for the whole day, while experiments were performed. The alternative eventually came from a rather obscure source. Pig's fore trotters were obtained from a local butcher and imaged. They provided a large flexor tendon, in a structure similar to the carpal tunnel. There were clearly no complaints from the subjects during imaging.

Sequences of differing repetition times were used to image the trotters and satisfactory images were obtained. Inversion recovery sequences were also used to attempt to image the tendons and the tendon sheaths. The tendons could not be imaged, no signal could be obtained from the tendon itself. On dissection the tendon sheath was found to be very thin and clearly could not have been identified with the current resolution.

After extensive trials using pigs trotters the sequences used in the study were chosen. These sequences were those which were already in use on the system for imaging other parts of the body, few software developments were required for the pilot study to commence.

There was a brief investigation into the use of coronal wrist imaging. Some images were collected, but the results coincided with those of the literature (Middleton et al. 1987). The images were good and the course of tendons could sometimes be tracked, but they were by no means as informative as the axial cross-sectional images used in the study.

The pilot study was then performed, 58 wrists of asymptomatic volunteers were imaged. The results are discussed in chapter 2.

After the pilot study the magnet was passively shimmed by a colleague. The details of the shimming are included in section 3.2.1 on system modifications. At the same time
the gradient DAC box was replaced. Both of these adjustments to the system required alterations.

The slice position was changed so that the centre slice was closer to the centre of the bore, this was known to be the area of best homogeneity. Changing the centre slice required changes in the software controlling the gradients. The excitation frequency had to be changed to facilitate these changes. Once the new slice position had been established, it was then confirmed using the same technique as that used prior to the pilot study.

As a result of the change in slice position the coil mount had to be redesigned so the coil could be positioned nearer the centre of the bore. The scales on the bed allowing positioning of the subject also had to be changed.

Complications were found when attempting to image subjects in the new position prior to the main study. Some of the more over weight subjects found it difficult to enter the system in the new position. There also seemed to be more interaction with the coil (The coil was closer to the subject's abdomen in the new position). It was therefore decided to image subjects in the old position, with the arm extended above the head, if difficulties with subject entry were encountered in the main study (This was later found to be the case in many of the subjects.).
6 CONCLUSIONS.
6.1 Developmental Conclusions.

A system for successfully collecting axial MRI images of human wrists was developed, including a new position to alleviate patient discomfort.

The system was tested via a pilot study in which 58 normal volunteer wrists were imaged.

6.2 Main Conclusions.

The intra-observer reliability was examined and was found to be adequate. Errors in the intra-observer reliability were attributed to the information processes of the observer.

The inter-observer reliability was examined. Differences were discovered in the inter-observer reliability, clinical systems must therefore be evaluated and data used carefully, as the results obtained by two different observers may differ. If the course of treatment of a patient is dependent on the results of analysis caution should be expressed.

Differences between the dominant and non-dominant carpal tunnel cross-sectional areas of control wrists were identified. The carpal tunnels of the dominant side were smaller than those of the non-dominant side. Further research is required to explain this result.

It was not possible to identify differences in carpal tunnel cross-sectional area between CTS cases and healthy controls using the MRI system reported in this study. It must be stressed that the negative result obtained in this study may be related to the resolution of the imaging system used.

MRI is an expensive and complex imaging technique and funds are becoming scarce for its use in even modestly sized case-control studies. There is concern about the number of cases in this study and the conclusions must be treated with caution. But, since there
Conclusions

is such an agreement with the recent CT literature it is thought that the results are valid.

One final and additional concern that arises from this study, is that images obtained from MRI and indeed CT systems should be treated with caution and by experienced observers. The resolution of the imaging system should be assessed objectively before conclusions are made. These problems lead to the conclusion that MRI does not, at present, have a role in the clinical management of CTS (Healy et al. 1990). If system resolution, cost and speed of imaging can be improved this situation may change.
7 REFERENCES.
References


Callison, J.R., Thomas, O.J. and White, W.L., (1968) Fibro-fatty proliferation of the median nerve, Plastic and Reconstructive Surgery, 42: 403-413


Crowder, M.J., (1988) Personal communication


References


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References


Liang, C-L., (1987) CT-scanning of cross-sectional area of the carpal tunnel in cases of carpal tunnel syndrome, Journal of the Japanese orthopaedic Association, 61: 1033-1045


Louis, D., (1990) Proceedings of Occupational disorders of the upper extremities (Ed. Armstrong, T.), University of Michigan, USA


Mahloudji, M., (1968) Familial Carpal-Tunnel Syndrome Due to Amyloidosis, The Lancet, 313: 1374


References


Nichols, L., (1982) BSc Project, Liverpool Polytechnic


Pomeroy, K., (1989) Personal communication


References


Templeton, A.W. and Zim, I.D., (1964) The Carpal Tunnel View., *Missouri Medicine*, 443-444

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References


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I The Anatomy of the Upper Limb.

I.1 Introduction.

For the purpose of this study it is only necessary to understand the anatomy of the distal section of the upper limb. This account of the anatomy will therefore only cover the radius and ulna, the carpus, metacarpus and the digits. Most of the information in this review was derived from Hamiltons' Textbook of Human Anatomy (1976).

I.2 Bones of the Upper Limb.

The radius and ulna comprise the forearm, in the anatomical position the radius is the most lateral while the ulna the most medial.

*Radius:* The radius consists of two ends and a body. The proximal end forms the head of the radius, which articulates with the capitulum of the humerus and medially with the radial notch of the ulna. The distal end of the radius forms a prominence on the side of the wrist known as the radial styloid process. The styloid process has a concave articular surface with which, the two most lateral bones in the proximal layer of carpus, articulate.

*Ulna:* The proximal end of the ulna forms the trochlear notch, which articulates with the grooved trochlear of the humerus. The notch separates into two projections, the upper forms the olecranon and the lower the coronoid process.

The radial notch allows the head of the radius to rotate, facilitating the movements of supination and pronation of the forearm. The body of the ulna is connected to that of the radius by the inter-osseous membrane.

Distally the head of the ulna forms a bony prominence known as the ulna styloid
process (fig 1.1 Hamilton p97). The head of the ulna does not directly articulate with the carpus, but via a triangular fibrocartilaginous articular disc, which also allows for articulation with the radius.
Fig 1.1 Left Carpal and Metacarpal Bones, and Phalanges; Anterior Aspect.
I.3 The Carpus.

The carpus consists of eight carpal bones arranged in two layers of four. They are held firmly together by ligaments, although considerable movement between the bones may occur. The proximal layer of bones consists of the scaphoid, lunate, triquetral and pisiform (lateral to medial). The distal layer consists of the trapezium, trapezoid, capitate and hamate (fig I.1).

The proximal surfaces of the scaphoid, lunate and triquetral provide the surfaces for articulation with the distal end of the radius. The palmar aspect of this is concave with raised sides formed by the tubercle of the scaphoid and trapezium on the lateral side and the pisiform and hook of hamate medially, forming the carpal tunnel. These structures provide attachment for the flexor retinaculum (the so called transcarpal ligament), which encloses the carpal tunnel. Tendons and other structures pass through this tunnel from the forearm to the hand.

The distal layer of carpal bones provide articulation with the metacarpal bones of the palm of the hand. The first metacarpal articulates with the trapezium, the second with the trapezoid, the third with capitate and the fourth and fifth with the hamate (fig I.1).

The proximal layer of carpal bones articulates with the distal row via a mid carpal joint. At the mid carpal joint the convexity formed by the hamate and capitate articulates with the concavity formed by the scaphoid, lunate and triquetral. The convexity of the distal surface of the scaphoid articulates with the concavity formed by the trapezium and trapezoid.

Interosseous ligaments connect the carpal bones. Those of the distal row are very strong and thick particularly between the hamate and capitate. The bones of the carpus are further connected to each other by palmar and dorsal intercarpal ligaments and the lateral and medial ligaments.
The pisiform articulates with the palmar surface of the triquetral via a joint, which is independent of all the other intercarpal joints. It is attached distally by ligaments to the hamate and fifth metacarpal bone via the pisohamate ligament and pisometacarpal ligament respectively.

I.4 The Metacarpals.

There are five metacarpal bones of which only the first (that of the thumb) has unrestricted mobility with the carpal bones. Each metacarpal consists of a proximal base, a body and a distal head (fig I.1).

The base of the metacarpals articulate proximally with the distal row of carpal bones. The rounded heads of metacarpals articulate with the base of its respective proximal phalanx.

I.5 The Phalanges.

There are two phalanges in the thumb and three in each of the medial four digits. They form the bones of the digits and are held in position by collateral ligaments on the lateral and medial surfaces and a palmar ligament on the palmar surface. This prevents hyperextension of the joint.
I.6 Synovial Sheaths of the Wrist and Hand.

The synovial sheaths of the wrist and hand are divided into those of the anterior and those of the posterior aspect of the wrist. The anterior synovial sheath consist of 3 sheaths, which lie deep to the flexor retinaculum. The posterior synovial sheaths are more dedicated to their respective tendon, with only one common sheath.

**Anterior Synovial Sheaths:**

i. The common synovial sheath for the tendons of flexor digitorum profundus and flexor digitorum superficialis is known as the ulnar bursa. It extends upwards from 2.5cm proximal to the flexor retinaculum, around the tendons of both the flexor muscles. Distally it extends beyond the flexor retinaculum to the middle of the palm, except for the tendon of the fifth digit, where it communicates with the synovial sheath to the fifth digit (Gray 1977 p401). The bursa envelopes the tendons on the medial side, but does not usually extend around the lateral side. There may also be communication with the radial bursa deep to the median nerve.

It is now known that the tendons are not absolutely free from the ulnar bursa. They are attached to the floors of the synovial sheaths by extremely fine transparent folds of synovial membrane known as the mesotendons (Zbrodowski et al. 1981). The mesotendons in the metacarpal region vary in shape, either wedge; trapezium; or parallelogram shaped where as those in the carpal region have a more consistent flattened shape.

ii. The synovial sheath for the tendon of flexor pollicis longus forms the radial bursa. It is wound around the medial side of the tendon and extends distally almost as far as the attachment to the distal phalanx.

iii. The synovial sheath for the tendon of flexor carpi radialis extends from 2.5cm proximal to the flexor retinaculum to its insertion of its tendon. It may communicate
with the radial bursa.

Each pair of flexor tendons for the medial four digits are enclosed by their own synovial sheaths in the phalangeal region. These extend from the metacarpophalangeal joints almost to the insertion of the profundus tendon on the distal phalanx.

*The Posterior Synovial Sheaths:* These are confined to the close proximity of the wrist from 1 cm proximal to the extensor retinaculum to the bases of the metacarpals. There is a common sheath for the tendons of abductor pollicis longus and extensor pollicis brevis on the lateral side of the styloid process of the radius; a common sheath for the tendons of extensor carpi radialis longus and brevis on the back of the radius, a common sheath for the tendon of extensor digitorum and extensor indicis. There are separate sheaths for the tendons of the extensor pollicis longus, extensor digiti minimi and extensor carpi ulnaris.
I.7 The Retinacula of Flexor and Extensor Tendons.

As the muscles and nerves pass from the arm into the hand they are held in position by ligaments known as the flexor and extensor retinacula.

*Flexor Retinaculum:* This is a rectangular sheet of fibrous tissue attached to the tubercles of the trapezium and scaphoid laterally and to the hook of hamate and pisiform medially. The proximal limit of the retinaculum occurs beneath the distal wrist crease on the anterior aspect of the wrist. The flexor retinaculum forms the palmar border of the carpal tunnel.

The flexor retinaculum prevents anterior bowing of the flexor tendons of the hand and fingers. If the contents of the carpal tunnel increase or the flexor retinaculum thickens to such an extent that the flexor retinaculum becomes tightened, compression of the median nerve occurs. This is the basis of CTS. One method of treatment is to section the flexor retinaculum to release this pressure on the nerve.

The blood supply to the flexor retinaculum was found by Zbrodowski and Gajisin (1988) to arise from arteries near the carpal region. It was also possible to identify a superficial and deep network of vessels in the structure. The superficial network is formed by unnamed branches from the radial and ulnar arteries. The radial artery sends out 3–5 small arterial branches forming a network with anastomoses between them. It is interesting that no arterial branches are formed from the thenar and hypothenar muscles.

The deep network is formed from 2 to 4 small branches from the superficial palmar arch, forming a network in the synovial membrane on the deep surface of the flexor retinaculum. Anastomoses are found between these networks thus supplying the flexor retinaculum from both sides. The implications of these blood supplies are of importance.
if the flexor retinaculum is to be sectioned during a carpal tunnel decompression operation (section 4.6).

*Extensor Retinacular*: This is a band attached medially to the distal end of the ulna, the medial carpal bones and the medial ligament of the wrist joint and laterally to the anterior border of the radius. Six compartments are formed beneath the extensor retinaculum through which the extensor tendons pass through on route to the dorsal aspect of the hand.
1.8 The Muscles of the Forearm.

The muscles of the forearm may be divided into two groups. The anterior muscles are generally flexors of the wrist and hand, whereas the posterior muscles are generally the extensor muscles of the wrist and hand.

1.8.1 The Anterior Muscles.

Table I.1 gives details of the origins, insertion, nerve supply and action of the anterior muscles of the forearm. Pronator teres and Pronator quadratus are both, as their names suggest, pronators of the wrist. The rest of the muscles are flexors, some acting only on the wrist (flexor carpi radialis, palmaris longus, flexor carpi ulnaris), while others act as flexors of the digits (fig I.2 Hamilton 1976 p 173).
<table>
<thead>
<tr>
<th>Muscle</th>
<th>Origin</th>
<th>Insertion</th>
<th>Nerve and Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pronator Teres</td>
<td>1. Medial epicondyle of humerus. 2. Coronoid process of the ulna.</td>
<td>Middle part of lateral surface of the radius</td>
<td>Median nerve.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pronation of the radius and ulna.</td>
</tr>
<tr>
<td>Pronator Quadratus</td>
<td>Front and lower quarter of ulna.</td>
<td>Front and lower quarter of radius.</td>
<td>Anterior interosseous.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pronation of the radius.</td>
</tr>
<tr>
<td>Palmaris Longus</td>
<td>Medial epicondyle of the humerus.</td>
<td>Palmar aponeurosis and the flexor retinaculum.</td>
<td>Median nerve.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Flexor of the hand and wrist.</td>
</tr>
<tr>
<td>Flexor Carpi Ulnaris</td>
<td>Medial epicondyle of humerus, medial ligament of the elbow joint, and medial side of the coronoid process of the ulna.</td>
<td>Pisiform bone.</td>
<td>Ulnar nerve.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Flexion and adduction of the hand at the wrist.</td>
</tr>
<tr>
<td>Flexor Carpi Radialis</td>
<td>Medial epicondyle of the humerus.</td>
<td>Bases of 2nd and 3rd metacarpals and the adjacent carpals.</td>
<td>Median nerve.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Flexion and abduction of the hand at the wrist.</td>
</tr>
<tr>
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<td>----------------------------------------------</td>
<td>-----------------------------------------------------------------</td>
</tr>
<tr>
<td>Flexor Digitorum Profundus</td>
<td>Anterior and medial surfaces of the ulna, via an aponeurosis to the posterior surface of the ulna and the interosseous membrane.</td>
<td>Four tendons insert on the distal phalanx of their respective digit.</td>
<td>Medial half: Ulnar nerve. Lateral half: Median nerve.</td>
</tr>
<tr>
<td>Flexor Pollicis Longus</td>
<td>Anterior surface of the radius and the interosseous membrane.</td>
<td>Base of the distal phalanx of the thumb.</td>
<td>Flexes the thumb at the interphalangeal joint.</td>
</tr>
<tr>
<td>Flexor Digitorum Superficialis</td>
<td>Medial epicondyle and the oblique line of the radius.</td>
<td>Four tendons insert on the body of the middle phalanx of their respective digits.</td>
<td>Flexion of the fingers at the proximal interphalangeal joint. Also flexion at the metacarpophalangeal joints.</td>
</tr>
</tbody>
</table>
I.8.2 The Posterior Muscles.

Table 1.2 gives details of the origin, insertion, nerve supply and action of the posterior muscles of the forearm. Some of the muscles act on the medial four digits extending the wrist and hand. Others act exclusively on the first digit extending and abducting the thumb.
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Extensor Digitorum</td>
<td>Lateral epicondyle</td>
<td>Tendon passes to each of the medial four digits, splits and inserts on the base of the middle and distal phalanx.</td>
<td>Radial nerve. Extends the fingers at the metacarpophalangeal joint and interphalangeal joint.</td>
</tr>
<tr>
<td>Extensor Digiti Minimi</td>
<td>Lateral epicondyle</td>
<td>Phalanges of the 5th digit.</td>
<td>Radial nerve. Extends the 5th digit.</td>
</tr>
<tr>
<td>--------------------</td>
<td>----------------------------------------------</td>
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<td>-------------------------------------------------------</td>
</tr>
<tr>
<td>Abductor Pollicis Longus.</td>
<td>Posterior surfaces of the radius and ulna and interosseous membrane.</td>
<td>Base of the first metacarpal.</td>
<td>Posterior Interosseous nerve. Abducts the hand at the wrist or the thumb at the carpometacarpal joint.</td>
</tr>
<tr>
<td>Extensor Indicis.</td>
<td>Posterior aspect of the ulna and interosseous membrane.</td>
<td>Tendon blends in with the medial side of the extensor digitorum tendon.</td>
<td>Posterior Interosseous nerve. As for extensor digitorum.</td>
</tr>
</tbody>
</table>
It is important to note which of the flexor tendons actually pass through the carpal tunnel. The tendon of palmaris longus (a muscle which is frequently absent and is of limited use) passes superficial to the flexor retinaculum and inserts in the palmar aponeurosis and the flexor retinaculum. It does not pass through the carpal tunnel. Neither does the tendon of flexor carpi ulnaris which inserts on the pisiform bone and this is attached to the hamate and fifth metacarpal ligament. The tendon of flexor carpi radialis inserts on the base of the second and third metacarpals and adjacent carpal bones. Although this tendon passes deep to the flexor retinaculum (Hamilton 1976 p171) it is not considered to be within the carpal tunnel. It has its own fibro-osseous tunnel outside the carpal tunnel (Robbins 1963). The tendons of the major wrist flexors do not actually pass through the carpal tunnel.

The tendons of flexor digitorum profundus and superficialis both pass through the carpal tunnel before inserting on their respective phalanges. Their position within the carpal tunnel are described in section 1.9. In addition to the flexor tendons of the medial four digits, the tendon of flexor pollicis longus also passes through the carpal tunnel, before insertion occurs at the base of the distal phalanx of the thumb.
Fig 1.2 Anterior Muscles of the Forearm. p173
I.10 The Short Muscles of the Hand.

There are a number of shorter muscles which are contained in the hand which provide the finer movements of the finger and thumb. There are four groups and are shown in fig 1.3 (Hamilton 1976 p176).

1. The muscles of the thenar eminence.
2. The muscles of the hypothenar eminence.
3. The lumbrical muscles coming from the tendons of flexor digitorum profundus.
4. The adductor muscles of the thumb and interossei muscles which have their origin on the metacarpal bones.
Fig 1.3 p176 Hamilton short muscles.
i. The muscles of the thenar eminence are the lateral muscles in the palm of the hand. They consist of abductor pollicis brevis, flexor pollicis brevis and opponens pollicis. Table I.3 gives details of their origin, insertion and nerve supply. They are usually supplied by the median nerve and have their origin on the flexor retinaculum, the tubercle of the trapezium and the tubercle of the scaphoid. These muscles of the thenar eminence are important when measuring the distal motor latencies of the median nerve (section 1.7.11).

ii. The muscle of the hypothenar eminence consist of abductor digiti minimi, flexor digiti minimi brevis and opponens digiti minimi. These muscles act on the little finger and the fifth metacarpal bone and are supplied by the ulnar nerve. Table I.4 gives details of their origin, insertion and nerve supplies.

In addition, a small but variable muscle (palmaris brevis) lies in the skin of the hypothenar eminence. Its action is to prevent the hypothenar eminence becoming flattened during palmar contraction.

iii. The lumbrical muscles are four slender muscles, attached in the palm to tendon of flexor digitorum profundus. The first and second lumbricals are attached to the lateral side of the tendons of the index and middle fingers respectively. The third and fourth to the adjacent side of the tendons between which they lie (ie. the tendon of the third, fourth digit and fourth and fifth digit respectively). The first and usually the second are supplied by the median nerve, the third and fourth by the ulna nerve, which may also supply the second.

They extend the fingers at the interphalangeal joints through the extensor digitorum tendons. With the fingers extended at the interphalangeal joints they flex the fingers at the metacarpophalangeal joints. Indeed, flexion at the metacarpophalangeal joints of the medial four digits with the interphalangeal joints kept extended, involves only the
lumbrical muscles (Hamilton, 1976, p 106). This was the reason for the measuring of the metacarpophalangeal joint flexion in the main study (section xx).

iv. The abductor muscle of the thumb (adductor pollicis) has 2 heads, a transverse and an oblique. The transverse has an origin on the palmar surface of the third metacarpal and the oblique from the base of the second and third metacarpal bones and the capitate (table I.5). It is responsible for pressing the thumb against the side of the index finger. It is supplied by the ulnar nerve.

The interossei muscles are arranged in 2 series palmar and dorsal. Details of their origin, insertion and nerve supply are given in table I.5. The palmar interossei adduct the other digits towards the third digit. The dorsal interossei adduct the medial three digits from a line drawn through the third digit.
<table>
<thead>
<tr>
<th>Muscle</th>
<th>Origin</th>
<th>Insertion</th>
<th>Nerve and Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abductor Pollicis Brevis</td>
<td>Anterior surface of the flexor retinaculum, tubercle of the trapezium and scaphoid.</td>
<td>Lateral side of the base of the proximal phalanx of the thumb.</td>
<td>Median nerve. Draws the thumb forward into a plane perpendicular to the palm.</td>
</tr>
<tr>
<td>Flexor Pollicis Brevis</td>
<td>Anterior surface of the flexor retinaculum.</td>
<td>Lateral side of the base of the proximal phalanx of the thumb.</td>
<td>Median nerve. Moves the thumb into the plane of the palm at the metacarpophalangeal joint.</td>
</tr>
<tr>
<td>Opponens Pollicis</td>
<td>Flexor retinaculum and the trapezium.</td>
<td>Lateral border of the first metacarpal.</td>
<td>Median nerve. Rotates the thumb so that the nail faces anteriorly, and flexes the thumb at the metacarpophalangeal joint.</td>
</tr>
<tr>
<td>Muscle</td>
<td>Origin</td>
<td>Insertion</td>
<td>Nerve and Action</td>
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<tr>
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<tr>
<td></td>
<td></td>
<td>phalanx of the 5th digit.</td>
<td>Abducts the 5th digit.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>phalanx of the 5th digit.</td>
<td>Flexion of the 5th digit at the</td>
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<td></td>
<td></td>
<td></td>
<td>metacarpophalangeal joint.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>metacarpal.</td>
<td>Pulls the 5th metacarpal anteriorly and rotates the</td>
</tr>
<tr>
<td>Palmaris Brevis.</td>
<td>Flexor retinaculum</td>
<td>Skin of the along the ulnar</td>
<td>digit so that the nail faces anteriorly.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>border of the hand.</td>
<td>Ulnar nerve.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Prevents the hypothenar eminence from becoming</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>flattened during the palmar grip.</td>
</tr>
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<td>-----------------------------</td>
<td>-------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Lumbricals</td>
<td>From flexor digitorum profundus tendons.</td>
<td>Into the lateral side of extensor expansions of the 2\textsuperscript{nd} to 5\textsuperscript{th} metacarpophalangeal joint.</td>
<td>1 and usually 2 median nerve. 3, 4 and (sometimes 2) ulnar nerve. Extend the fingers at the interphalangeal joints through the extensor digitorum tendons, flexion of fingers at metacarpophalangeal joint (when fingers extended).</td>
</tr>
<tr>
<td>Palmar interossei</td>
<td>1 and 2 medial side of shaft of 1\textsuperscript{st} and 2\textsuperscript{nd} metacarpals</td>
<td>Into extensor expansion of digit of respective metacarpal.</td>
<td>Finger adduction.</td>
</tr>
<tr>
<td></td>
<td>3 and 4 lateral side of shaft of 4\textsuperscript{th} and 5\textsuperscript{th} metacarpals</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dorsal interossei</td>
<td>4 muscles each attached via 2 heads to adjacent metacarpal shafts.</td>
<td>Into extensor expansion of the respective proximal phalanx.</td>
<td>Finger abduction.</td>
</tr>
<tr>
<td>Adductor Pollicis</td>
<td>2 heads: 1. Palmar surface of the 3\textsuperscript{rd} metacarpal.</td>
<td>Medial side of the base of the proximal phalanx of the thumb.</td>
<td>Ulnar nerve.</td>
</tr>
<tr>
<td></td>
<td>2. Base fo 2\textsuperscript{nd} and 3\textsuperscript{rd} metacarpal and capitate</td>
<td></td>
<td>Presses the thumb against the 2\textsuperscript{nd} digit.</td>
</tr>
</tbody>
</table>
I.11 The Blood Supply to the Hand and Wrist.

At the cubital fossa the brachial artery splits and forms the radial and ulnar arteries which, continue to supply the hand and wrist.

1.11.1 The Radial Artery.

The radial artery descends down the arm on the lateral side of the forearm, lying adjacent the tendons of flexor pollicis longus on its medial side and brachioradialis on its lateral side. It is just proximal to the wrist where the pulse is usually taken from the radial artery. It then passes downwards and backwards below the styloid process of the radius and deep to the extensor tendon of the thumb, it passes forwards between the proximal ends of the first and second metacarpals and traverses the adductor pollicis muscle to enter the palm. In the palm it anastamoses with the deep division of the ulnar artery to form the deep palmar arch. The superficial palmar branch evolves just before the artery leaves the anterior aspect of the wrist, this anastomoses with the superficial division of the ulnar artery.

1.11.2 The Ulnar Artery.

The ulnar artery passes down the medial side of the forearm lateral to and overlapped by flexor carpi ulnaris. It ends on the lateral side of the pisiform bone in front of the flexor retinaculum, there it divides into a superficial and a deep branch. The superficial branch curves downwards and laterally with the palm deep to palmaris brevis and the palmar aponeurosis. It usually communicates with a small branch of the radial artery to complete the superficial palmar arch. The deep division of the ulnar artery passes downwards and backwards into the palm, through the hypothenar muscles on the medial side of the hook of hamate. This joins the terminal part of the radial artery to form the deep palmar arch.

The common interosseous artery arises just distal to the communicant of the ulnar artery, where it divides into the anterior and posterior interosseous arteries. It is from
the anterior interosseous artery that a long slender branch, the median artery evolves, which accompanies the median nerve into the palm. This artery may become enlarged or "persistent" as it accompanies the median nerve into the palm (Gray 1977 p543). This is sometimes responsible for compression of the median nerve in the carpal tunnel.
I.12.1 The Normal Anatomy of the Median Nerve.

The median nerve arises in the brachial plexus and is formed by the union of a lateral root from the lateral cord and the medial root from the medial cord (fig 1.4). It therefore contains fibres the 5th, 6th, 7th, and 8th cervical nerves and the 1st thoracic nerve. It descends down the arm and arrives at the cubital fossa on the medial side. It gives off no branches in the upper arm.

In the forearm the median nerve runs down the middle of the arm (hence its name median). Shortly after entering the forearm it gives off an anterior interosseous branch, which lies deep to the interosseous membrane and supplies the deep flexor muscles in the forearm (table I.1).

At the wrist it lies deep to the palmaris longus tendon and gives off a palmar cutaneous branch, before entering the palm through the carpal tunnel deep to the flexor retinaculum. The palmar cutaneous branch may easily be damaged during injuries to the wrist or even during the carpal tunnel decompression surgery. Therefore, care must be taken not to damage the nerve during the initial incision. Taleisnik (1973) advised a longitudinal incision on the ulnar side of the axis of the ring finger ray. This incision should extend through the skin, subcutaneous tissue and ligament, thus keeping all three tissue layers and the palmar cutaneous branch of the median nerve intact. Post operative problems could also be avoided using this method.

Distal to the flexor retinaculum the median nerve gives off an important thenar branch, providing the motor supply to the thenar muscles of the hand. The median nerve ends in five palmar digital cutaneous branches, which provide sensory supply to the 1st, 2nd and 3rd digits, the lateral half of the 4th digit and the whole of the palmar surface. Sensory supply is also provided to the dorsal surface of the distal part of the middle phalanx and the whole of the distal phalanx, including the nail bed. The median nerve sensory distribution is shown in fig 1.1. It is important that sufferers of CTS actually have the symptoms in these areas. Digital motor branches supply the 1st lumbrical
muscle and sometimes the 1st interosseous muscle (table I.5). The second lumbrical muscle is supplied by the digital branch to the adjacent sides of the middle and ring fingers.
Fig I.4 Anatomy of the Brachial plexus.
I.12.2 Anatomical Abnormalities of the Median Nerve.

Communications in the forearm between the median and ulnar nerves have been reported in the literature. (Iyer and Fenichel 1976). This 'Matin-Gruber' anastomoses was estimated to occur in 15% of the population. Such anastomoses may cause problems when attempting to measure NCV in the forearm.

Variations in the thenar motor branch have also been reported. The thenar branch usually leaves the median nerve distal to the flexor retinaculum. Lanz (1977) examined 246 hands during surgery and found variations of this branch to exist, these were classified into four groups.

i. Variations in the course of the thenar branch. Lanz (1977) found 46% of the thenar branches to be normal and divided from the median nerve distal to the flexor retinaculum. In 31% of nerves investigated, the thenar branch left the median nerve within the carpal tunnel under the flexor retinaculum. In 23% the thenar branch actually perforated the flexor retinaculum, this may cause compression of the nerve by the ligament.

ii. Accessory branches of the median nerve distal to the carpal tunnel. Double motor branches were reported but only very rarely (7%). However, those which are encountered during surgery should be preserved.

iii. High division of the median nerve. The high division of the median nerve rarely occurred (3%) and was normally associated with a large median artery. Two median nerves occur in the forearm often of the same diameter, separated by the median artery.

iv. Accessory branches proximal to the carpal tunnel. Branches of the thenar motor branch very rarely occurs (2%) and could be responsible for unusual electrophysiological test results.
Variations in the median nerve do occur and should be considered when diagnosing CTS and electrophysiological tests are inconclusive.
I.13 Cross Sectional Anatomy.

The arrangement of the carpal bones is difficult to perceive from cross-sections of the wrist as there is considerable overlap of the bones from slice to slice. It is important to know of the arrangement of the bones, tendons, ligaments, muscles and nerves when examining images. This section gives an overview of the cross-sectional anatomy of the wrist (and in particular of the carpal tunnel), starting with the most proximal section and moving distally.

First consider the wrist in cross-section at the very distal end of the radius and ulna. The extensor tendons are arranged on the dorsal aspect of the wrist in close proximity to the radius. On the palmar side of the arm the flexor tendons of the digits are arranged in a flattened shape. The tendons of flexor digitorum profundus are arranged in a line of four, deep to the tendons of flexor digitorum superficialis. These are arranged in 2 rows of 2 tendons. The median nerve is at this point separate from the flexor tendons, as no flexor retinaculum exists this far up the arm. The carpal tunnel has yet to be formed.

Next consider the slice at the proximal border of the flexor retinaculum. The carpal tunnel is now formed by an osseous trough, via the scaphoid, capitate, hamate, triquetral and pisiform bones. The flexor retinaculum bridges the trough from the scaphoid to the pisiform thus enclosing the carpal tunnel. The superficialis and profundus flexor tendons surrounded by ulna bursa, as well as flexor pollicis longus surrounded by radial bursa, are contained within the carpal tunnel along with the median nerve. Flexor carpi radialis is now distinct from the carpal tunnel and continues down the wrist separate from it. The tendons of palmaris longus overlie the median nerve with the flexor retinaculum intervening. The ulnar artery and nerve lie outside the carpal tunnel in the canal of Guyon (Robbins 1963).

2.5cm distal to its origin of the carpal tunnel the extensor tendons are now arranged in
a more flattened style around the dorsal aspect of the wrist. The carpal tunnel is now formed by osseous structure on 3 sides by trapezium, trapezoid, capitate and hamate bones. A thicker flexor retinaculum now completes the tunnel. An important feature of this slice is the hook of hamate on the medial side of the carpal tunnel. The median nerve at this point is more flattened and in contact with the tendon of flexor pollicis longus on its lateral side. The tendon of flexor carpi radialis is now completely distinct from the carpal tunnel on its own by a splitting of the flexor retinaculum (Hamilton 1976 p177).

The head of the first metacarpal is present in this slice, as well as the muscles of the thenar and hypothenar eminences. The tendon of palmaris longus is now very thin and flattened as it prepares to insert on the flexor retinaculum and palmar aponeurosis.

The final slice considered here is actually in the palm of the hand. The osseous boundaries of the carpal tunnel are now formed by the bases of the 5 metacarpal bones. The tendons inserting on the bases of these metacarpal bones are now absent as the slice is distal to their insertions. The thenar and hypothenar muscles are well developed at this point. The flexor retinaculum is no longer present, although the palmar aponeurosis continues to keep the tendons tightly packed. The tendon of flexor pollicis longus is still in close proximity to the more flattened median nerve. This point is just proximal to where the median nerve divides and sends branches off to their respective digits.

In summary the carpal tunnel contains the tendons of flexor pollicis longus, flexor digitorum profundus and superficialis, the median nerve and its artery. The flexor carpi radialis has its own fibro-osseous tunnel outside the carpal tunnel. The ulnar artery and nerve run superficial to the flexor retinaculum in Guyon's canal. Throughout the carpal tunnel the tendons of flexor digitorum profundus and superficialis are surrounded by the ulnar bursa, the tendons of flexor pollicis longus by the radial bursa. The median
nerve does not run within any of these bursae.
II Magnetic Resonance Imaging Background and Theory.

II.1 Introduction to Nuclear Magnetic Resonance.

The principles of Nuclear Magnetic Resonance (NMR) are complex, they are difficult to understand and indeed there is no simple way to explain them. It requires a knowledge of physics, chemistry and mathematics to fully grasp the basic principles. Further, knowledge of quantum physics is required for a complete understanding of these principles. This explanation of NMR theory does not delve into the complexities of quantum physics, nor does it ask the reader to understand how certain equations are obtained. Instead, the classical theory of NMR is explained, in a form which most scientists should be equipped to grasp, by tapping their background knowledge of basic physics and mathematics.

The clinical value of NMR is realised when the principles are applied to imaging. Magnetic Resonance Imaging (MRI) is now used to obtain cross-sectional images of human tissue in vivo, in a similar way to a Computed Tomography body scan. The fundamental difference between MRI and Computed Tomography is that tissues are relatively transparent to the short wave length x-rays used in Computed Tomography (Fig II.1). Thus, a Computed Tomography image is in effect a back projection or a shadow of the bony tissue, whereas MRI provides an image of the water and thus the tissue of the sample.

Fig II.1 The Electromagnetic Spectrum. (Gadian 1982 p. 3)
Moving through the intermediate wave lengths of the electromagnetic spectrum, tissue becomes opaque to Ultra-violet, through visible light, infrared and on to microwaves. At the longer wave lengths, in the radio frequency (RF) region, the tissue becomes transparent once more. RF is used in NMR to safely probe deep inside the body. Information can be obtained directly from a tissue of interest, with regard to its chemical makeup and its position within the body. Thus MRI can provide us with a vast array of data, with a high degree of safety.
II.2 The History of NMR.

The principles of NMR have been known since the mid 1940's. The use of NMR for imaging purposes progressed slowly, until the computer technology had advanced sufficiently to allow the complex calculations required during imaging to be performed in seconds rather than hours. MRI has only been available for clinical use for the last decade.

Work on NMR was carried out before World War II, but due to poor selection of materials, negative results were obtain by Gorter et al. (1936) when attempting to detect nuclear spins in Lithium and Aluminium salts. The break through came in 1946, when two independent groups simultaneously published work about their successful NMR experiments. Bloch et al. (1946) reported work carried out at Stanford University, while Purcell et al. (1946) reported work at Harvard University. It was only after discussion that the two groups realised that they had both observed the same phenomenon.

The first strong proton NMR signal from living human tissue, was obtained when Bloch inserted his own finger into the RF coil at Stanford University, soon after his original publication. Two years later in 1948, Purcell and a colleague put their heads inside a 2 Tesla field. The only noticeable affect to date, was a sensation of an EMF in the fillings of their teeth, whilst inside the field.

The true impact of both groups work was realised in 1952, when Felix Bloch and Edward Purcell were jointly awarded the Nobel prize for Physics.

NMR progressed slowly up to the 1960's, when higher fields, providing better resolution became available. But it was not until 1973, when Lauterbur (1973) demonstrated how a gradient could be used to obtain one dimensional spatial information, that imaging really developed rapidly. A series of gradients was used to obtain a two dimensional projection of an object. The image was reconstructed in a similar way to Computed Tomography.
(The back projection method was used in these early studies). The pixel coordinates of an object are determined by obtaining a profile along the x and y axis. Using information from at least 1 more view the true coordinates of the object may be obtained.

Within a decade of the Lauterbur publication clinical MRI systems have been manufactured for use in hospitals throughout the world. Due to the high profile of these systems in the media and medical establishment, spending on imaging has far outstripped that on other areas of NMR research. Although MRI systems are expensive to purchase, install and run, they are now challenging the other conventional imaging techniques.

The original two dimensional projection techniques have been replaced by faster two dimensional Fourier transform methods. More recently three dimensional imaging has meant that once data has been collected, any slice may be reconstructed. Techniques such as gating have meant that even cardiac movements maybe eliminated and images of the heart are now a reality.
Appendix II

II.3 Basic NMR Theory.

II.3.1 Magnetic Fields.

A magnetic field is the area in which the magnetic forces of a magnet exist and so act on an object. These forces may exist between the ends of a bar magnet, the arms of a horse shoe magnet or indeed through a solenoid coil (as used in imaging system). The effect of a magnetic field may be visualised by scattering iron filings over the area of the field. The filings will arrange themselves along the magnetic field lines of the magnet. These field lines exist inside as well as outside the magnet, they are the so called magnetic flux, representing the density of the field. The closer together the lines are, the higher the flux density and the stronger the field.

The magnetic flux of a solenoid electromagnet used for imaging, may be considered in the same way as the bar magnet although the solenoid magnet does not have poles. The field is generated by wire solenoid coils carrying an electric current. A single wire will generate a field around the wire at right angles to it. If the wire is arranged in a coil, the field will pass through the centre of the coil. The magnetic flux will be most dense and homogeneous in its centre. Imaging systems require a uniform magnetic field, so a solenoid coil arrangement of wire coils is used to obtain an homogeneous field in the centre of the core of the magnet. It is in the centre of the coil where the sample to be imaged is placed.

Magnetic flux (Φ) is measured in volt seconds (Vs) or using the SI units the Weber (Wb). The flux density (B) is a function of the magnetic flux and the area of the field (A) according to equation II.1;
\[ B = \frac{\Phi}{A} \text{ Units } \text{Wb m}^{-2} \]

equation II.1

B may be expressed in the SI units the Tesla (T) or Gauss (G).

\[ 1 \text{ T} = 1 \text{ Wb m}^{-2} = 10,000 \text{ G} \]

It was mentioned earlier that the homogeneity of the field is most important to imaging systems. Typical imaging systems have homogeneities of the order of 10 ppm or better over the imaging region.
II.3.2 The Properties of Atomic Nuclei in Magnetic Fields.

Nuclei are the core of the atoms which make up all of the molecules in the universe. Apart from the nucleus of hydrogen, which contains a solitary proton, all other nuclei consist of protons and neutrons. Since protons are positively charged and neutrons have no charge, all nuclei have a positive charge. Atomic nuclei with an odd number of neutrons or protons, or both, will exhibit a phenomena known as spin (Gadian 1982). In a similar way to that of a spinning top spinning on its axis (fig II.2.1), some nuclei spin on their own axis (fig II.2.2). But the top has to be spun, whereas nuclear spin is a fundamental property of nature, they need no external torque to make them spin. Two thirds of stable nuclei exhibit this property.
Appendix II

Fig II.2.1 Top G

Fig II.2.2 nucleus $B_0$
Since nuclei with spin possess a charge, the spinning will create a magnetic field. This may be considered to be a physical vector quantity, known as the magnetic moment (\(\mu\)), expressing the size and direction of the nuclei's own magnetic field. This magnetic moment will cause the nucleus to behave as a microscopic bar magnet, with specific poles.

In the absence of an external magnet field the nuclei will be randomly orientated. Returning to the analogy of the spinning top, the top will not only spin on its own axis, it will also precess about the direction of the gravitational field of the earth (\(G\)). In a similar way, nuclei with spin will experience a torque when placed in a magnetic field. This causes them to precess about the field, the motion being known as the 'Larmor precession' (Gadian 1982). The nuclei precess at an angle \(\Theta\) to the direction of the field \(B_0\), but out of phase with each other. The combination of all of the nuclei in the sample, will result in a net magnetisation along the axis of the main field. No component of magnetisation in the plane perpendicular to the field will be observed, because the nuclei precess out of phase with each other.
Fig II.3 Parallel vs Anti-parallel.
The nuclei in a sample will exist in one of two energy states with respect to $B_0$. Any nucleus may point towards or against the direction of $B_0$. These two orientations are known as the 'parallel' and the 'anti-parallel' states respectively. They differ by a value $\Delta E$, the parallel state being slightly lower in energy than the anti-parallel (fig II.3). The difference ($\Delta E$) is of the magnitude of the thermal energy generated by random collisions between molecules. The populations of nuclei in the two energy states are determined by the Boltzmann distribution (Slichter 1980 p.6) according to equation II.2 (Where $n^-$ and $n^+$ are the number of nuclei in the parallel and anti parallel states respectively, $\Delta E$ is the difference in energy, $k$ is the Boltzmann constant and $T$ is the temperature.). When the sample has reached thermal equilibrium, the nuclei in the parallel state will out number those in the anti parallel state according to equation II.2. The sample is then said to be magnetised. This net magnetisation is the result of all the nuclei in the sample and not just that of one single nucleus.

$$\frac{n^-}{n^+} = e^{-\Delta E/kT} \quad \text{equation II.2}$$

II.3.3 The Larmor Relationship.

If you consider a sample in a uniform magnetic field $B_0$, a proportion of the nuclei will align themselves with the field, and will precess at a characteristic frequency; known as the larmor frequency. The larmor frequency of precession ($\omega_0$) is directly proportional to $B_0$ as shown in equation II.3 (Gadian 1982 p.83).

$$\omega_0 \propto B_0 \quad \text{equation II.3}$$

By introducing a constant ($\Gamma$) for each type of nucleus, the equation may be completed as in equation II.4.

$$\omega_0 = \Gamma B_0 \quad \text{equation II.4}$$
(Where $\Gamma$ is the gyromagnetic ratio of the particular nucleus of interest.)

The frequency of precession of nuclei in a magnetic field is directly related to the strength of that field, according to equation II.4. This relationship is fundamental in NMR studies.

II.3.4 The Gyromagnetic Ratio.

The gyromagnetic ratio varies depending on the nucleus being examined. Nuclei of different elements precess at different rates in the same magnetic field, due to their different gyromagnetic ratios. The units of the gyromagnetic ratio in the larmor equation are given as units of angular frequency over unit magnetic field strength. Angular frequency should be expressed in radians per second. Dividing by $2\pi$, the angular frequency may be converted into cycles per second or Hertz (The SI unit of frequency). In NMR terms the field strength is usually expressed in Tesla and frequency in Mega Hertz (MHz). The values for $\Gamma$ of various nuclei are given in Table II.1.

<table>
<thead>
<tr>
<th>Isotope</th>
<th>$\Gamma$ (MHz/T)</th>
<th>Sensitivity relative to $^1$H</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^1$H</td>
<td>42.58</td>
<td>1</td>
</tr>
<tr>
<td>$^{19}$F</td>
<td>40.05</td>
<td>0.830</td>
</tr>
<tr>
<td>$^{31}$P</td>
<td>17.24</td>
<td>0.066</td>
</tr>
<tr>
<td>$^{23}$Na</td>
<td>11.26</td>
<td>0.093</td>
</tr>
<tr>
<td>$^{12}$C</td>
<td>10.71</td>
<td>0.016</td>
</tr>
<tr>
<td>$^{16}$O</td>
<td>5.77</td>
<td>0.029</td>
</tr>
</tbody>
</table>

MRI systems use magnets of various field strengths, so it is desirable to know the larmor frequency of a particular nucleus at these various field strengths. The larmor equation
may be solved for frequency in Hz (f) as in equation II.5. \( \Gamma \) has to be divided by \( 2\pi \) to convert it from radians per second into Hz.

\[
f = \frac{\Gamma B_0}{2\pi}
\]

\text{equation II.5}

If the \( \Gamma \) of a nucleus is known, along with \( B_0 \) the larmor frequency may easily be calculated. Some examples are shown in table II.2.

By carefully choosing the correct frequency of RF with which to excite the nuclei in a sample, the type of nuclei to be excited may also be selected (See section xx on RF pulses). Due to the abundance of hydrogen in tissue, the proton has been chosen as the nucleus to excite by the majority of MRI systems. However, systems with high field strengths are now using phosphorous and sodium as the nuclei to image. These images are not of the same quality as the proton imaging systems.

---

Table II.2 \( \Gamma \) of nuclei at different field strengths.

<table>
<thead>
<tr>
<th>Isotope.</th>
<th>Field Strength (T)</th>
<th>Larmor frequency (MHz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(^1\text{H})</td>
<td>0.04</td>
<td>1.703</td>
</tr>
<tr>
<td>(^1\text{H})</td>
<td>0.15</td>
<td>6.387</td>
</tr>
<tr>
<td>(^1\text{H})</td>
<td>0.5</td>
<td>21.29</td>
</tr>
<tr>
<td>(^1\text{H})</td>
<td>1.00</td>
<td>42.58</td>
</tr>
<tr>
<td>(^1\text{H})</td>
<td>2.00</td>
<td>85.16</td>
</tr>
<tr>
<td>(^31\text{P})</td>
<td>0.5</td>
<td>8.62</td>
</tr>
<tr>
<td>(^31\text{P})</td>
<td>1.00</td>
<td>17.24</td>
</tr>
<tr>
<td>(^31\text{P})</td>
<td>1.5</td>
<td>25.86</td>
</tr>
<tr>
<td>(^31\text{P})</td>
<td>2.00</td>
<td>34.48</td>
</tr>
<tr>
<td>(^23\text{Na})</td>
<td>2.00</td>
<td>22.52</td>
</tr>
</tbody>
</table>
11.3.5 Magnetisation.

The net magnetisation ($M$) is the magnetisation of all of the nuclei in the sample. It is comprised of two components; longitudinal and transverse magnetisation ($M_z$ and $M_{xy}$ respectively). At equilibrium the longitudinal component of magnetisation ($M_z$), which represents the magnetisation in the z direction, will be at a maximum (Fig II.4). $M_{xy}$ can be further decomposed into its constituents; the magnetisation in the x and y axis ($M_x$ and $M_y$ respectively).

![Diagram of magnetisation components](image)

Fig II.4 $M$, $M_z$, $M_{xy}$

$M_z$ is known as $M_0$ when in this equilibrium position, this allows us to recognise when $M_z$ has returned to its equilibrium value. As its name suggests, the transverse component of magnetisation ($M_{xy}$) represents the magnetisation in the x y plane. When $M_z$ equals $M_0$, the magnetisation in the x y plane will be zero.
II.3.6 The Rotating Frame of Reference.

The concept of a precessing nucleus, in a uniform magnetic field, is not only difficult to perceive, but also difficult to depict diagrammatically. Especially when the movement of the nucleus becomes more and more complex. The rotating frame of reference is used to simplify the situation and represent the nucleus and the magnetisation in the static field.

If you consider an observer, at a point in space, monitoring the flight path of a ball as it drops to earth, the earth would appear to rotate on its own axis; the observer would be stationary. The ball dropping to earth would not only move towards the surface, but would also follow the rotation of the earth. Its path would be a complex parabola, with respect to the observer. To a second observer, positioned on earth, the earth would appear stationary and the universe would seem to rotate about it. The ball would seem to follow a direct path towards the earth, the path appearing straight in the direction of the earth's gravitational field (G).

It is easier to observe the ball from the point of view of the spinning universe and stationary earth as with the second observer, rather than the spinning earth and stationary universe. In the same way it is easier to represent the precessing nucleus from the point of view of the spinning universe and stationary nucleus, rather than the spinning nucleus. For this reason the precessing nucleus may be considered to be a stationary object and the field rotating about it. This concept is known as the rotating frame of reference.

The coordinates of the rotating frame of reference correspond to the laboratory coordinates xyz, but to distinguish them from the laboratory frame they are suffixed with an apostrophe. They are therefore known as x', y' and z', as shown in fig II.5, although z and z' are conventionally in the same direction.
Fig II.5 The Rotating Frame vs Laboratory Frame of Reference.

The three orthogonal axis are included in fig II.5 to complete the picture. The direction of the field is conventionally said to be in the z direction, although the magnetisation vector of the nucleus may change depending on its state of relaxation. This net magnetisation vector (M) is represented as an arrow in the direction of the net magnetisation. Arrows representing the longitudinal and transverse components of magnetisation (M_\perp and M_{xy} respectively) may also be included in the diagram. Since the arrows are vectors, their size and direction are indicative of the size and direction of the magnetisation of all of the nuclei in the sample.
II.3.7 Radio Frequency (RF) Pulses.

If we consider the situation of a sample in a static field $B_0$. The net magnetisation will precess about the direction of the main field $z'$, at an angular frequency $\omega_0$, according to the larmor equation. The transverse magnetisation $M_{xy}$ would be zero (fig II.6).

![Fig II.6 The Magnetisation in the Rotating Frame at Equilibrium.](image)

If we apply a field $B_1$ along the $x'$ axis, the nuclei will precess about $B_1$ at an angular frequency $\Gamma$. $B_1$. This effect is seen because in the rotating frame of reference, the only apparent field experienced by the nucleus would be $B_1$. If $B_1$ is applied for a time $t_p$ the nuclei will rotate through an angle $\Theta$ according to the equation II.6 (Gadian 1982 p.84).

$$\Theta = \Gamma B_1 t_p$$  \hspace{1cm} \text{equation II.6}

If $\Theta = \pi/2$ rad and $t_p$ satisfies the equation II.6, the net magnetisation ($M$) will be tipped through an angle of 90° from the $z'$ axis into the direction of the $y'$ axis. This combination of $t_p$ and $B_1$ is known as the 90° pulse or a 90\_x pulse (The \_x specifies that the $B_1$ field is positioned along the x axis). In the same way a 180° pulse will tip the magnetisation from the $z'$ direction into the negative $z'$ direction (fig II.7). The variables $B_1$ and or $t_p$ would have to be modified, so that $\Theta$ in equation II.6 would equal $\pi$. If a
shaped pulse is used the strength of $B_1$ is modified instead of changing $t_p$. Otherwise $t_p$ would be changed when shaped pulses were not required.

Fig II.7 90° and 180° pulses.

By using a field $B_1$ in the $x'$ direction for a time $t_p$, the nuclei may be rotated through a desired angle about the $x'$ axis into the $y'$ axis. The field $B_1$, is static in the rotating frame of reference, but in the laboratory frame it may be considered to be rotating about the $z$ axis, with angular frequency $\omega_0$. This $B_1$ field may be generated by passing an oscillating electric current through a transmitter coil, orientated so that the field $B_1$ is along the $x$ axis. A pulse of RF at the larmor frequency may be delivered to the coil by amplifiers. Thus the field $B_1$ for the 90° and 180° may be changed by changing the amplitude of the RF, ie the strength of $B_1$ is controlled by the attenuation of the RF pulse or by changing $t_p$.

On the application of a 90° pulse the magnetisation will be moved into the $x$ $y$ plane. In this situation $M_z$ would be zero, there will be no component of magnetisation in the $z$
direction. This seems obvious since the magnetisation has been tipped through 90°, as does the fact that $M_{xy}$ reaches a maximum at this point. The net magnetisation would be in the $xy$ plane.

II.3.8 Free Induction Decay (FID).

Following a 90° RF pulse, which provides a $B_1$ RF field, the net magnetisation will be tilted into the $x'y'$ plane by the pulse. It will then begin to precess about $B_0$ at the larmor frequency ($w_0$). $M_{xy}$ will be at a maximum and $M_z$ will equal zero. Since the precessing nuclei possess charge and are moving in a magnetic field, an electromotive force (EMF) will be induced in a coil (Gadian 1982 p.85). This may be detected using a coil receiver situated close to the sample. The EMF induced in the coil, will oscillate at a frequency $w_0$ and the amplitude will be proportional to $M_{xy}$ (fig II.8). The signal will be greatest immediately after the RF pulse, when $M_{xy}$ will be greatest.

![Fig II.8 Graph of $M_{xy}$ vs time](image-url)
The coil surrounding the sample, will only detect an EMF induced by the precession of the transverse magnetisation $M_{xy}$. It is the precession of $M_{xy}$ which induces the EMF itself. Thus, the signal detected by the coil reflects the behaviour of $M_{xy}$. Immediately after the 90° pulse, when $M_{xy}$ is at a maximum, the EMF induced in the coil will be at a maximum, $M_{xy}$ will then return to its equilibrium value. This relaxation will result in an exponential reduction in the EMF induced in the receiver coil. The term Free Induction Decay (FID) has been used to represent this process.

*The characteristics of the FID;* (Philips 1984)

1. The oscillating signal detected in the receiver coil will oscillate at the larmor frequency for that nucleus in that field strength.

2. The initial signal amplitude will relate to the density of the nuclei in the region of excitement.

3. The FID will decrease with time, as a function of the relaxation processes of the particular nuclei.

The FID in reality would not be as simple as that represented in fig II.7. It would not be composed of a single frequency, factors such as chemical shift and the local field inhomogeneities would result in the FID being composed of a variety of component frequencies. These factors may be used to the advantage of the imaging process.
II.3.9 The Equations of Motion.

The behaviour of the magnetisation in the magnetic field was explained by Bloch in terms of time dependent differential equations. These are known as the Bloch equations.

The classical equation of motion is the starting point in deriving the Bloch equations. The rate of change of the angular momentum ($\mu$) of the spinning nucleus is dependent on the torque exerted on it by the field. The vector product of the magnetic moment and the field, ($\mu \times B$), gives the torque on the nucleus. This may be multiplied by $\Gamma$ to obtain an expression for the rate of change of the angular moment (equation II.7)

$$\frac{d\mu}{dt} = \Gamma \mu \times B$$  \hspace{1cm} \text{equation II.7}

If $M$ is the vector sum of all of the magnetic moments then equation II.8 will express the macroscopic magnetisation of the sample.

$$\frac{dM}{dt} = \Gamma M \times B$$  \hspace{1cm} \text{equation II.8}

The vector product may be expanded to obtain the components in all of the Cartesian axes.

$$M \times B = M_x B_x \hat{i} + (M_y B_z - M_z B_y) \hat{j} + (M_z B_x - M_x B_z) \hat{k}$$

(Farrar and Becker 1971 p.7)  \hspace{1cm} \text{equation II.9}

The field $B$ in the equation II.9 represents the static field $B_0$ as well as the magnetic vector of the RF field $B_1$. This may be considered to be a rotating field about the $z$-
axis with angular frequency $\omega_0$. The component fields of $B$ may be expressed as in equation II.10.

$$B_x = B_1 \cos \omega t \quad B_y = B_1 \sin \omega t \quad B_z = B_0 \quad \text{equation II.10}$$

These expressions may be substituted into equation II.8 to obtain expressions for the rates of change of the three components of magnetisation.

$$\frac{dM_x}{dt} = \Gamma (MyB_0 + M_z B_1 \sin \omega t)$$

$$\frac{dM_y}{dt} = \Gamma (M_z B_1 \cos \omega t - M_x B_0)$$

$$\frac{dM_z}{dt} = \Gamma (M_x B_1 \sin \omega t + M_y B_1 \cos \omega t) \quad \text{equation II.11}$$

In order to complete the equation, relaxation has to be taken into account. Bloch included time constants to allow for relaxation, these constants are discussed later and are known as $T_1$ and $T_2$. Hence the final Bloch equations may be written as in equation II.12, which take into account the return of $M_x$ and $M_y$ to their equilibrium value of zero, and the return of $M_z$ to the equilibrium value of $M_0$.

$$\frac{dM_x}{dt} = \Gamma (MyB_0 + M_z B_1 \sin \omega t) - M_x / T_2$$

$$\frac{dM_y}{dt} = \Gamma (M_z B_1 \cos \omega t - M_x B_0) - M_y / T_2$$

$$\frac{dM_z}{dt} = \Gamma (M_x B_1 \sin \omega t - M_y B_1 \cos \omega t) - M_z - M_0) / T_1 \quad \text{equation II.12}$$

The use of different sequences allow $T_1$ and $T_2$ to be calculated because the known
variables may be cancelled out.
11.3.10 Relaxation of Nuclei.

After excitation by an RF pulse the nuclei will return to their equilibrium position. They will lose the energy gained from the RF pulse by transferring it to the surrounding molecules. At the same time they will induce a current in the coil surrounding the sample. The process of transferring energy to the surroundings is known as relaxation and commences on excitation. Both the longitudinal and transverse relaxation times of a nucleus will depend upon many factors; such as molecular structure of the material the nucleus is in; its physical state; and the temperature of the sample.

\[ T_1 \text{ Relaxation.} \]

The mechanism which characterises the return of \( M_z \) to its equilibrium position is known as \( T_1 \). Other terms commonly used to describe this relaxation include Longitudinal, Spin-lattice and Thermal relaxation times. These are discussed briefly here;

\textit{The Longitudinal} relaxation time as it represents the behaviour of the longitudinal magnetisation \( M_z \) in the magnetic field.

\textit{The Spin Lattice} relaxation time as it represents how fast energy is transferred from the spinning nucleus to its surroundings (the lattice) in which the nucleus is embedded. Energy is transferred by random collision with other nuclei.

\textit{The Thermal} relaxation time as it is a measure of the rate at which thermal equilibrium is restored after being disturbed.

After the \( 90^\circ \) RF pulse, \( M_z \) will equal zero and \( M_{xy} \) will be at a maximum (fig II.8). As relaxation occurs \( M_z \) increases, as the magnetisation returns to the equilibrium value \( M_0 \) (fig II.9).
Although $M_z$ and $M_{xy}$ are the component vectors of $M$, the rate of $M_z$ increase is not necessarily proportional to the rate of $M_{xy}$ decrease; ie. there is not a simple correlation between the rate growth of $M_z$ and the decay of $M_{xy}$. In fact due to the dephasing of $M_{xy}$, it may disappear completely long before $M_z=M_0$. The $M_z$ relaxation time also increases with increased magnetic field strength.

The magnitude of $T_1$ may vary from about 50 milliseconds to a few seconds in biological tissue. Again the time is dependent on the kind of nuclei being stimulated, the strength of the main field and the chemical and physical environment surrounding the nuclei. Very pure liquids have long $T_1$'s, compared to the so called impure liquids found in biological tissue.
Appendix II

The mechanism which characterises the return of the transverse magnetisation $M_{xy}$ to its equilibrium value is known is the $T_2$ relaxation. Other terms are commonly used to describe $T_2$, these include spin-spin relaxation and the transverse relaxation time. It is clear that the transverse relaxation time refers to the rate at which the transverse relaxation returns to its equilibrium position. However, the spin-spin term is not quite so obvious. It refers to the way the relaxation process involves interactions with other nuclear spins, without any exchange of energy with the lattice.

At equilibrium the nuclei precess about the field, but out of phase with each other, so no component of $M_{xy}$ exists. After the 90x pulse the net magnetisation will lie along the $y'$ axis. The magnetisation will precess about $z'$ at a frequency $\omega_0$. Immediately after the 90x pulse, the nuclei would be in phase with each other and $M_{xy}$ would be at a maximum. Interaction between the spins and their neighbours will cause changes in the local magnetic field. The local magnetic field variation will cause the spins to precess at different frequencies, some faster and some slower than others. There will be a divergence of frequencies of precession of the spins about $\omega_0$ of magnitude $\Delta \omega_0$. As the $\Delta \omega_0$ increases, so the spins dephase more and more in the $x'$ $y'$ plane. Thus $M_{xy}$ decays and eventually all of the spins will be out of phase with each other and $M_{xy}$ will again equal zero.

The time constant $T_2$ characterises this decay of $M_{xy}$. Equation II.13 describes the exponential return to the equilibrium position of $M_{xy}$ with the constant $T_2$.

$$\frac{dM_{xy}}{dt} = -\frac{M_{xy}}{T_2}$$

If the spin-spin interactions were the only factors affecting the field experienced by the nuclear spins, then $M_{xy}$ would relax with the time constant $T_2$. However, in reality this
may never be the case, due to main field inhomogeneities. These have the same effect as changes in the local field. The nuclear spins will have even more field differences, so $\gamma \omega_0$ will increase much faster than if it were only subjected to spin-spin interactions. The term $T_2^*$ is used to describe the $M_{xy}$ relaxation in the presence of main field inhomogeneities.

$T_2$ tends to be very short indeed in solids (the order of microseconds). The fixed molecules in solids will maintain local field variations. The $T_2$ of liquids tends to be much longer (the order of seconds), $T_2$ of materials found in biological tissue tends to range from about 40 milliseconds to around a second. To complicate matters further the $T_2$ of materials found in-vivo, would not exhibit a simple single exponential decay. Instead, due to the multitude of component tissue types a multi-exponential behaviour is exhibited.
11.3.11 The Spin-echo Sequence.
Due to $B_0$ inhomogeneities, the measurement of $T_2$ is not possible using a single 90° pulse. However, the effect of these inhomogeneities may be removed, by simply refocussing the magnetisation after it has been affected by the main field.

By applying a 90° pulse, the magnetisation is tilted into the $x'$ $y'$ plane of the rotating frame of reference (fig II.10.1). If all of the spins precess at the same frequency ($w_0$), then $M_{xy}$ would remain along the $y'$ axis. But, the $B_0$ inhomogeneities cause the spins to precess at slightly different frequencies, causing dephasing or 'fanning out' of the spins (fig II.10.2). The fanning out will occur in the $x'$ $y'$ plane. This dephasing will result in a reduction in the amplitude of the signal observed. If a 180° pulse is then applied, at a time $\tau$ after the 90° pulse, the spins would be inverted into the direction of the $-ve$ $y'$ axis (fig II.10.3). The partially dephased spins will still be subject to the same $B_0$ inhomogeneities. However those spins which were spinning at a high frequency than $w_0$, would then slow down, and vice-versa for the spins precessing at a lower frequency. (fig II.10.4). The spins will eventually precess at the same frequency, $w_0$ at a time $\tau$ after the 180° pulse (fig II.10.5).

The situation may be clarified by using an analogy of runners on a circular running track, on a windy day. If the runners all set off at their own pace, some faster and some slower than others, their abilities and the wind would cause them to spread out around the track. If at a time $\tau$ they are ordered to turn around and run in the opposite direction, eventually they will all arrive at the start, at a time $2\tau$, separated only by the random effects of the wind. The faster runners would have further to run back, but could make up the distance faster than the slower runners. The same is true of the spins in the magnetic field. At a time $\tau$ after the 180° pulse the magnetisation would refocus and an 'echo' will be detected. $M_{xy}$ would then be refocussed, although slightly smaller than before because of $T_2$ decay.
This echo will be detected as an FID of opposite phase to that observed after the 90x pulse, because it will be positioned in the -ve y' axis. The size of the echo will be dependent on the relaxation, which has occurred during the 2r sec which have elapsed after the 90x pulse. The T2 relaxation is responsible for this reduction. The magnitude of the signal will diminish by a factor $\exp(-2r/T2)$. This allows T2 to be evaluated by measuring the size of the echo.

By using a train of 180x pulses separated by a time 2r, the echo may be refocussed many times; thus allowing a more accurate determination of T2.
Fig II.10 Spin Echo Sequences.
II.3.12 The Calculation of T1.

When using conventional NMR techniques T1 is usually calculated by using a train of single 90° pulses or an inversion recovery sequence. When imaging the spin-echo sequences is used. This allows the time in the sequence for the gradients to be applied. The basis for the calculation is derived from a simplified form of the equations of motion (section II.3.9). Equation II.14 is the basic simplified equation used, in which a two point measure is used. The sample is exposed to 2 types of spin-echo sequence for the purpose of this calculation. Both sequences have the same τ but differ in their Tr.

The magnetisation (M) may be obtained from the image for each of the sequences, however M0 is unknown. It should be stressed that this measure of T1 is not the actual measure of T1 that could be derived using the other methods mentioned earlier. It can however, be used in comparisons within this study.

Sequence 1 uses a Tr of long duration (2000ms).

\[ M_1 = M_0 \left(1 - e^{-\text{Tr}/T1}\right) e^{-2\tau/T2} \]  

Since Tr is large the value of \( e^{-\text{Tr}/T1} \) tends to zero. Thus \( 1 - e^{-\text{Tr}/T1} \) will tend to 1 and can be cancelled from the equation. The equation of motion for a sequence with a long Tr may be expressed as in equation II.15.

\[ M_1 = M_0 e^{-2\tau/T2} \]

\[ M_0 = M_1/ e^{-2\tau/T2} \]  

sequence II.15

Sequence 2 uses a shorter Tr (500ms) than sequence 1. By substituting the expression for \( M_0 \) (equation II.15) into the basic equation II.14 the \( M_0 \) component may be removed thus leaving equation II.16.
Appendix II

\[ M_2 = M_1 \left(1 - e^{-\frac{T_r}{T_1}}\right) e^{-2\frac{\tau}{T_2}/e^{-2\frac{\tau}{T_2}}} \]  

equation II.16

Since the same \( \tau \) is used in both sequences the \( e^{-2\frac{\tau}{T_2}} \) cancels leaving an expression with only one unknown (\( T_1 \)) as in equation II.17.

\[ M_2 = M_1 \left(1 - e^{-\frac{T_r}{T_1}}\right) \]  

equation II.17

This may be solved for \( T_1 \);

\[ T_1 = \frac{-T_r}{\ln \left(\frac{M_2}{M_1}\right)} \]  

equation II.18

(Where \( T_r=500 \), \( M_2 \) and \( M_1 \) are the signal intensities from the image for the \( T_r = 500 \) and 2000ms sequences respectively.)

Thus an estimate of \( T_1 \) may be derived from two spin-echo sequences.
II.4 Magnetic Resonance Imaging.

II.4.1 Imaging Introduction.

It has already been discussed how some physical information can be obtained from a sample by using the principles of NMR. It is also possible to construct images of the sample by using the NMR properties of frequency and field. Spatial information has to be obtained for an image to be constructed, the details of which are to be discussed later in this section.

The process of obtaining images using the NMR phenomenon has been given a variety of names in the past including following;

- NMR imaging
- Magnetic Resonance Imaging (MRI)
- Spin Imaging
- Spin Mapping
- NMR Tomography
- Zeutamography
- Proton Imaging

Most of these names indicate that the principles of NMR are being employed for the imaging process. However, to the uninitiated the last five names would be meaningless. NMR imaging and Magnetic Resonance Imaging (MRI) are favourable because they both indicate the use of nuclear magnetic resonance as the imaging technique. However, the latter of the two is most favourable, because the reference to nuclear has been dropped, thus removing the suggestion of the use of ionising radiation. It also removes any confusion with the basic principles of NMR, which may be used for other purposes such as chemical analysis of the sample.

The process of capturing a magnetic resonance image is complex. Not only does spatial information have to be collected in the plane of the image, but a slice of the sample
must be selected before a meaningful image can be constructed.

II.4.2 Obtaining Spatial Information.

Slice selection.

To obtain an image a slice of the sample must be selected, otherwise information over the whole sample would be collected. It would not be possible to interpret this as a two dimensional image. Selective excitation is used to obtain a slice of the sample. This slice can then be used so as to obtain a two dimensional image in the plane of that slice (as described in the previous two sections). If an RF pulse, of frequency \( w_0 \), is applied to a sample in the \( B_0 \) field, all of the nuclei experiencing the \( B_0 \) field will be excited, as long as the larmor relationship is satisfied (equation II.4).

A frequency encoding gradient may be used to obtain spatial information in one dimension, the same principle maybe used in reverse to selectively excite a slice of the sample to image. By applying a known gradient in the \( z \) direction, the larmor frequency of precessing the nuclei may be known. If the \( z \) gradient increases linearly along the \( z \) axis, then the larmor frequency will also increase linearly along the \( z \) axis. The relationship between distance along the \( z \) axis (\( z \)) and the frequency (\( w_z \)) is expressed in equation II.20.

\[
    w_z = \Gamma B_0 + \Gamma B_z z
\]

If the position and width of the required slice are known, then the frequency of excitation and band width may be calculated for that slice and thickness. The thickness of the slice \( n_z \) is directly proportional to the band width of frequencies \( n w_z \) according to equation II.21.

\[
    n w_z = \Gamma n_z B_z
\]
The band width of frequencies with which to excite the correct slice of the object may now be calculated. All that is left to do is to obtain the correct $B_1$ field, with which to excite the slice with this range of frequencies. The RF pulse which provides the $B_1$ field must contain this range of frequencies. By applying a Fourier transform to the spectrum of component frequencies of the required band width, a sinc shaped RF pulse is obtained. This will ensure that the frequency of excitation will correspond to the larmor frequency of the nuclei in the required slice. Any nuclei not in that slice will not experience any RF at their larmor frequency and will therefore remain unexcited. Technically the shaped pulse should be calculated using complex algorithms, however after passing through the pulse generating electronics of the imaging system, any changes from a Gaussian weighted sinc shaped pulse would be lost.

The gradient used for the selective excitation is known as the slice select gradient. It must be applied for the duration of the RF pulse and is normally in the $z$ direction of axial imaging and one other direction for sagittal or coronal imaging. However, during the RF pulse, the nuclei at different positions in the slice will experience different field strengths and will thus precess at different rates. At the end of the RF pulse they will be out of phase with each other, some precessing faster and some slower than others. No signal will be detected. Another gradient of opposite sign must be applied to correct this dephasing. This gradient is applied directly after the RF pulse and is aptly known as the rephase gradient.

*Frequency Encoding.*

It has already been discussed that the angular frequency of precession of the spinning nucleus ($\omega$) is directly proportional to the field strength ($B$) experienced by the sample (according to the larmor relationship equation II.4). If this field strength was constant across the whole sample, all of the nuclei would precess at the same angular frequency.
In practice the field strength will not be perfectly constant across the sample, so frequencies of precession will vary across it. This property may be used to the advantage of the experimenter if the field strength can be varied linearly, by a known amount. A magnetic field gradient is used for this purpose.

By applying a linear field gradient along one axis, in the plane of the image, the frequency of precession may be varied linearly along that axis. In equation II.22 a field gradient \((G_x)\) is applied along the \(x\)-axis, the frequency of precession \((\omega_x)\) whilst the gradient is applied is directly proportional to the sum of the strength of the main field \(B_0\) and the strength of the field gradient \(G_x\), at that point along the \(x\)-axis. The strength of the field gradient is proportional to the distance \(x\) along the \(x\)-axis. Hence, the frequency \(\omega_x\), is directly proportional to the distance \(x\) along the \(x\)-axis, the encoding of spatial information has thus been achieved.

\[ \omega_x = \Gamma B_0 + \Gamma x G_x = \Gamma B_z \]  

\textit{equation II.22}

The actual field experienced by the nucleus at a point in space can be expressed as \(B_z\).

The spatial information obtained in this manner, may be used to obtain a one dimensional signal intensity profile of the sample (along the \(x\)-axis). The frequency of precession of the nuclei is proportional to the distance along the \(x\)-axis. Early techniques used frequency encoding in both the \(x\) and \(y\) axis. This method was superseded by the technique detailed here because main field inhomogeneities resulted in errors in the image reconstruction when data from gradient 180° apart were compared. The frequency/phase encoding technique does not suffer this problem, as the gradients do not change their orientation with respect to the main field.

This information is collected by the receiver coil in the form of an FID signal, produced by the precessing nuclei. The FID will contain a whole spectrum of
component frequencies, all expressed as a function of time. Since we must be able to obtain the intensities of each component frequency, some method of transforming the data, from a function of time into a function of frequency, must be employed. The component frequencies must be isolated and their intensities calculated, before any spatial information can be obtained.

The Fourier transform is a commonly used mathematical function for expressing complex wave forms in their component frequencies. The details of Fourier transforms are not discussed here, but it should be noted that the intensity of the component frequencies of the FID may be obtained, hence providing the basis for spatial information in one dimension.

This method of imparting spatial information is usually expressed as frequency encoding. During the collection of the FID, after the RF pulse has been delivered, the frequency encoding gradient has to be applied. This provides the linear variation in the $B_z$ field during data collection and thus allows spatial information to be collected.
Phase Encoding.

Frequency encoding in two dimensions has been followed by frequency in one and phase in the other. As well as frequency the phase angle of the signal can be altered. A gradient is applied in the y axis, prior to the collection of the FID, which in effect alters the phase angle (φ) of the precessing nuclei. The frequency of the precessing nuclei is proportional to the distance (y) along the y axis according to the equation II.23.

\[ \omega_y = \Gamma (B_0 + yG_y) \]  
\[ \text{equation II.23} \]

Since the frequency may vary along the y axis, the phase angle φ will also change. Therefore φ is proportional to the distance along the y axis, directly after the application of G_y. The time (t_y), or the magnitude of the gradient applied is vital. The longer or larger G_y the more φ will change. Equation II.24 shows how φ is related to the strength of G_y, the distance along the y axis (y) and the time of application of G_y (t_y).

\[ \phi = \omega_y t_y = \Gamma (B_0 + yG_y)t_y \]  
\[ \text{equation II.24} \]

When no gradient is applied all of the magnetisation vectors will be in phase with each other. As the y gradient increases the magnetisation will dephase, those magnetisation vectors which are 180° out of phase with each other will cancel out. Only the magnetisation vectors which are in the correct position along the y axis, will be selected by the phase encoded Fourier transform. Thus a column of the slice may be treated with the frequency encoding gradient. By increasing the y gradient the columns which are selected move along the y axis. The phase encoding gradient usually starts off at a maximum, steps down through zero and on to a negative maximum of the same magnitude.

The data once collected (1024 points) is Fourier transformed in the frequency direction.
Appendix II

The final stage is to Fourier transform the data array in the phase encoding dimension to obtain the coordinates and magnitude of each pixel. So two Fourier transforms are performed on the data, hence the name of the imaging technique, two dimensional Fourier transform imaging (2DFT).
II.4.3 The MRI System at the University of Surrey.

The Magnet.

The magnet was a resistive type which necessitated the use of a water cooling unit situated outside the building. Chilled water was pumped around the cooling system on the magnet and the power supply. The heated water was then removed to chillers outside and the heat dissipated outside. Problems occurred when the cooling system pumps became overloaded due to the deposition of calcium scaling in the pipes. The magnet regularly tripped out when over heating occurred. After inspection the fault was traced to the cooling pipes and the system was descaled. Further problems with tripping out were only rarely encountered.

Since the magnet was of a resistive type the running costs were high. This was exacerbated by the need to keep the magnet on for 24 hours a day during the operational period. The field took at least 2 hours to stabilise after being switched off during the night. When studies were being performed this would have meant excessive periods of down time. Hence the magnet was left on for 24 hours a day, and only switched off on days when it was not required. The power consumption was estimated to be in the region 10 KWatts. The electricity bill, kindly met by the Physics department, was to say the least expensive.

The bore of the magnet measured 55 cm in diameter. However, this was reduced to 50 cm when the gradient coils were in position. When a whole body coil was being tested for its feasibility the bore was even further reduced. It transpired that the whole body coil was not to be used due to technical problem of RF supply and coil design. For the purposes of this study the bore measured 50 cm in diameter.

In the time period between the pilot and the main study the field was shimmed (Pomeroy 1989). Passive wire shims were taped to the inside of the gradient housing and the field plotted to assess improvements. The results of the shimming experiments
Appendix II

The Patient Bed and Supporting Blocks.

During imaging the subject lay on a bed mounted on rollers. This allowed the subject to be positioned in the coil prior to being moved into the magnet for imaging. For the pilot study the subjects lay on blocks to raise their torso above the level of the bed. The coil was positioned under the abdomen so the blocks had to be deep enough to allow sufficient clearance for the patients body over the coil and allow enough space for the subject to fit into the bore of the magnet. When in the imaging position the coil had to be in the horizontal plane of the centre of the bore, although it was off set form the vertical plane.

The blocks were designed under these criteria. The block edge adjacent to the coil was 15 cm above the level of the bed to allow clearance of the body over the coil. These blocks were tapered to a height of 12 cm above the bed to allow increased access to the bore. The other blocks were all 12 cm above the bed.

After the shimming was performed the slice position was moved closer to the centre of the bore into the region of greater homogeneity. Problems with access for the subjects arm were also encountered in the pilot study. It was decided to redesign the coil position using anthropometric data of the 18-65 year old population (Pheasant 1984) under the following design criteria.

i. The coil had to be positioned so that the 95th percentile male could enter the system with sufficient elbow clearance. The centre slice to bore edge distance had to be greater than 30.5 cm.

ii. The internal elbow clearance had to be less than the 5th percentile female elbow clearance. The distance from centre slice to the tendon of biceps brachi at the elbow
Appendix II

had to be less than 21.0 cm.

To satisfy these design criteria the centre slice had to be at least 30.5 cm from the side of the bore and at most 21.0 cm from the side of the foam support block. The centre slice was offset from the centre of the bore by 4.5 cm. This allowed 32.0 cm clearance with the side of the bore, thus satisfying the first design criteria. The support block was shaped to allow minimum clearance of 16.0 cm thus satisfying the second design criteria. With these design alterations 95% of the population would be able to fit their arm into the coil arrangement.

The Gradients.
The gradients were formed by windings mounted on the bore of the magnet. They were driven by dedicated laboratory amplifiers. The shapes of the gradient pulses were provided by the data general computer via the DAC boxes. The timing of the pulse was controlled by the BBC computer. The usual three gradients were used in the system; the slice select gradient (z-axis), the frequency and phase encoding gradients (x and y axis). Problems were encountered when both the gradient amplifiers and the DAC boxes malfunctioned.

After the pilot study the power supply to the amplifiers was overhauled by the physics department technician. Unfortunately the supply to each of the amplifiers was connected incorrectly, resulting in the overheating and failure of all three amplifiers soon after installation. The repairs took a number of months to complete. A disconnected earth wire on a solder iron resulted in the destruction of the original DAC chips. These are now unavailable, so a new DAC box had to be designed and built before progress could be made. The gradient field strengths all had to be redefined before the system could be used again. The gradient system was responsible for much of the down time of the system.
The same gradient strengths were used for imaging both sides (left and right wrists). Only the excitation frequency was changed to alter the slice position.

*The RF System.*

The RF was delivered by a 10 cm diameter solenoid coil (Plate 2.2). The signal was transmitted to the coil down 50 Ω braided coaxial cable via a tuning box. The tuning box contained 2 variable capacitors, one in series and the other in parallel with the RF circuit. The capacitors were bathed in transformer oil to avoid shorting between the capacitor plates. Occasionally loose connections occurred in the tuning box. This meant regularly overhauling the box when a loose connection was suspected. This was not an enjoyable task as the transformer oil tended to leak from the box (usually onto the person handling it) when ever it was disturbed.

The RF signal was amplified by a water cooled amplifier. The signal to the amplifier was formed in the pulse generation tray. Pulse shapes were sent to the tray by the Data General computer according to the programme run. The RF wave form was supplied by a frequency synthesiser, also under the control of the Data General. The pulse generation tray combined the shapes of the pulses with the RF wave form and then attenuated the size of the pulses to suit the sequence in use. Timing of the pulses was provided by the BBC computer.

*Sequences.*

Prior to the pilot study experiments were carried out on pigs trotters. They were considered a suitable alternative to human wrists, and a good source of tendons to image. During the experiments the pigs trotters were imaged using various imaging sequences. The most appropriate were found to be those used in the pilot and main studies. Although the tendons of the pigs trotters could not be imaged, it was anticipated that imaging human (or tendon sheaths) would be more successful.
Data Acquisition and Analysis.

After passing through the pre-amp close to the magnet, the signal entered the data acquisition tray via an attenuation box. The signal was then prepared for analysis by the Masscomp. Erroneous frequencies were removed by filtering the signal and the signal was split in two. The two channels entered the masscomp were an array processor carried out the analysis of the signal.

The Masscomp was controlled by the BBC. A "get data" pulse was sent to the Masscomp to inform it when to start collecting data. The signal was sampled 8 ms after the get data pulse.

Once the image had been constructed it was stored on the system directory. The images were displayed on the graphics terminal. This also acted as an oscilloscope, producing a trace of the set up signals when required.

Problems were encountered when the data acquisition board in the Masscomp was overloaded. This happened three times resulting in the replacement of the board by the engineer. The cause of the fault was never discovered so the input cables had to be disconnected when ever the system was not in use. It was thought that a spike was produced in the system which overloaded the Masscomp data acquisition board.

Central Timing Control.

The BBC computer controlled the timing of the other systems. The repetition rate and the time to echo was set on the BBC. The Data General computer was responsible for the production of the RF pulses and gradient control. Also the type of sequence to be used was controlled by the Data General. Programmes were written which supplied the appropriate shape of pulse, RF and gradient pulses. The Masscomp was dedicated to the collection and analysis of the data, construction and display of the images. A general
imaging programme was used for all of the imaging on the Masscomp. The programmes on the Data General and the Masscomp were selected by the operator and the programmes started simultaneously. The system is displayed schematically in fig II.11.
Fig II.11 Schematic diagram of the system.
A logical method of naming the images was employed. The image name allowed the operator to identify; which subject the image was from; which wrist (right or left); the imaging plane; the type of sequence used in the imaging session; and the number of the image in a multi-slice sequence.

The was achieved using the following criteria;

1. The subjects initials made up the first letters of the filename. As many names as possible were accounted for, to avoid complications with filename repetitions of subjects with the same initials. The first two, if not three letters of the filename thus represented the subjects name.

2. The next letter was either an "R" or an "L" depending on whether the imaging was of the right or left wrist respectively.

3. The usual imaging plane was the trans-axial plane, thus the next letter in the filename was usually a "T". Coronal or sagittal images would be labelled with the letters "C" and "S" respectively.

4. The sequence was abbreviated to; "D" for density imaging with long repetition times such as the multi-slice images (Tr 2000ms); and "SR" for the saturation recovery sequences with short repetition times (Tr 500ms).

5. Finally the image number was automatically added to the end of the filename by the system computer. A single slice sequence would have a "1" added to it, whereas the multi-slice image would have its position in the multi-slice sequence recorded according the order explained in chapter 2.
Thus the third image, in a multi-slice, density, trans-axial sequence of the authors (ARN) left wrist, would have the filename "ARNLTD3". This convention was followed throughout the duration of the entire study.
Dear

You saw me recently about your wrist and we found you were suffering from carpal tunnel syndrome. I am currently engaged in some research, at the University of Surrey, to try and find out more about the condition you are suffering from. I would be most grateful if you would be prepared to help us with our research. It will involve you coming to the University to have your wrists imaged in a body scanner and have some other tests done.

The body scanner is of a new type called MRI (Magnetic Resonance Imaging), which uses a strong magnet and some radio waves to look into the body without touching it. There are no risks involved, no x-rays or any ionising radiation and you will feel nothing. All you have to do is to lie inside the magnet for about half an hour for each wrist. The other tests will involve measuring your arms and hands and asking you to fill in a questionnaire.

The researcher at the University (Mr Andrew Norman) will contact you shortly to see if you wish to participate in the study. If you do, he will arrange a convenient time for you to come and be imaged. You can arrange with him to be collected and taken to the University and back home, if you wish. All information will be treated in the strictest confidence and you may withdraw from the study at any time.

Yours sincerely,

Mr J. Older FRCS Consultant Orthopaedic Surgeon

Contact Address:
Andrew Norman
Ergonomics Research Unit,
Robens Institute,
University of Surrey,
Guildford,
Surrey.
GU2 5XH

Tel: 0483 571281 ask for extension 2434
CONSENT FORM

Volunteers Participating in The Musculoskeletal Disorder and Associated Risk Factors Study

I, __________________________________________ (Block Letters)
of _______________________________________


agreed to participate in the musculoskeletal disorder risk factors study on the following terms:

1. The experimental protocol, the objectives and the methods have been explained to me.

2. All the relevant information relating to the procedures and substance(s) to be used and samples to be taken has been explained to me.

3. I understand that I have the right to withdraw from the trial at any time.

4. I am over 18 years of age.

Signed ___________________________ Date ___________________
Dear Sir/Madam,

In our Health and Safety Institute at the University of Surrey we undertake many studies of health problems that may occur through the work and other activities that people do. We often need to carry out surveys to find out how common particular problems are. These rely on questionnaires such as this one.

We would be very grateful therefore if you would fill in this questionnaire and return it when it has been completed.

Please try to answer all the questions as fully as possible and ask for assistance if you need it. All the information that you provide will be treated as strictly confidential and cannot be traced back to you.

Thank you very much for your co-operation in this important research study.

Yours faithfully,

Dr. Peter Buckle

Mr. Andrew Norman

The Robens Institute,
University of Surrey,
Guildford, Surrey.
INSTRUCTIONS

Please answer the questions as fully as possible; some questions require you to give written information, some only require you to tick a box.

BACKGROUND INFORMATION

Today's date: Day __________ Month __________ Year __________
The time now: __________ am □ pm □
Year of birth: 19 __________
Sex: Male □ Female □
Height: __________ ft __________ ins Weight: __________ st __________ lbs

Are you: Right-handed □ Left-handed □ Both □

Are you: A Smoker □ A Non-Smoker □

If you are a smoker, how much do you smoke per day? __________

In which town, village or city do you live? __________

(If you live in the country, write down the nearest town or village)

Do you take part in any sporting activities and/or hobbies? NO □ YES □

If 'YES' please list them and write down the approximate time you spend on each per week:

<table>
<thead>
<tr>
<th>SPORT or HOBBY</th>
<th>TIME SPENT PER WEEK</th>
</tr>
</thead>
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<tr>
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</tbody>
</table>

SECTION A

1. a) What is your job or occupation? _______________________

b) Please describe the main things that you do in this job? _______________________

c) How long have you worked in this job? ______ yrs. ______ mths.

2. Have you had any other jobs before this one? NO □ YES □

If 'YES' please give details and dates where possible:

<table>
<thead>
<tr>
<th>JOB DESCRIPTION</th>
<th>FROM</th>
<th>TO</th>
</tr>
</thead>
<tbody>
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</tr>
</tbody>
</table>

330
3. How many hours do you work on average each week? 

4. How many hours do you work on average each day? 

5. a) Do you change the type of work that you do during the day or week? 
   b) If 'YES', please describe each job and indicate how long you spend doing each type of work:
   
<table>
<thead>
<tr>
<th>TYPE OF WORK</th>
<th>HOURS PER WEEK</th>
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</thead>
<tbody>
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</table>

6. Is your work of a repetitive nature? 

7. Does your work involve the use of your hands and arms? 
   b) If 'YES', please describe the task(s) and indicate how many hours you spend on each per day:
   
<table>
<thead>
<tr>
<th>TYPE OF WORK</th>
<th>HOURS PER WEEK</th>
</tr>
</thead>
<tbody>
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</tr>
</tbody>
</table>

8. a) Do you use any hand held tools in your job? 
   (Non motor-driven/Non power tools ONLY) 
   b) If 'YES', please describe the tools and indicate how many hours on average that you use them per day:
   
<table>
<thead>
<tr>
<th>TOOL</th>
<th>HOURS PER DAY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

9. a) Do you use any hand held motor driven 
or power tools / machines in your job? 
   b) If 'YES', please describe the tools and indicate how many hours on average you spend on each per day:
   
<table>
<thead>
<tr>
<th>MACHINE TOOL</th>
<th>HOURS PER DAY</th>
</tr>
</thead>
<tbody>
<tr>
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</tbody>
</table>
Appendix III

SECTION B

THIS SECTION IS ABOUT REGULAR AND OCCASIONAL PAIN OR DISCOMFORT

Please tick the boxes to indicate your answer to each question

1. Have you had any pain or discomfort in any part of your body in the last 12 months?  
   NO ☐  YES ☐

   If 'NO' Please go to Section C on page 6

2. Have you had regular pain or discomfort in any part of your body in the last 12 months?  
   (Regular means that the pain or discomfort should have occurred at least once a week for at least two months)

   NO ☐  YES ☐

Please shade on the diagram below any areas where you have had regular pain or discomfort in the last 12 months.

Please describe the pain for each area and indicate whether you can connect it with anything that you do (eg. work, sports, hobbies etc...).

Regular pain or discomfort

Please describe the pain for each area and indicate whether you can connect it with anything that you do (eg. work, sports, hobbies etc...).

Regular pain or discomfort
3. Have you had occasional pain or discomfort in any part of your body in the last 12 months? (Occasional means that the pain or discomfort has not occurred regularly or has occurred less than once a week).

Please shade on the diagram below any areas where you have had occasional pain or discomfort in the last 12 months.

Please describe the pain for each area and indicate whether you can connect it with anything that you do (eg. work, sports, hobbies etc...).
SECTION C

THIS SECTION IS ABOUT ACHES AND PAINS

*Please make sure that you tick either the 'NO' or 'YES' box in each line*

1. Have you ever had pain or discomfort in any of these parts of the body?

<table>
<thead>
<tr>
<th>Part</th>
<th>NO</th>
<th>YES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neck</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper arm</td>
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<tr>
<td>Shoulder</td>
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<td></td>
</tr>
<tr>
<td>Elbow</td>
<td></td>
<td></td>
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<tr>
<td>Upper Back</td>
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<tr>
<td>Lower arm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower Back</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wrist</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leg</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2. Do you have pain at the moment in any of these parts of the body?

<table>
<thead>
<tr>
<th>Part</th>
<th>NO</th>
<th>YES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neck</td>
<td></td>
<td></td>
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<tr>
<td>Upper arm</td>
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<tr>
<td>Shoulder</td>
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<td>Elbow</td>
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<tr>
<td>Upper Back</td>
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<tr>
<td>Lower arm</td>
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<td>Lower Back</td>
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<tr>
<td>Wrist</td>
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<tr>
<td>Hand</td>
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</tbody>
</table>

3. Have you ever sought medical advice for pain in any of these parts of the body, (e.g. from a doctor, physiotherapist etc...)?

<table>
<thead>
<tr>
<th>Part</th>
<th>NO</th>
<th>YES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neck</td>
<td></td>
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<tr>
<td>Upper arm</td>
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<tr>
<td>Shoulder</td>
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<td>Elbow</td>
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<td>Upper Back</td>
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<td>Lower arm</td>
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<td>Lower Back</td>
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<td>Wrist</td>
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<td>Hand</td>
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</table>

4. Have you ever had any medical treatment for pain in any of these parts of the body (e.g. from a doctor physiotherapist etc...)?

<table>
<thead>
<tr>
<th>Part</th>
<th>NO</th>
<th>YES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neck</td>
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<td>Upper arm</td>
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<td>Hand</td>
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5. If you have answered 'YES' to any part of question 3 or 4 please would you provide us with the following information:-

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Year</th>
<th>Area Affected</th>
<th>Cause</th>
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334
6. a) Did you have any sick leave in 1989? 
   NO □ YES □
   b) If 'YES' how many days sick leave did you have? ________ days

7. a) Did you have any sick leave in 1989 related to problems with any of these areas of the body?
   
   | Neck | NO □ YES □ | Upper arm | NO □ YES □ |
   | Shoulder | NO □ YES □ | Elbow | NO □ YES □ |
   | Upper Back | NO □ YES □ | Lower arm | NO □ YES □ |
   | Lower Back | NO □ YES □ | Wrist | NO □ YES □ |
   | Leg | NO □ YES □ | Hand | NO □ YES □ |

   b) If 'YES' how many days sick leave did you have and which part of the body was it related to?
   
<table>
<thead>
<tr>
<th>DAYS OF SICK LEAVE</th>
<th>PART OF BODY AFFECTED</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

8. a) Have you ever broken any bones? 
   NO □ YES □
   b) If 'YES' which bone(s)? __________________ and when? _________________

9. a) Have you ever sought medical advice for a sprain or dislocation? 
   NO □ YES □
   b) If 'YES' was it for any of the following joints? If 'YES' When? (YEAR)
   
   | Neck | NO □ YES □→19__ | Upper arm | NO □ YES □→19__ |
   | Shoulder | NO □ YES □→19__ | Elbow | NO □ YES □→19__ |
   | Upper Back | NO □ YES □→19__ | Lower arm | NO □ YES □→19__ |
   | Lower Back | NO □ YES □→19__ | Wrist | NO □ YES □→19__ |
   | Leg | NO □ YES □→19__ | Hand | NO □ YES □→19__ |

10. Have you been diagnosed by your doctor as having arthritis, rheumatism or 'wear and tear'? 
   NO □ YES □
   b) If 'YES' was it for any of the following joints? If 'YES' When? (YEAR)
   
   | Neck | NO □ YES □→19__ | Upper arm | NO □ YES □→19__ |
   | Shoulder | NO □ YES □→19__ | Elbow | NO □ YES □→19__ |
   | Upper Back | NO □ YES □→19__ | Lower arm | NO □ YES □→19__ |
   | Lower Back | NO □ YES □→19__ | Wrist | NO □ YES □→19__ |
   | Leg | NO □ YES □→19__ | Hand | NO □ YES □→19__ |
11. Have you ever been diagnosed by a doctor as suffering from any of the following? (Please indicate when this condition was first diagnosed)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Diagnosis Status</th>
<th>First Diagnosed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypothyroidism</td>
<td>NO</td>
<td>-19</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>NO</td>
<td>YES -19</td>
</tr>
<tr>
<td>Kidney failure</td>
<td>NO</td>
<td>YES -19</td>
</tr>
<tr>
<td>Amyloidosis</td>
<td>NO</td>
<td>YES -19</td>
</tr>
<tr>
<td>High blood pressure</td>
<td>NO</td>
<td>YES -19</td>
</tr>
<tr>
<td>Acromegaly</td>
<td>NO</td>
<td>YES -19</td>
</tr>
</tbody>
</table>

The following questions are for WOMEN only

12. Have you had a pregnancy? NO □ YES □

If 'YES' have you had numbness/tingling in your hands during pregnancy NO □ YES □

13. Have you ever menstruated? NO □ YES □

If 'YES' have you had numbness/tingling in your hands prior to menstruation NO □ YES □

14. Have you passed through the menopause? NO □ YES □

If 'YES' have you had numbness/tingling in your hands since passing through the menopause NO □ YES □

15. Have you undergone gynaecological surgery? NO □ YES □

If 'YES' have you had numbness/tingling in your hands since you underwent gynaecological surgery NO □ YES □

16. Have you ever used oral contraceptives? NO □ YES □

If 'YES' have you had numbness/tingling in your hands whilst using oral contraceptives NO □ YES □

Please check that you have answered every question.

Thank you for your co-operation.
OCCUPATIONAL CHECK LIST.

These questions are designed to help us find out more about the job you do and the kind of tasks you do in your job.

1. Do you have to grip or hold any object in your palm with your fingers and thumb during your job?  
   - NO ☐   YES ☐
   
   If "YES" do you repeat this task more than once every 30 seconds?  
   - NO ☐   YES ☐
   
   Do you have to exert a force (> 4 Kg) as part of this task?  
   - NO ☐   YES ☐
   
   Could you estimate how long you spend doing this task during a day at work?  
   ____________________ hours per day.

2. Do you have to pinch or hold any object between your fingers and thumb during your job (Not in your palm)?  
   - NO ☐   YES ☐
   
   If "YES" do you repeat this task more than once every 30 seconds?  
   - NO ☐   YES ☐
   
   Do you have to exert a force (> 4 Kg) as part of this task?  
   - NO ☐   YES ☐
   
   Could you estimate how long you spend doing this task during a day at work?  
   ____________________ hours per day.

3. Do you have to flex your fingers in your job?  
   - NO ☐   YES ☐
   
   If "YES" do you repeat this task more than once every 30 seconds?  
   - NO ☐   YES ☐
   
   Do you have to exert a force (> 4 Kg) as part of this task?  
   - NO ☐   YES ☐
Appendix III

4. Apart from gripping movements, do you have to bend your thumb during your job?  
   NO □ YES □

   If "YES" do you repeat this task more than once every 30 seconds?  
   NO □ YES □

   Do you have to exert a force ( > 4 Kg) as part of this task?  
   NO □ YES □

   Could you estimate how long you spend doing this task during a day at work?  
   _____________________ hours per day.

5. Do you have to twist your wrist in your job?  
   NO □ YES □

   If "YES" do you repeat this task more than once every 30 seconds?  
   NO □ YES □

   Do you have to exert a force ( > 4 Kg) as part of this task?  
   NO □ YES □

   Could you estimate how long you spend doing this task during a day at work?  
   _____________________ hours per day.

6. Do you bend your wrist up and down during your job?  
   NO □ YES □

   If "YES" do you repeat this task more than once every 30 seconds?  
   NO □ YES □

   Do you have to exert a force ( > 4 Kg) as part of this task?  
   NO □ YES □

   Could you estimate how long you spend doing this task during a day at work?  
   _____________________ hours per day.
Appendix III

Patient Check list

1. Do you notice any change in the severity of the symptoms during the course of:

   The Day  YES ☐  NO ☐  DON'T KNOW ☐
   The Night YES ☐  NO ☐  DON'T KNOW ☐
   The Week  YES ☐  NO ☐  DON'T KNOW ☐
   The Month YES ☐  NO ☐  DON'T KNOW ☐
   The Year  YES ☐  NO ☐  DON'T KNOW ☐

If "YES" please indicate when these were at their worst________________________

2. Have any members of your family experienced such symptoms? YES ☐  NO ☐  DON'T KNOW ☐

   If "YES" please give details (relationship etc) ___________________________

3. How long have you been suffering from your present condition?____________________

4. Is this your first attack or have you suffered from it before?_____________________

   Please give details of any previous attacks____________________________________

5. What was your job or occupation at the time of onset of your present condition?

6. As a result of your condition; have you changed your life style in any of the following:
   (please indicate when and why you had to change)?

   Sports and Hobbies__________________________________________________________

   Job__________________________________________________________

   Other__________________________________________________________
EDINBURGH HANDEDNESS INVENTORY

Please indicate your preference, in the use of hands, in the following activities by circling the appropriate letter.

OL  := you use ONLY the LEFT hand for that task unless absolutely forced to use the right.
L   := you normally use the LEFT hand for that task.
E   := you may use EITHER hand for that task.
R   := you normally use the RIGHT hand for that task.
OR  := you use ONLY the RIGHT hand for that task unless absolutely forced to use the left.

Some of the activities require both hands. In these cases the part of the task, or object, for which hand preference is wanted is indicated in brackets.

Please try to answer all of the questions, and only leave blank if you have no experience at all of the object or task.

<table>
<thead>
<tr>
<th>Activity</th>
<th>OL</th>
<th>L</th>
<th>E</th>
<th>R</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Writing</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drawing</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Throwing</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scissors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toothbrush</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knife (without fork)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spoon</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pliers</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Broom (upper hand)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strike match (match)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opening box (lid)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Oldfield (1971)
Please shade on the diagrams where your pain or discomfort occurs.

Name__________________________
<table>
<thead>
<tr>
<th>Anthropometric Details.</th>
<th>LEFT</th>
<th>RIGHT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrist breadth: styloid</td>
<td>_____mm</td>
<td>_____mm</td>
</tr>
<tr>
<td>Wrist breadth: distal crease</td>
<td>_____mm</td>
<td>_____mm</td>
</tr>
<tr>
<td>Wrist depth: distal crease</td>
<td>_____mm</td>
<td>_____mm</td>
</tr>
<tr>
<td>Wrist circumference: styloid</td>
<td>_____mm</td>
<td>_____mm</td>
</tr>
<tr>
<td>Palm width</td>
<td>_____mm</td>
<td>_____mm</td>
</tr>
<tr>
<td>Hand length</td>
<td>_____mm</td>
<td>_____mm</td>
</tr>
<tr>
<td>Radius length</td>
<td>_____mm</td>
<td>_____mm</td>
</tr>
<tr>
<td>Palmaris longus?</td>
<td>______</td>
<td>______</td>
</tr>
<tr>
<td>PIP joint angle</td>
<td>______</td>
<td>______</td>
</tr>
<tr>
<td>MCP joint angle</td>
<td>______</td>
<td>______</td>
</tr>
<tr>
<td>Height</td>
<td>_____m</td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td>_____Kg</td>
<td></td>
</tr>
<tr>
<td>Strength tests</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grip strength MVC</td>
<td>left</td>
<td>_____Kg</td>
</tr>
<tr>
<td></td>
<td>right</td>
<td>_____Kg</td>
</tr>
<tr>
<td>Diagnostic tests</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distal Motor Latency</td>
<td>median</td>
<td>left</td>
</tr>
<tr>
<td></td>
<td>ulnar</td>
<td>______</td>
</tr>
<tr>
<td>Phalens test</td>
<td>______</td>
<td>If positive note time in seconds ______</td>
</tr>
<tr>
<td>Flick Test</td>
<td>______</td>
<td></td>
</tr>
</tbody>
</table>
Pixel Conversion Factors.

To determine the conversion factors for both linear and area measurements a phantom of known dimensions (diameter and area) was imaged.

In converting the linear and area measurements from pixels to cm and cm² respectively, the known dimensions were divided by the respective linear and area pixel counts. Thus a conversion factor for linear and area pixels into cm and cm² was derived.

During image analysis the linear pixel counts were magnified by a factor of 4 to aid analysis. Therefore, the absolute linear pixel counts were 4 times greater than those calculated by area. For example, a square of area 4 area pixels (sides 2 x 2 area pixels) would have sides measuring 8 x 8 linear pixels. The calculation on page 144 should be re-defined to account for this difference as follows;

Linear measures;  
Bottle diameter = 5.6 cm  
Image diameter = 144.5 / 4 linear pixels  
→  
1 linear pixel = 5.6 / (144.5 / 4) = 0.155 cm

Area measures;  
1 square area pixel = 0.0232 cm²

If the linear pixel conversion factor (0.155 cm) is squared an area conversion factor can be obtained (0.02403 cm²). When this is compared to the area conversion factor determined directly from the phantom (0.0232 cm²) a difference of less than 0.001 cm² is observed. A similar calculation using the same principles can be applied to the data on page 116.

Since the conversion factors were based on these absolute values and thus fully accounted for any magnification, the calculation of dimensions in cm and cm² were accurate. The data used throughout this thesis were therefore not affected by this magnification factor.