2002

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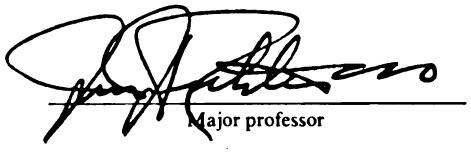
USE OF MAGNETIC RESONANCE IMAGING EXAMINATION TO ASSESS COMPARTMENT CHANGES IN THE FOREARM AND WRIST WITH EXPOSURE TO REPETITIVE TYPING

presented by

Gail A. Shafer-Crane

has been accepted towards fulfillment
of the requirements for

Ph.D. degree in Anatomy



Major professor

Date 8-15-02

USE OF MAGNETIC RESONANCE IMAGING EXAMINATION TO ASSESS COMPARTMENT CHANGES IN THE FOREARM AND WRIST WITH EXPOSURE TO REPETITIVE TYPING

By

Gail A. Shafer-Crane

A DISSERTATION

Submitted to
Michigan State University
In partial fulfillment of the requirements
for the degree of

DOCTOR OF PHILOSOPHY

Division of Anatomy and Structural Biology
Department of Radiology

2002

ABSTRACT

USE OF MAGNETIC RESONANCE IMAGING EXAMINATION TO ASSESS COMPARTMENT CHANGES IN THE FOREARM AND WRIST WITH EXPOSURE TO REPETITIVE TYPING

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Dimensional, positional and fluid content changes of soft tissues of the forearm and wrist as a response to typing were analyzed in this study using magnetic resonance imaging. Axial images were taken at the mid-forearm, proximal to the transverse carpal ligament, at the longitudinal level of the pisiform, hamate and base of the metacarpals levels. The intent was to contrast muscles more and less active through magnetic resonance imaging (MRI) examinations, and note changes in morphology of the median nerve at the wrist related to exposure to typing. Thirteen female professional typists, six asymptomatic and seven symptomatic, underwent three MRI examinations of the dominant forearm and wrist at baseline, after three hours of typing, and after eight hours of rest. Three investigators blinded to the subjects' exercise status analyzed forearm muscle and wrist compartment images with respect to T2 signal intensity and nerve morphology. Compartmental constituent fluid and shape changes were correlated with typing. Forearm flexors were more active in typing than extensors and thumb muscles (P=.0016). Progressive variations in T2 as well as size and shape of the median nerve highly correlated to typing. MRI analysis following exercise (typing) in this study revealed significant changes in both muscles and nerves, suggesting a relationship between exposure to typing and these findings.

In loving memory of Esther Mary Loersch and Shirley Evelyn Barry, my grandmother and mother ... and to the women who came before us, and will come after.

Carpi Diem.

ACKNOWLEDGMENTS

My road to completion has taken many twists and turns through the maze of classes, research projects, testing, teaching and finally writing. Through this long haul, my family has shown heroic patience and support. We have given up much time together, and delayed or rearranged every sort of family activity. Dan has patiently waited for his college student wife to come home for meals, activities and just to be at home. Many times Mike and his wife Elizabeth or Stephanie were drafted to help with the research project, volunteer for imaging, or help in some way. Thanks to all of you.

This work would have never been started without the direction, patience and vision of Robert Hubbard, PhD. He listened to an enthusiastic, naïve graduate student hopeful wandering about, looking for the entrance to the road to PhD, and heard the germ of a worthy idea. Joseph Vorro admitted me into the Anatomy program, and assigned by original committee: James Rechtien as my mentor, and Lawrence Ross, Kenneth Stephens, and Robert Werner. Though the committee changed because of the loss of the original project, these individuals have continued to offer their support and direction. Particularly Dr. Rechtien, whose patience and perseverance is unmatched.

So many others were instrumental in my successful completion of this project. Marcy Schlinger, the primary investigator of the study, helped format and edit many forms of posters and preliminary articles. Drs. Lee Bennett, Kevin Robinson and Joseph Pernicone radiologists spent countless hours pouring over images. Tom Cooper and Dr. Ronald Meyer ran the MRI through our very lengthy imaging sessions on Sundays and evenings.

And, finally, thanks to my committee: James Rechtien, advisor, J.I. Johnson, William Falls, Ron Meyer, Lee Bennett and Arlene Sierra. Each offered their time and expertise in this endeavor. I have learned so much thanks to these people, and to so many others. One may only hope to pass along the knowledge and opportunity to others.

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Table of Abbreviations

ANOVA	Analysis of variance
APL	Abductor pollicis longus
AWS	Advantage Windows Workstation
C5,6,7,8	Cervical nerve number 5, 6, 7, and 8
CNS	Central Nervous System
CTS	Carpal Tunnel Syndrome
DIP	Distal interphalangeal joint
DOMS	Delayed Onset Muscle Soreness
DRUJ	Distal radioulnar joint
ECR	Extensor carpi radialis
ECRB	Extensor Carpi Radialis Brevis
ECU	Extensor carpi ulnaris
ED	Extensor Digitorum
EDM	Extensor digiti minimi
EPB	Extensor pollicis brevis
EPL	Extensor pollicis longus
ETL	Echo train length
FCRL	Flexor carpi radialis longus
FCU	Flexor carpi ulnaris
FDP	Flexor digitorum profundus
FDS	Flexor digitorum superficialis
FOV	Field of view
FPL	Flexor pollicis longus
FSE	Fast spin echo
GRE	Gradient echo image, in this study T2 weighted
IP	Interphalangeal joint
MRI	Magnetic Resonance Imaging
NIOSH	National Institute of Occupational Safety and Health
PIP	Proximal interphalangeal joint
RF	Radio frequency pulse
RSI	Repetitive Stress Injury
T1	MRI value T1 where fat is brighter than water
T1	Thoracic nerve number 1
T2	MRI value T2 where water is brighter than fat
TCL	Transverse Carpal Ligament
TE	Echo time
TR	Relaxation time
UCRIHS	University Committee on Research Involving Human Subjects
UNIX	A proprietary computer operating system that allows simultaneous multiple level interactions between software with multiple users

Glossary of Magetic Resonance Imaging Terms

Fast Spin Echo	In conventional spin echo, the radio frequency pulse is applied to provide a 90° excitation pulse which is followed by rephasing pulses at 180°. These pulse sequences are adjusted for T1 (short TE and short TR), proton density (short TE and long TR), and T2 weighting (long TE and long TR). In fast spin echo multiple 180° rephasing pulses are used during data acquisition. These are referred to as echo train, and the total pulses used are defined as the echo train length (ETL). The fast spin echo pulse sequence allows more information to be recorded for each image in a shorter period of time.
Fat saturation	Fat saturation in image collection voids the signal from fat, nullifying the signal. The hydrogen atom is linked to carbon in fat, giving it a specific rate of precession. A 90° radio frequency pulse can be applied to "pre-saturate" the tissue in the FOV, followed by the excitation RF pulse is then applied, and the signal from fat is voided.
Gradient Echo	Gradient echo images (GRE) require the application of additional gradient echo pulses to refocus the echoes. This takes less time than FSE, which requires application of the radio frequency pulse. The result is a faster imaging time. The GREs used in this study were T1 weighted, and provided contrast between the median and ulnar nerves and the surrounding connective tissue.
Gyromagnetic ratio	As the axis of an atom rotates, the vector of the axis caused by its interaction with an applied magnetic field is called the gyromagnetic ratio.
Larmor equation	The Larmor equation ($\omega_{0=}B_0 \times \gamma$) provides the method for calculating the value of the precession frequency under different applied magnetic fields. The processional frequency (ω_0) is equal to the applied magnetic field (B_0) times the gyromagnetic ratio (γ). Each type of molecule has a different precessional frequency, allowing identification of the substance through its unique electrical signature.

Longitudinal magnetization	When a body is placed in a strong magnetic field, the axis of the magnetic active atoms align with the magnetic field.
Precession	The axis of an atom rotates in a cone shaped path at a rate that is consistent with the element's characteristics. This rate varies with exposure to different magnetic fields, and calculated using the Larmour calculation. Each element has its own rate of precession.
Resonance	Resonance causes the NMV to move out of alignment with the applied magnetic field, forming a "flip angle." The term used to describe B_0 is the longitudinal axis. The plane at 90° to the longitudinal axis is termed transverse plane. During resonance, the magnetic moments also begin to move in phase with one another. This is when the NMV's all precess at the same rate (the Larmor frequency for hydrogen) and are located in the same position throughout their paths of precession.
RF pulse	A radio frequency pulse is an applied radio frequency wave that is at the same frequency as the precessional frequency of an element, usually hydrogen. It is this pulse that perturbs the atoms, causing some of them to spin into a higher energy configuration, and to spin in phase with each other (resonance).
T1 recovery time	T1 is determined by the length of time in milliseconds it takes for the nuclei to recover longitudinal magnetization.
T2 relaxation time	T2 relaxation time, or decay, is the length of time in milliseconds that it takes for 63% of the transverse magnetization to be lost following a radio frequency perturbation. The energy loss resulting in T2 is through the interaction of the magnetic fields of nearby nuclei, also termed *spin spin relaxation* or *spin lattice relaxation.* The energy lost takes the form of heat, which is dispersed through the surrounding tissue or lattice.
TE	Time between the application of the radio frequency pulse and the peak of the signal induced in the coil measured in milliseconds.
TR	The time between radio frequency pulses

Transverse magnetization	When an RF pulse is applied, the axis of atoms whose natural oscillation matches the frequency of the pulse absorb energy. This causes them to move out of alignment with the longitudinal, applied magnetic field, or spin. If sufficient energy is applied, the axes of these atoms will move to 90 degrees out of alignment, this is transverse magnetization. It is the degree of transverse magnetization that produces the electrical field that is received by the receiver coils and transformed into the MRI signal.

Chapter I

INTRODUCTION

Repetitive stress injuries (RSIs) are a plague on modern society. They affect the quality of life for millions of people worldwide. Delayed onset pain or paresthesias are a cardinal symptom of these disorders, and are poorly understood. This study was undertaken to advance the understanding of the normal anatomical functions of nerves and muscles exposed to repetitive activity, and how those functions might differ in symptomatic individuals. A study model, which may be used in future studies, was developed to examine the effects of a variety of vocational activities upon the muscles and nerves of the forearm.

Societal and personal costs of RSIs are significant. Knowledge of these costs mandates that we explore the etiologies of these devastating syndromes. These disorders have been observed throughout recorded history. Despite the attempts of the earliest healers through modern physician scientists to define the etiologies of RSI, the causal factors are not, as yet, completely understood.

A brief summary of these subjects will be presented in this chapter. A brief history of RSIs and specifically the most prevalent RSI, carpal tunnel syndrome will be presented. RSI will be defined, and several disorders of the forearm will be discussed. Methods of study will be summarized, and the hypotheses of this study will be presented at the conclusion of this introductory chapter.

Medical and Physical Costs of Repetitive Stress Injuries

The National Institute of Occupational Safety and Health (NIOSH) report of 2001 documents over 582,000 cases of repetitive stress injuries (RSIs) for the year 1995 [65]. Over the period included in that report, this number accounted for one out of three of all injuries and illnesses with days away from work. Manufacturing and service industries each account for around 26 percent of RSIs, followed by retail trade with nearly 16 percent. This NIOSH report focuses on injuries and illnesses resulting in the longest periods of time away from work. This emphasis helps clarify risk levels of particular vocations. The report uses median days away from work as the key survey measure of severity. The median number of lost workdays for all cases of RSI was 6 days in 1999, with one fourth of the cases resulting in 21 days or more away from work. The injury-illness with the highest median of work days lost was carpal tunnel syndrome (CTS) at 27 lost days. Fractures were second with 20 days, and amputations required 18. Repetitive motion resulted in the longest absences from work as a leading event and exposure category at a median of 17 days [65].

Carpal tunnel syndrome, an entrapment neuropathy, is the most common of all RSIs accounting for 90% of the compensable injuries reported through workers compensation [65]. The Department of Labor statistics of 1999 reports CTS as the diagnosis responsible for the most days missed from work for that year, and barely second to back injuries as the most costly to rehabilitate. Cases involving surgery may average $250,000 in medical costs alone [13]. Despite the epidemiological evidence, and the increased incidence among workers in specific trades, a controversy remains over categorization of CTS as an RSI in both research and clinical studies [34].

The prevalence of RSIs in the general population is significant. Actual percentages vary widely depending on the study. NIOSH reports a 4.2 % prevalence in women, and 1.3% in men in a 1996 survey. A similar Dutch study reports 6.8% in women, and 1.2% in men [13, 18, 65]. Prevalence in working populations varies by task. Cherniack reports the highest risk in fish and meat workers at 60%, followed by grocery store clerks also at about 60%, with office workers at 10-26%. These figures were determined by the Bureau of Labor Statistics Survey of Occupational Injuries and Illnesses (1995), with high percentages either confirmed or identified by physical examination [65].

The survey, which defined an expected number of cases, differs from the number actually reported to either workers compensation by the Physician's First Report, or to the health department. The number of cases reported by workers compensation reports is somewhat lower. This inconsistency may be because cases are not reported to either the employer or workers compensation system, or because of the existence of a report latency between case identification and the reports to various agencies responsible for ongoing surveillance of RSIs.

Electrodiagnostic methods used in surveillance have defined cases not reported clinically. These latent cases are reported as positives by some investigators and not reported by others. They would not be included in reports of work related injuries to the health department, for example, but would be included in longitudinal studies of specific industries independent of governmental reporting mechanisms. Peak age ranges also vary by study. Cherniack reports a peak age range of 45-54 years; other studies report a peak age range of 35-44 years [13, 29, 56, 70].

History of Repetitive Stress Injuries

The earliest recording of RSI is from Egyptian hieroglyphics taken from the Hanoverian obelisk now on display in the Louvre Museum in Paris, France. This refers to "white finger disease" in stonecutters for the Pharaohs' pyramids. References to this problem have been made in the medical literature of the 19th and 20th centuries as well [33, 52]. These more recent references are of fish and meat processors working with knives in a cold environment, and stone masons and heavy construction workers using jack hammers and other heavy tools with either a component of impact and/or vibration. The exposure of the worker to low frequency vibration, prolonged power grasping, and percussion also increases the risk of repetitive neural trauma that may lead to RSI [13].

Carpal tunnel syndrome, thoracic outlet syndrome and cubital tunnel syndrome were described in the medical literature of the 1800's. Medical scientists of that period often defined these entities as circulatory disorders of the nerves. It may be helpful to review the history of CTS as an example of the evolution of modern understanding of the etiologies of RSIs.

History of Carpal Tunnel Syndrome

(The following is paraphrased from The History of Carpal Tunnel Syndrome [66] with additional information from other sources as cited).

Late Nineteenth Century

Sensory changes associated with CTS were first clearly defined by James Putnam in 1880. He was the first to document nocturnal paresthesias. He eventually suggested that this new disease entity was caused by circulatory disturbances affecting the median nerve at the wrist. He ruled out more proximal lesions in the brachial plexus because there is often bilateral involvement and the symptoms are inconsistent. Franz Schultz, a contemporary of Dr. Putnam, described sensory symptoms in the median nerve distribution in his patients. The Schultz study also reported a population similar to that of Dr. Putnam. These patients were women of middle age who described nocturnal pain or paresthesias [66].

Early Twentieth Century

Thenar atrophy was described as a separate, unrelated entity. James Ramsey Hunt described thenar atrophy in 1909, 1911, 1914 and 1950, relating atrophy to mechanical compression of the motor branch of the median nerve by the transverse carpal ligament (TCL). He determined that this disorder was caused by occupational overuse. However, Dr. Hunt did not believe that the sensory nerve syndrome described by Dr. Putnam was related to the motor impairment and thenar atrophy.

Pierre Marie and Charles Foix documented compression of the median nerve at the TCL as the cause of thenar muscle atrophy in a report to the French Neurological Society in 1913. They described the post mortem dissection of the median nerve of an 80-year-old woman whose symptoms were known to the physicians before her death. They

were able to describe swelling of the median nerve, thinning distal to the TCL, formation of a nodule or neuroma just proximal to the TCL, and demyelinization of the median nerve beneath the TCL.

Early carpal tunnel/median nerve decompression surgeries were performed in the 1920's [2],[52]. Further definition of "median neuritis" and eventually the term "carpal tunnel syndrome" was attributed to Drs. Brain and Phalen in the 1940's and 1950's [2]. Advances in both diagnosis and treatment of carpal tunnel syndrome have been made as the prevalence in the population has grown. According to Arle, only 12 cases were known in the 1950's, while as many as 15.8% of the working population is known to have CTS in the current population [3].

Mid Twentieth Century

Post World War II, women entered the work force in unprecedented numbers, many taking jobs that required hours of typing, filing, and other tasks deemed "light work"[34]. It was not expected that this type of work could elicit similar symptoms as the heavy work previously associated with RSI. As reliance upon the computer expanded in the 1980's, studies began to suggest an epidemic of CTS. Dire predictions of 80-90% of the workforce likely to experience some form of RSI during their work life began to gain attention. In the 1990's, CTS rivaled back injury for the most expensive of covered injuries under workers' compensation in most developed countries [3]. In recent years, there has been a deluge of epidemiological, medical and ergonomic research in the area of RSI and related workstations, physical and medical risk factors, and remedies. Yet no

precise cause and effect relationship between specific vocational tasks and characteristics of CTS in particular, and RSIs in general, has been defined.

The History of Inflammation

Inflammation is often an early sign of RSI. Several disorders, which are considered RSIs, are referred to as inflammatory disorders. They will be discussed in greater detail later in this chapter. Knowledge of the historical development of the understanding of inflammation may be helpful in understanding the anatomy, histology and physiology of RSI. (The following history of inflammation was paraphrased from Inflammation, an Upjohn Company publication by Grueme B. Ryan and Guido Majno.)

1650 B.C.

The earliest references to inflammation have been translated from the Smith Papyrus, a scroll writing in Egypt around 1650 BC, which was derived from an earlier work that was as much as 1000 years older. This earliest reference to inflammation was intermingled with the then current knowledge of wounds and infection. The Greeks continued to relate inflammation and infection closely for a millennium. Roman medicine did not alter this understanding of the close relationship between infection and inflammation. However, the Roman writer Cornelius Celsus enumerated the four cardinal clinical signs of inflammation: redness and swelling with heat and pain.

Late Eighteenth/Early Nineteenth Century

It was not until 1793 that Scottish surgeon John Hunter separated inflammation from infection, as a "salutary reaction." Julius Cohnheim, in 1867, wrote the first description of inflammatory processes in frog mesentery that he was studying under the microscope in the living state. He observed arteriole dilation with associated increased blood flow, which eventually decreased. As blood flow slowed, he observed white blood cells beginning to line the blood vessel walls. He then described diapedesis for the first time. His hypothesis stated that the permeability of the blood vessels increased during the inflammatory process. He related his observations to the four cardinal signs of inflammation, and most of the basis for the modern understanding of the inflammatory process was established.

Virchow, in his *Cellular Pathology*, published in 1858, added a fifth sign of inflammation to the body of knowledge. This sign indicates that an inflamed organ does not behave normally.

Nineteenth and Twentieth Century

The increase in permeability of the endothelium of the capillary system has been gradually confirmed and defined over the last 100 years. Most recently, electron microscopy has captured the various processes of inflammatory changes in the endothelium. Diapedesis and the increased permeability of the venules to allow the escape of antibodies and antitoxins and fluid have been documented by electron microscopy.

The flow of fluid into the tissues, and subsequent accumulation of this fluid, causes the acute edema in the early stages of inflammation. Fibroblast infiltration with the exudate allows new connective tissue to be added to, or replace, the fluid that has accumulated in the tissue. Inflammatory swelling is usually accompanied by pain, which is either evident episodically or with motion or palpation [75].

Definition of Repetitive Stress Injuries

Repetitive stress injuries (RSI) refer to a category of conditions of the neuromuscloskeletal system thought to be caused by the performance of repetitive tasks [4, 33, 34], often including repetitive forceful grasping, pinching, pushing, lifting, pulling or triggering. Examples of high risk activities include use of a computer mouse, air tools, typing and hand tools. RSI is usually either vocational or avocational, resulting in a cumulative trauma to soft tissue. This category of disorders is not a diagnosis. Many terms are used in conjunction with these disorders. Cumulative trauma disorder, over-use syndrome, repetitive motion disorder, repetitive strain injury, and musculo skeletal disorders are among the most popular terms in the literature [33]. For the purposes of this study, we will use the term repetitive stress injury (RSI) to represent these conditions. Advances in technology continue to uncover the secrets of the various etiologies of repetitive stress injuries. Clarification of the definitions of RSI as used in this study will provide the basis for subsequent discussion of the Methods of Study and Hypotheses.

Clinicians divide repetitive stress injuries into two categories, neurocompressive disorders and inflammatory disorders. Common neurocompressive disorders, carpal tunnel syndrome, cubital tunnel syndrome, and Guyon's canal syndrome, affect the

median and the ulnar nerves. They represent compression of these peripheral nerves in specific compartments of the wrist and elbow. Inflammatory disorders of the forearm include lateral and medial epicondylitis and tenosynovitis. These three disorders affect specific muscles at their point of insertion or at their myotendinous junction, or in their synovial tendon sheaths.

Neurocompressive disorders

Neurocompressive disorders are caused by mechanical compression, either because of posture, invasive tissue, edema, or injury to a compartment that increases the pressure on a nerve sufficiently to reduce or occlude perineural circulation. A brief review of normal anatomy, histology and physiology as they relate to RSI follows.

Normal anatomy, histology and physiology

Peripheral nerves are usually mixed nerves, and have their beginnings as spinal nerves [81]. The nerve cell is made up of three parts, the cell body, axon, and bouton or terminus. Motor nerve cell bodies (efferent) are located within the gray matter of the spinal cord [53]. The axon is often several feet long and branches to terminate on as few as one, or as many as 30,000 muscle fibers to form a motor unit. As these axons exit the spinal cord, they protrude between vertebrae through intervertebral foramina and proceed through connective tissue compartments to their terminations in the extremities [60]. Sensory nerve cells (afferent) are housed within the dorsal root ganglion. Specialized nerve endings, which are located in all tissues, may be chemoreceptors, mechanoreceptors, or nociceptors. Action potentials initiated in these sensory organs, are

propagated along their long axons which are eventually housed within the spinal nerve. They will finally synapse on the interneurons of the central nervous system.

Nutrients, neural transmitters and other less known substances are manufactured in the nerve cell body and transported to the terminus of the nerve in a process called axonal transport [81]. Depending on the substance, either fast or slow axonal transport moves it along toward the terminus of the nerve. Sustenance of both the nerve and the muscle cells making up the motor unit is dependent on robust axonal transport [81].

Normal anatomy of the peripheral nerves permits sufficient mobility of the nerve to allow it to slide as the position of the upper limb is moved through its normal range of motion. This excursion of the nerve may be as much as 23 mm at the elbow or wrist [37, 87]. Along the length of the nerve, also gliding with it, is a capillary plexus. This plexus is in two parts, the longitudinal and transverse capillaries. The capillaries are located within and supply the perineurium, and penetrate deep between the fascicles [45].

Similarities between neurocompressive disorders and inflammatory disorders

Persistent nocturnal or delayed onset pain has been used for decades by clinicians as the definitive symptom to diagnose repetitive stress injuries, including lateral epicondylitis, tenosynovitis and CTS [64]. These symptoms often follow exposure to prolonged exercise. Patient complaints are often transient, non-specific reports of pain, weakness, and paresthesias in the upper limbs [33, 34]. These symptoms may crescendo over time. With continued exposure to the injuring force, the symptoms of inflammation increase until the patient is unable to tolerate the precipitating activity. Once the individual has been subjected to a repetitive stress injury, the tissue involved continues to

be more susceptible to further injury. Recovery is lengthy, and may require a variety of interventions including absolute rest, change in activity method or resistance, medication, physical rehabilitation and/or surgery [2, 13, 34, 65]. If one is aware of causal factors, these injuries are more easily prevented than treated.

Differences between neurocompressive disorders and inflammatory disorders

The most apparent difference between neurocompressive disorders and inflammatory disorders is the anatomical structure involved in the injury. The mechanism of injury is also different.

Neurocompressive disorders occur when there is an increase in intracompartmental pressure inhibiting normal perineural circulation. This pressure increase may occur because of an individual sustaining an awkward posture, repetitive increases in finger tip pressure as in typing, or because of forceful grasp [71, 72, 86]. A neurocompressive disorder often has an insidious onset. Seldom can a specific date or incident be identified as the causal factor. It is more likely to be a lengthy exposure to an aggravating activity. The more severe disorders may cause compression sufficient to displace axons, or interrupt myelination. Diagnostic testing of neurocompressive disorders is done through electrodiagnostic testing. Nerve conduction studies are the "gold standard" for defining neurocompressive disorders [41, 52, 55, 56].

Inflammatory disorders often occur after a change in job status, a sudden exposure to a new task or a change in equipment [33]. Inflammation of muscle is characterized by an increase in interstitial fluid, complaints of soreness, stiffness or pain at a specific point in the muscle. Tenosynovitis may be characterized by difficulty in

smoothly moving a digit (trigger finger), palpation of fibrous or fluid filled nodules along the synovial tendon sheath, and pain with active range of motion of the joint moved by the inflamed tendon. Clinical assessment including manual muscle testing, observation of edema at the insertion of muscle, and/or pain with palpation over the muscle belly or insertion of the muscle are classic signs.

Normal Anatomy of Forearm Compartments

The Carpal Tunnel

The carpal tunnel is a rigid, bony 'C' shaped canal formed from the eight carpal bones that make up the wrist. Across the roof of the carpal tunnel is the transverse carpal ligament, a thickened band of forearm fascia that closes the tunnel. The tendons of the flexor digitorum profundus, flexor digitorum superficialis, and flexor pollicis longus muscles, as well as the median nerve, traverse the wrist through the carpal tunnel.

The Cubital Tunnel and Guyon's Canal

The ulnar nerve traverses the elbow in the cubital tunnel. The floor of the cubital tunnel is the lateral collateral ligament, which covers a bony groove in the medial proximal ulna; the roof is a connective tissue retinaculum. The tendon of the flexor carpi ulnaris inserts into the retinaculum. The nerve then passes between the muscle bellies of the flexor carpi ulnaris and flexor digitorum superficialis muscles in the forearm. The ulnar nerve traverses the wrist with the ulnar artery and vein through Guyon's canal, a triangular connective tissue compartment. The floor of Guyon's canal is the transverse

carpal ligament, the roof is the palmar carpal ligament, and the medial wall is the medial side of the pisiform bone.

Normal Accommodations of the Peripheral Nerves

The cross sectional shape of many peripheral nerves is typically elliptical. The elliptical shape allows the nerve to alter shape as the flexible compartments are compressed through muscle contraction or postural changes. The area of the nerve does not change with the change in shape [48]. This has been shown to be a protective response to changes in pressure within the compartment [71, 72, 86]. A more detailed review of the normal anatomy and histology of the median and ulnar nerves may be found in Chapter II on pages 24-41.

Altered anatomy, histology and physiology of the peripheral nerves of the forearm

Many authors have reported shape, circulatory and histological changes of the peripheral nerves of the forearm resulting from increased intracompartmental pressure. These changes may impact neural function in a transient, reversible way or they may cause permanent, irreversible changes including axonal loss [17, 46, 47, 52, 63].

Carpal tunnel syndrome has been often studied, no doubt because it is vastly more prevalent than other neurocompressive disorders [13, 18, 65]. Studies of median nerve compression at the wrist document transient circulatory effects and the subsequent symptoms, e.g. transient numbness and tingling or pain. Diagnostic testing may document measurable effects, e.g. diminished circulation measured by Doppler

flowometry and slowed nerve conduction [1, 17, 37, 46, 78]. More information on the compartments of the wrist, including the carpal tunnel is in Chapter II on pages 32-37.

Compression within a compartment sufficient to occlude perineural circulation, even if only briefly, will cause an interruption in the oxygen supply to the nerve axon and a local, reversible physiological block [46]. If the compression is short lived, damage to the axon may be completely reversed by relieving the compression. If the compression is sustained for long periods, or is repeated with sufficient frequency, the injury may cause demyelinzation and or retrograde degeneration of the nerve cell (Wallerian degeneration) [46]. Ischemia is often mentioned as one of the most prevalent forces contributing to the blockage of axonal transport, and to increased impact of compression on the nerve.

Anatomical Considerations in Inflammatory Disorders

Inflammation is generally thought of as a symptom. In the context of this study, we will define inflammatory disorders as those whose primary characteristic is inflammation. The culprit in these injuries is most often the connective tissue of the bursa, tendon insertion, tendon sheath, or muscle belly. In order to understand the implications of inflammation, it is necessary to review the normal anatomy, histology and physiology.

Normal Anatomy, Histology and Physiology

Fascia covers all cellular components of the body. This is called myofascia when it covers muscle. This continuous loose irregular connective tissue envelope is non-contractile, or "inactive." This is important because proprioceptors, pressure receptors

and other sensory organs that provide kinesthetic, proprioceptive, stretch, and deformation feedback to the central nervous system are housed within this non-contractile connective tissue [38, 39]. Muscle, tendon, and ligament sensors coordinate with the fascial sensors to provide comprehensive postural and movement information to the central nervous system (CNS). The CNS provides feedback to the muscles for coordination of motion and protection from sprains and strains [38].

Dense Connective Tissue

Tendons, made up of dense regular connective tissue, attach muscles to bone. Dense regular connective tissue is comprised of parallel collagen fibers with a noticeable wave, or "crimp" [39]. This allows shock absorption and tolerance to prolonged or repetitive strain without damage to either the tendon or muscle under normal loads. The muscle fibers are also covered with loose irregular connective tissue (myofascia). This tissue envelops the muscle, and as it nears the point of origin or insertion (myotendinous junction), the connective tissue thickens and joins with the tissue of the tendon.

Muscle

Muscle is highly vascularized by prolific capillary beds that penetrate the muscle along connective tissue layers, branch to supply adequate nutrition to the muscle fibers, and transport waste materials out of the muscle [53]. During exercise, water is shifted between intercellular muscle fiber compartments due to osmotic changes from the accumulation of lactic acid, a by-product of exercise [80]. This is a simplification of one

theory that explains the changes in muscle tissue that allows the identification of active muscle by magnetic resonance imaging. This will be discussed later in this chapter.

Muscle contraction may take one of three forms. Concentric contraction is when the muscle shortens in length during activation. Isometric contraction is when there is no change in muscle length during activation. And eccentric contraction is when the muscle lengthens during activation [53, 79-81]. More information on muscle anatomy and histology is available in the Anatomy chapter on pages 32-41.

Altered anatomy, histology and physiology

Increased strain in prolonged resistance, or repeated strain will cause connective tissue fibers to straighten [38]. During cumulative repetitive activities a tendon may lengthen and eventually remain in its lengthened state making it more susceptible to damage at either the osteotendinous or the myotendinous junction [39]. Inflammatory changes may occur when exposure to repetitive trauma accumulates, causing microhemorrhages and dissociation between muscle fibers and their points of insertion into the tendon [34, 69, 77]. Edema is one of the first signs of inflammation, which is characterized by the accumulation of fluid in the intercellular space.

Delayed Onset Muscle Soreness

Delayed onset muscle soreness (DOMS) is the onset of muscle pain hours or days after the exposure to the activity that caused the injury [53, 79]. Histological changes are implicated in DOMS as evidenced by the accumulation of intercellular fluid [53, 79].

DOMS has been defined as one of the cardinal symptoms of repetitive stress injury [33, 34, 52].

Examples of Neurocompressive Disorders

Median neuropathy

Carpal Tunnel Syndrome

Carpal tunnel syndrome is the neurocompressive disorder of the median nerve at the wrist. The median nerve is compressed beneath the transverse carpal ligament within the carpal tunnel. Some causal factors include prolonged wrist flexion and repetitive power grasp or pinch. These actions separately, or more powerfully in combination, cause the long flexor tendons to compress the median nerve against the transverse carpal ligament, collapsing the perineural circulation. Other common causal factors may include wrist fracture, edema, and encroachment of muscle fibers from anomalous lumbricals that invade the carpal tunnel. CTS is characterized by pain or paresthesias in the thumb and radial two fingers, and the radial half of the third. Tinel's sign is hypersensitivity of the nerve to mechanical stimulation. Tinel's sign is often elicited along the course of the median nerve in CTS. If untreated, atrophy of the thenar muscles and subsequent loss of grip and pinch strength may develop [33].

Pronator Syndrome

Compression of the median nerve may also occur as it passes through the pronator teres muscle in the proximal forearm. The patient presents initially with complaints of volar forearm pain that may follow repetitive forceful elbow motion [59]. Asking the patient to pronate the forearm against resistance exacerbates the paresthesias or pain.

Ulnar neuropathies

Guyon's Canal Syndrome

Ulnar nerve compression at the wrist occurs in Guyon's canal, a small connective tissue compartment located superficial to the transverse carpal ligament (TCL), beneath the palmar carpal ligament and just lateral to the pisiform bone. Awkward postures of the wrist, especially ulnar deviation and wrist flexion during power grasping are causal factors [34]. Because Guyon's canal is a soft tissue compartment, this syndrome is vastly less prevalent than CTS. Numbness, paresthesias, or pain in the small and ulnar half of the ring fingers are symptoms of this disorder.

Cubital Tunnel Syndrome

Cubital tunnel syndrome is a common neurocompressive disorder of the ulnar nerve caused by repeated valgus stress on the elbow. Because the cubital tunnel is somewhat superficial, the ulnar nerve is exposed to potential mechanical trauma within its confines. It may also be exposed to repetitive trauma from forceful flexion of the elbow against resistance, or with percussive force as in hammering. The ulnar nerve may also be tethered by anomalous connective tissue or scar tissue within the cubital tunnel. Pain, paresthesia, and hypoesthesia that radiate about the elbow as well as proximally and distally along the course of the ulnar nerve, are symptoms and signs of cubital tunnel syndrome [34, 64].

Examples of Inflammatory Disorders

Lateral Epicondylitis

Lateral Epicondylitis is an inflammation of the common extensor tendon of the forearm. The tendons of four wrist and finger extensor muscles combine to form this broad tendon: the extensor carpi radialis brevis (ECRB), extensor carpi ulnaris, extensor digitorum (ED), and extensor digiti minimi. The proximal attachment of the tendon arises from the lateral epicondyle [60]. The tendon of the ECRB is most commonly inflamed in this disorder [64]. The combined action of repetitive flexion of the index finger during powerful grasping, as in activating the trigger of an air nailer, is a common causal factor of lateral epicondylitis. This motion appears to require eccentric contraction of the ECRB to stabilize the wrist. When the tolerance of this muscle is exceeded, it becomes inflamed resulting in lateral epicondylitis. The backhand tennis strike is also such a common causal factor, that this disorder is nicknamed "tennis elbow" [64]. Delayed onset muscle soreness (DOMS) is a common symptom. The onset of pain may be delayed for hours or days from the causal activity, which allows continuation of the activity and increased severity of the disorder [72]. Once pain has begun, it recurs during the provocative activity [34].

Medial Epicondylitis

Medial Epicondylitis is inflammation of the tendons of the pronator teres and/or flexor carpi ulnaris as they insert into the medial epicondyle. Repetitive forceful flexion of the wrist while grasping a fairly large object is a common causal factor. This disorder is sometimes called golfer's elbow and housemaid's elbow. DOMS is a common

symptom. Once there is onset of pain, repetition of the provocative activity and/or pressure on the insertion site will cause moderate to severe pain [34].

Tenosynovitis

Tenosynovitis and peritendinitis in the forearm, wrist and hand refers to inflammation of the tendon sheaths of the long finger and wrist muscles [33, 34]. Forceful, repetitive use of the digits is a major causal factor. Often characterized by palpable nodules along the length of the tendon sheaths or tendons, localized edema, and palpable trigger points at the myotendinous junctions, these diagnoses are made through clinical signs [34]. The patient may be able to indicate a specific date of overuse resulting in the injury, or may relate a range of dates, wherein changes in the activity level were noted. Onset of pain, while somewhat delayed, is often more acutely related to a specific activity, where a specific incident of injury in a compressive disorder is less well defined. [34].

Method of study

The characteristics of inflammation and repetitive stress suggest that exposure to repetitive activity would present observable changes in muscles and nerves and their respective compartments after a short exposure to the activity. These changes would include vessel dilatation, changes in T2 relaxation times (T2 relaxation time is a parameter of fluid content in tissue, see Glossary) of muscles and nerves, and increased fluid levels in the compartments of the wrist and elbow. It would further be expected that

some or all of these changes would resolve with prolonged rest. The research design was developed with these concepts in mind.

Typing as the exercise exposure of choice

Typing was chosen as the exercise exposure because clerical workers represent a high percentage of the workforce who lose time from work because of RSI. Typing has been shown to increase intracarpal tunnel pressure [72]. Furthermore, a design using typing made possible the control of exercise posture, along with maintenance of proximity to magnetic resonance imaging (MRI) equipment.

Study population

Women experience CTS and some other RSIs more frequently than men. The ratio of women to men is as high as 5:1 in some populations [13]. For that reason, it was decided that women would be recruited as subjects for this study. Clerical workers, specifically professional typists, are more likely to experience some form of RSI, though clerical workers are more likely to experience symptoms that are transient and poorly localized. Our asymptomatic subjects were screened for history of previous injury, diagnosis or recent symptoms. The symptomatic cohort was recruited because they were experiencing symptoms of upper extremity pain or paresthesias at the time of the study. Each individual also reported a diagnosis. Two reported diagnoses of CTS, four reported diagnoses of lateral epicondylitis, and one reported a diagnosis of tenosynovitis. All had similar symptoms of forearm pain and/or paresthesias. Some reported delayed onset (DOMS) or nocturnal pain and/or paresthesias.

Imaging Method

Magnetic Resonance Imaging (MRI) was chosen as the evaluation technique. This non-invasive technique provides high-resolution axial images that lend themselves well to quantification of size, fluid content and changes in shape or position of the tissue under study. More information on the MRI techniques used in this study is available on pages 45-46.

Summary of Findings

Muscle T2 Changes and active muscle identification

Investigators in this study were able to differentiate between muscles more and less active during typing through the use of MRI T2 relaxation times. T2 weighted images show unbound water as brighter than bound water. During exercise a number of metabolic factors that are well documented in the literature combine to briefly increase the T2 relaxation time in muscles performing concentric contraction [19-21, 68]. While the most intense interval of T2 relaxation time increase is short lived, approximately 30 minutes, this phenomenon allowed the investigators to identify particular muscles active in typing.

Changes in morphology of the nerves at the wrist

The investigators were further able to observe the median and ulnar nerves at the wrist, and to compare and contrast their morphology at baseline, prior to activities of the day, immediately after typing, and after 8 hours of rest. T2 changes were measured and

the visible morphologic changes in the nerves and their compartments were documented in the dominant forearm of each subject by MRI.

More complete information on the methods used in this study is available in Chapter III on pages 42-52.

Hypothesis development

Contrasting muscles more and less active in typing

At the outset of this study, several hypotheses were developed from the literature. It is known, for example, that exercising muscle has a measurable increase in T2 relaxation time when compared to rest. One expectation of this study was to contrast muscles active and inactive in typing. Inflamed tissue has the tendency to have increased T2 relaxation time [55, 56] with MRI examination. For that reason it was expected that the T2 relaxation time increases in muscles of symptomatic subjects after typing would be more dramatic than those of asymptomatic individuals. This was not what was found.

Changes in Neural Morphology

Nerve morphology changes when challenged by increases in pressure from muscle contraction or posture. Investigators in this study expected the shape and size of the nerves of symptomatic subjects to change more than those of the asymptomatic subjects. This proved to be incorrect. As the study progressed, an explanation became apparent, and will be discussed in Chapters IV and V.

Study investigators also expected T2 relaxation times of nerves of both symptomatic and asymptomatic subjects to vary with exposure to typing when compared to rest. The variation and trend of the changes became one of the most interesting aspects

of this study. More information on results can be found in Chapters IV and V, pages 63-72, 83-87.

CHAPER II

ANATOMICAL REVIEW OF THE UPPER EXTREMITY AS IT RELATES TO REPETITIVE STRESS INJURY

Human function is unique, in part, because we are able to use our hands to carry out complex tasks. The upper limb is designed to execute these tasks as quickly as the brain invents them. High levels of communication between the central nervous system and the upper extremity make this possible. The muscles that provide motor function to the hand have one of the highest ratios of motor neurons, connecting the hand muscles with the central nervous system, to muscle fibers [81]. The skin of the hand is similarly invested with sensory receptors [81]. The combination of sensibility and motor control creates one of the most sensitive and coordinated systems of the body. The distance these neurons travel makes them vulnerable to compression as they twist and turn through a system of compartments traveling from their origins in the central nervous system to their points of termination. It is necessary to understand the course of the nerve and blood supply from their beginnings to identify distal neural impairments.

Neural and Vascular Pathways

Neural and vascular structures have different origins. Nerves, veins and arteries join to form neuro-vascular bundles that allow them to travel together from their proximal origins to their distal terminations. The bony skeleton and connective tissue compartments that provide conduits for the neuro-vascular bundles support the neuro-vascular bundles. An understanding of the close physical and functional associations between neural and vascular structures will be valuable in this study of repetitive stress injuries (RSIs). Many RSI syndromes have both neural and vascular components,

etiologies, and symptoms. RSIs are usually associated with particular anatomical regions. The following anatomical review of the upper extremity will define anatomical regions and several of the associated repetitive stress injuries.

First, it is necessary to review a few terms that allow anatomical descriptions to be consistent and concise. Examination of the body can be accomplished using many imaging techniques (such as Magnetic Resonance Imaging, x-ray, or ultrasonography) or through more hands on examination (such as physical, palpatory or goniometric techniques). Anatomical nomenclature is used to identify consistent reference points and perspectives. The present study will use a number of Magnetic Resonance Imaging (MRI) methods. The images that are a result of MRI techniques are often referred to as "slices." Sagittal sections (at the mid-line) and parasagittal sections (on either side of the mid-line) divide the left side of the body from the right. Coronal slices run from side to side, dividing anterior from posterior. Axial slices are perpendicular to the longitudinal plane [60]. Axial examinations are the most useful for the assessment of the compartments of the upper limb and are the images primarily used in this study (Figure 2.1).

A brief summary of the anatomical structures that are involved in repetitive stress injuries follows. Included in the summaries of the anatomy are examples of the mechanisms of common RSIs. Anatomical structures will be reviewed regionally, proximal to distal.

The Neck and Shoulder

The head is borne by the vertebral column. The cervical vertebrae provide both mobility and support for the head, while acting as a conduit for sensory and motor neural components and sites of origin for neck and shoulder muscles. The vertebral foramina are areas of potential impingement. Herniation of the intervertebral discs, arthritic changes reducing the size of the foramina, or an injury causing impingement of the nerve roots (radicals) may cause a radiculopathy. A radiculopathy affects motor and sensory function the full length of the peripheral nerve. Symptoms are usually exacerbated with range of motion of the neck, which increases the pressure on the impinged spinal nerve [52].

The Brachial Plexus

The brachial plexus is the nerve center for the upper extremity. It is formed from the anterior primary rami of cervical nerve roots C5 – T1. As the anterior rami emerge from the foramina, they form the trunks of the brachial plexus and pass between the anterior and middle scalene muscles. If these muscles are hypertrophied from overuse or are in spasm, they may compress the roots or trunks directly. The scalene muscles originate from the transverse processes of the cervical vertebrae and insert on the first and second ribs.

Hypertonicity or spasm of the anterior and middle scalenes may cause the first rib to compress the brachial plexus and/or the subclavian artery, which travels with the brachial plexus as it passes through the scalene muscles. This is one causal factor of Thoracic Outlet Syndrome (TOS), which may be either a circulatory disorder of the upper limb, or a neurogenic disorder. Neurogenic TOS is caused by direct compression of the

brachial plexus, and often causes poorly localized paresthesias, hypoesthesia and pain. An anomalous cervical rib may compress either the brachial plexus or the subclavian artery and cause TOS. Symptoms/signs of TOS are paresthesias, sometimes well localized and sometimes spread throughout the upper extremity, and circulatory changes including cyanosis of the affected arm. The patient will have decreased tolerance for overhead activities such as washing, styling or drying their hair [52].

Trunks, Divisions, Cords and Branches

Distal to the nerve roots, the anterior rami combine to form the superior (C5 and C6), middle (C7) and inferior (C8, T1) trunks. The trunks then divide into the anterior and posterior divisions. The lateral cord is formed by the anterior divisions of the superior and middle trunks. The medial cord is formed by the continuation of the anterior division of the inferior trunk. The posterior cord is comprised of the unification of all the posterior divisions of the three trunks. The lateral, posterior and medial cords tuck under the clavicle with the subclavian artery. The cords then divide into branches, which become the named nerves supplying the shoulder, arm and forearm. The lateral pectoral (thoracic), musculocutaneous, and lateral component of the median nerve derive from the lateral cord. The ulnar nerve and medial contribution of the median nerve derive from the medial cord, as do the medial pectoral, medial brachial cutaneous, and medial antebrachial cutaneous nerves. The upper subscapular, thoracodorsal and lower subscapular nerves derive from the posterior cord just proximal to the formation of its terminal branches, the axillary and radial nerves [45, 60].

Nerves of the Upper Extremity

These nerves enter the arm just inferior to the glenohumeral joint. The musculocutaneous nerve exits the axilla and is located between the biceps brachii and brachialis after piercing the coracobrachialis muscle. The lateral antebrachial cutaneous nerve is the continuation of the musculocutaneous nerve [60]. The median nerve exits the axilla with the brachial artery. They traverse the arm on the surface of the brachialis muscle. The ulnar nerve lies parallel to the median nerve, brachial artery and veins until approximately mid-humerus. It then separates and penetrates the medial intermuscular septum to enter the posterior compartment. It completes the path through the arm on the medial aspect of the triceps muscle [74]. The radial nerve leaves the axilla between the long and medial heads of the triceps muscle. It enters the radial groove with the radial artery where it wraps around the humerus from medial to lateral.

The Skeletal Armature

The thoracic vertebrae not only support the cervical vertebrae, but the rib cage as well. Each rib articulates first with the thoracic vertebra, then encircles the neck or chest and articulates with the sternum, either directly through their own costal cartilage (true rib) or indirectly through the costal cartilage of the rib immediately above (false ribs) with the exception of the last two ribs which do not articulate with the sternum (floating ribs) [60]. The clavicle, or collarbone, is an 'S' shaped long bone that articulates with the sternum proximally and the scapula distally. The synovial sternoclavicular joint is the only articulation between the axial skeleton and the upper extremity [60]. The very dense

interclavicular ligament provides limited mobility and tremendous strength to this articulation. A fibrocartilage disc provides shock absorption within the joint.

Osteology of the Shoulder

The bony structure of the upper limb, the appendicular skeleton, is designed to allow maximal mobility as a priority, with the sacrifice of some stability and weight bearing ability compared to the more ligamentous and bony joints of the lower limb. The proximal articulations of the arm include the shoulder joints. This complex joint includes the articulation of three bones, the clavicle, scapula and humerus. The clavicle provides the only direct articulation with the axial skeleton at the sterno-clavicular joint. Mobility of the shoulder is enhanced by the muscular attachment of the scapula to the dorsal rib cage and vertebral column. The concave anterior scapula, encased in muscle, glides over the convex rib cage.

The shoulder joint is formed by a "ball and socket" joint at the apex of the posterior scapula. The humeral head articulates with the scapula at the glenoid process (glenohumeral joint). This relatively small articular fossa is enlarged by the glenoid labrum, a ring of fibrocartilage, which increases the articular surface and depth of the glenoid fossa. Shoulder stability is maintained through the acromioclavicular joint superior to the glenohumeral joint [59, 60, 74].

The Course of Neural and Vascular Structures Supplying the Upper Limb

Circulatory structures that supply the upper extremity are of interest to the investigators in this study of repetitive stress injuries. Arteries provide oxygenated blood

to the extremities. Deep veins accompany, and are usually named for, the associated arteries. Deep veins, arteries and nerves often travel together in neuro-vascular bundles.

A description of the arterial pathways helps to summarize the course of the major vessels through the upper limb. Arterial vessels branch from the arch of the aorta. The brachiocephalic trunk branches into the right subclavian and carotid arteries; on the left the subclavian and carotid arteries branch directly from the aorta. The subclavian artery ascends and crosses the length of the clavicle, then crosses the first rib distally where it becomes the axillary artery. The axillary artery changes names again, to the brachial artery, after it crosses the teres major muscle and enters the arm. At approximately one third of the length of the humerus, the deep brachial artery branches off to accompany the radial nerve in the radial groove of the humerus, while the brachial artery continues through the arm, accompanied by the median nerve, between the brachialis and biceps brachii muscles [60].

The Elbow

The course of the Radial Nerve

The radial nerve emerges between the brachialis and the brachioradialis muscles to cross the elbow laterally, entering the cubital fossa lateral to the biceps brachii tendon as the biceps inserts into the radius. The radial nerve divides into the deep (muscular) and superficial (sensory) branches. The deep branch pierces the supinator muscles in a fibrous band, known as the "arcade of Frohse," to become the posterior interosseous nerve, and is vulnerable to impingement from spasm of the supinator [2]. This is sometimes diagnosed as a vocational repetitive stress injury.

The Course of the Median Nerve

The median nerve also crosses the elbow in the cubital fossa medial to the biceps brachii tendon, deep to the bicipital aponeurosis. It follows the continuation of the brachial artery into the cubital fossa, and then accompanies the ulnar artery distally, finally passing through the flexor/pronator compartment of the forearm between the flexor digitorum superficialis (FDS) and flexor digitorum profundus (FDP) without an accompanying artery, or less commonly, with the persistent branch of the median artery. Here it innervates the majority of the extrinsic muscles and provides articular innervation to the elbow [60]. The median nerve continues through the forearm between the FDS and FDP until it enters the wrist.

The Course of the Ulnar Nerve

The ulnar nerve enters the arm anterior to the subscapularis muscle and teres major and minor, and then follows the triceps muscle to the elbow. It traverses the elbow within the cubital tunnel at the ulnar notch of the medial epicondyle. This tunnel is formed by the aponeurosis between the two heads of the flexor carpi ulnaris muscle distally, and a thin fibrous structure extending from the olecranon to the medial epicondyle known as the cubital tunnel retinaculum. The ulnar nerve then joins the ulnar artery in a neurovascular bundle between the FCU and FDS. The ulnar nerve continues through the forearm between these muscles until it enters the wrist superficial to the transverse carpal ligament in Guyon's canal [25, 26, 60].

The cubital tunnel is an area of compression of the ulnar nerve, as is Guyon's canal. Ulnar neuropathies are the second most common peripheral neuropathy of the upper extremity. One possible cause of compression is thickening of the cubital retinaculum. According to Fritz, 22% of the population is subject to this anatomical variation, which causes dynamic compression. In 11% of the population an anomalous muscle, the anconeus epitrochlearis, which causes static compression of the ulnar nerve, may replace the retinaculum [25]. Trauma to the ulnar nerve is more likely at the cubital tunnel than at Guyon's canal because of the distance the ulnar nerve travels superficially, exposing it to a higher potential for trauma [2].

Compartments of the Forearm

Muscles that move the wrist, hand and fingers attach at the elbow and along the length of the forearm. The muscles are divided into flexor and extensor compartments within the bony and fascial compartments of the forearm (Figure 2.2). These compartments are defined by location, function and innervation. Neurovascular bundles travel between muscles in fascial compartments [60].

The Extensor Compartment

The extensor-supinator compartment components are the extrinsic (outside the hand) extensor muscles of the wrist, fingers and thumb. The radial nerve and its branches innervate the muscles in this compartment. These muscles extend the wrist and fingers as well as adduct, abduct, and supinate the forearm. The extensor carpi radialis longus (ECRL) originates on the lateral supracondylar ridge of the lateral epicondyle. The

tendons of the extensor carpi ulnaris (ECU), extensor digitorum (ED), extensor carpi radialis brevis (ECRB) and extensor digiti minimi (EDM) form the common extensor tendon as it inserts on the lateral epicondyle. The supinator muscle partially originates on the lateral epicondyle, as well as the radial collateral and annular ligaments of the elbow, supinator fossa and crest of the ulna before it wraps around the circular radial head where it inserts. The thumb muscle group (extensor pollicis brevis (EPB), extensor pollicis longus (EPL) and abductor pollicis longus (APL)) is also within this forearm compartment [59, 60, 74].

The Flexor-Pronator Compartment

The flexor-pronator compartment is on the anterior surface of the forearm, separated from the extensor-supinator compartment by the interosseus membrane of the radius and ulna. The flexor-pronator compartment is further divided into deep and superficial muscles. The five superficial muscles primarily attach to the medial epicondyle through the common flexor tendon. The pronator teres, flexor carpi radialis (FCR), palmaris longus, flexor carpi ulnaris (FCU) and flexor digitorum superficialis (FDS) are forearm pronators, wrist flexors and extrinsic finger flexors. Deep muscles in this group include the flexor digitorum profundus (FDP), flexor pollicis longus (FPL) and pronator quadratus. FDP and FDS are extrinsic (outside the hand) flexors of the digits (fingers). The FDP flexes the distal interphalangeal joint of the fingers; the FDS flexes the proximal interphalangeal joints (PIP). The FPL flexes the IP joint of the thumb [59, 60, 74].

The Wrist

The wrist is the highly dynamic link between the forearm and the hand. It is the main conduit of nerves and circulatory vessels that serve the hand. The complex bony joints of the wrist provide both strength and mobility for hand position and function. The wrist provides the bony fulcrum for long flexor and extensor tendons, and allows infinite repositioning of the hand during activity. Significant research has been done to characterize "accessory motions", the intercarpal motions of the carpal bones and their ligaments, as they respond to the demands of voluntary activity.

In the current literature the accessory motions of the carpus, as well as primary motions of the articulations of the long bones of the forearm and hand with the carpus, have been described as causing minute deformations of the bony carpal tunnel and its soft tissue constituents [43, 44, 71, 72]. These deformations create the potential for compromise of neural, vascular, connective, and lymphatic tissues that pass through the finite space of the carpal tunnel. Risk of repetitive trauma increases with the rates of force, speed, and repetition of the task, which in turn, increases the effect upon the contents of the carpal tunnel.

Magnetic Resonance Imaging studies of carpal tunnel syndrome (CTS) have shown particular characteristics of the median nerve and other soft tissue constituents of the carpal tunnel. These include increased T2 signal intensity of the median nerve, increased fluid content of the tendon sheaths and other compartments, and bowing of the flexor retinaculum over the median nerve [55, 56, 58, 61]. The axial imaging levels at which these phenomena occur are identified by prominent bony landmarks of the wrist clearly visible on magnetic resonance images. A description of these levels follows.

Proximal to the Transverse Carpal Ligament

For the purposes of this study, the area just distal to the distal radioulnar joint and the radial and ulnar styloids, but before the appearance of the proximal lunate as it articulates with the distal radius, is defined as "Proximal to the Transverse Carpal Ligament" (Figure 2.3). The transverse carpal ligament (TCL) is used interchangeably in the literature with the flexor retinaculum.

The distal radioulnar joint (DRUJ) is bound on the palmar aspect by ligaments, which give rise to the floor of the carpal tunnel. The radius fits into the radial sulcus of the distal ulna and is able to rotate about the ulna, permitting pronation and supination of the forearm. The pronator quadratus is one of the prime movers of pronation in its position covering the palmar surfaces of the distal radius and ulna. A thin layer of fat fills the Parona space covering the pronator quadratus. This underlies the bed of the flexor tendons, median and ulnar nerves, and the vessels of circulation that supply the wrist and hand. The forearm fascia, which encases the forearm just deep to the skin, thickens and is referred to as the palmar carpal ligament at this level [60].

Current studies of median nerve compression (carpal tunnel syndrome) describe changes in the shape of the median nerve visible on MRI examination [6, 8, 12, 47, 55]. The median nerve is usually round or oval in undiagnosed or asymptomatic subjects at this point, and is often flattened in symptomatic subjects [54]. The median nerve may be swollen and demonstrate an increased T2 signal intensity in patients with CTS. The sheath of connective tissue and fat surrounding the nerve is expected to be relatively thin

at this point. A definite separation between the nerve and connective tissue is often visible as a dark line on T2 weighted images.

The ulnar nerve is usually oval at this level. It may be triangular or flattened in patients with ulnar neuropathy at the wrist. While this has not been quantified to date, characteristics similar to those of CTS may be noted. These include increased T2 signal intensity, flattening or shape changes of the ulnar nerve, soft tissue inflammation and fluid within Guyon's canal.

The long flexor tendons of the flexor digitorum profundus (FDP) and superficialis (FDS), flexor pollicis longus (FPL) as well as the median nerve organize into layers as they prepare to enter the carpal tunnel. They are enveloped in tendon sheaths from proximal to the flexor retinaculum to the distal metacarpals (fifth finger to distal phalanx). The flexor carpi radialis (FCR) tendon is not considered to be a constituent of the carpal tunnel, even though it passes through the bony compartment. It enters the wrist in its own fascial compartment along the radial aspect of the carpal tunnel before inserting on the second metacarpal. The palmaris longus tendon is central and superficial to the TCL, and terminates in a long thin tendon that blends into the palmar fascia. The flexor carpi ulnaris tendon is the most medial structure in the volar wrist. It inserts first on the pisiform bone, then the fifth metacarpal [60, 74].

The extensor, or dorsal, compartment proximal to the transverse carpal ligament houses the extensor and abductor tendons of the digits. These tendons are housed within tendon sheaths, which produce synovial fluid to provide lubrication. One surface landmark used in examination of the wrist is the anatomical snuffbox. This hollow depression in the lateral wrist is formed by the tendons of the abductor pollicis longus

(APL) and extensor pollicis brevis (EPB) ventrally, and the extensor pollicis longus dorsally. The cephalic vein overlies the anatomic snuffbox and is one of the visible landmarks helpful in orienting one's self when one is studying images of the wrist. Dorsally the radial artery passes deep to the APL and EPB to enter the anatomic snuffbox. The extensor pollicis longus courses radially, superficial to the extensor carpi radialis longus and brevis tendons.

Level of the Pisiform

The bony landmark used to define the proximal segment of the carpal tunnel is the pisiform bone. The bones of the proximal carpal row, from lateral to medial are the scaphoid, lunate, and triquetrum. The sesamoid bone, Pisiform, rests on the anterior surface of triquetrum. The transverse carpal ligament (TCL) is formed when the volar component of the antebrachial fascial thickens distal to the distal radioulnar joint. The term "transverse carpal ligament" is used interchangably with the term "flexor retinaculum of the wrist [31, 35]."

The TCL only attaches to carpals. The lateral attachments are proximally the scaphoid and distally the trapezium. Medial attachments are the pisiform proximally and the hook of the hamate distally. The TCL forms the roof of the carpal tunnel. The flexor tendons, flexor digitorum superficialis (FDS), flexor digitorum profundus (FDP) and flexor pollicis longus (FPL) organize into layers to pass through the finite space of the carpal tunnel. The tendons of the FDP are deep, whereas the FDS tendons are more superficial and medial to the FPL. The median nerve has some variability in its location. However, it is usually superficial to the FDS, lying between the FDS and the tendon of

the FPL [51]. The retinaculum is least rigid in this region as it attaches on the mobile Pisiform medially, with a rigid base at its lateral attachment to the scaphoid [60].

Guyon's canal is medial and superficial to the carpal tunnel. The floor is the transverse carpal ligament as it covers the pisiform and hamate bones (distally), the roof is the palmar carpal ligament, and the medial wall is the pisiform bone. Guyon's canal houses the ulnar nerve (medial), artery and vein (lateral) (Figure 2.4). A small fat pad provides cushion for the ulnar artery and nerve within the canal. The ulnar nerve, artery and vein enter Guyon's canal just palmar and external to the roof of the flexor retinaculum on the ulnar side of the wrist. As the ulnar nerve and artery pass distally in Guyon's canal, they divide into their superficial and deep branches. The veins follow a similar course to the arteries.

Level of the Hook of the Hamate

Bones of the distal carpal row from medial to lateral are the hamate, capitate, trapezoid and trapezium. The hook of the hamate forms the ulnar wall of the carpal tunnel, as well as the attachment site of the TCL and deep wall of Guyon's canal [59, 60].

The TCL is generally seen as straight or slightly convex at this level as it extends between the hamulus of the hamate to the tubercle of the trapezium on MRI. The palmar capitate-scaphoid and palmar capitate-trapezium ligaments contribute to the deep walls of this segment of the carpal tunnel (Figure 2.5) [59, 60, 74]. The median nerve maintains its relationship to the other carpal tunnel structures as described at the level of the proximal carpal tunnel, but may assume atypical positions and shapes depending on the position of the wrist.

The Hand

No anatomical review of the upper limb is complete without at least a brief summary of the hand. Because the hand is the termination of the muscles, nerves and blood vessels discussed throughout this study, a basic understanding of its systems provides insight into the effects of RSI.

Osteology of the Hand

Distal to the carpal bones are the five metacarpals. These form the palm and the base of the thumb. The transverse carpal ligament ends just proximal to the heads of these long bones. The metacarpals maintain a concave transverse arch from their articulations on the carpals (Figure 2.6). Articulating with each of the metacarpals are the phalanges, or finger bones. These long bones provide the bony support and levers for grasp and pinch. Each articulation is designed to provide either single plane motion, as in the hinge joints of the interphalangeal joints, or mobility as in the saddle joint of the carpometacarpal joint of the thumb.

Hand muscles: Intrinsic

Intrinsic muscles originate and insert within the hand. The intrinsic thenar, or thumb, muscles originate from the TCL, trapezium and the scaphoid bones. The hypothenar, or small finger, muscles arise from the pisiform bone, the hamate bone, the tendon of the flexor carpi ulnaris, and the flexor retinaculum. The interosseous muscles are divided into the palmar and dorsal interosseii. These muscles lie between the

metacarpals, where they attach in order to abduct and adduct the fingers. There are four lumbrical muscles, numbered from lateral to medial, which flex the metacarpophalangeal joints and assist in full extension of the proximal interphalangeal joints. They arise from origins on the sides of the extensor expansions of the digits, and insert on the tendons of the flexor digitorum profundus [60].

Hand muscles: Extrinsic

The tendons of the long finger and thumb flexors fan out from the carpal tunnel as they approach their insertions on the digits. The flexor digitorum superficialis terminates on the proximal middle phalanx of digits 2-5, where it is a primary flexor of the proximal interphalangeal (PIP) joints. The flexor digitorum profundus inserts on the distal phalanges of digits 2-5, where it is the only flexor of the distal interphalangeal (DIP) joints. The flexor pollicis longus inserts on the base of the distal phalanx of the thumb, where it is the only flexor of the interphalangeal joint of the thumb.

Integument and fascia

The skin of the palm is very thick and is characterized by deep flexion creases. The palmar fascia is a continuation of the antebrachial fascia. It is well defined and thick in the central palm, but it is thinner where it covers the thenar and hypothenar eminences. This fascia provides excellent padding for the soft tissue structures of the hand [60].

The dorsal skin is wrinkled, with especially deep wrinkling present over the joints of the digits. This permits the skin to stretch over the joints and enhances flexibility of the hand.

Nerves, Arteries and Veins of the Hand

The radial and ulnar arteries and veins form the superficial and deep arterial arches of the palm. The superficial arch gives origin to the common and digital arteries and veins of the digits. The median and ulnar nerves fan out as they emerge from the carpal tunnel and Guyon's canal to supply both motor and sensory innervation to the hand. The median nerve supplies the lateral hand, as well as the thumb, index, long, and lateral half of the ring fingers with sensation. The recurrent median, a branch that typically arises just distal to the TCL, innervates the muscles of the thenar eminence.

The deep branch of the ulnar nerve innervates the adductor pollicis, the hypothenar muscles, palmar and dorsal interosseii, and the medial two lumbricals. Its sensory distribution includes the medial hand, medial half of the ring finger, and the little finger. The superficial radial nerve terminates as it provides sensory innervation to the lateral, dorsal hand and thumb [59, 60].

CHAPTER III

Materials and Methods

Clerical workers have been shown to be at higher risk than the general population for repetitive stress injuries. Long hours of rapid data entry with minimal postural changes, poorly designed workstations, and poor upper extremity conditioning for the work are some of the risk factors [52, 65]. The population with the highest incidence of repetitive stress injuries of the upper extremity includes women between the ages of 21 and 55 [3, 12, 13, 82].

Study Population

Thirteen female volunteers between the ages of 21 and 52 were recruited from the patient base of physicians participating in the study as investigators and a local rehabilitation center, Michigan State University clerical employees, and contract transcriptionists associated with the physician practices, the rehabilitation center, or a local hospital. All subjects were active as typists with a job requirement of three hours of production typing per day. This is equal to the length and rate of typing exposure for this study.

The asymptomatic cohort included 6 female typists; ages 21 – 52 mean age 38. The symptomatic cohort included 8 female typist subjects 21 – 52, mean age 44 (Figure 3.1). A standard 'T' test was used to show that the difference in mean ages between cohorts was not statistically significant. One subject from each cohort acted as a non-typing control as well as a typing subject.

Study Objectives

The intent of this study was to establish an imaging and exercise protocol and test hypotheses related to symptoms of delayed onset sensory disturbances including pain and paresthesia. We elected to include symptomatic subjects previously diagnosed with any repetitive stress injury of the forearm for this small cohort, as long as the subject reported symptoms of forearm pain and/or paresthesias. All symptomatic subjects were previously diagnosed with either carpal tunnel syndrome, tenosynovitis, or lateral epicondylitis of the dominant limb.

Experimental Design

Subject Selection

Subjects were interviewed for medical and work history, and then placed in either the asymptomatic or symptomatic cohort. Each subject identified her right hand as dominant. Volunteers with a history of previous injury or surgery to the dominant wrist, metabolic conditions such as diabetes or rheumatoid arthritis, or current pregnancy were excluded from this study. Each subject completed a medical history questionnaire (Figure 3.2), an informed consent form (Figure 3.3) approved by the University Committee on Research Involving Human Subjects (UCRIHS), and the Levine Carpal Tunnel Syndrome Symptom Severity Scale (Figure 3.4), and Functional Status Scale (Figure 3.5). The investigators used the results from these surveys to quantify symptoms and complaints [50, 76]. Subjects in the asymptomatic group scored 1.0-1.125 on the Levine Symptom Severity Scale and 1.0 on the Functional Status Scale. Symptomatic subjects

scores ranged from 1.36 to 2.37 on the Levine Symptom Severity Scale, and from 1.0 to 3.0 on the Functional Status Scale.

Physical Examination

Following placement in the appropriate cohort, each subject was scheduled for a physical examination of the dominant extremity. The physical examination was used to document performance differences, if any, between subjects and between the symptomatic and asymptomatic groups. The physiatrist or physiatry resident recorded the results of the physical examinations on a standard form (Figure 3.6).

The physical examination included provocative testing used by many clinicians to diagnose repetitive stress injuries. Among the provocative tests, the examiner attempted to elicit Tinel' s sign. The examiner used percussion of his/her finger tips along the course of the median and ulnar nerves at points as they approach the skin in an attempt to elicit shooting pain or paresthesia. The examiner also performed Phalen's test, which elicits radiating pain and/or paresthesia if positive. Each subject was directed to place the backs of her hands together in what may be described as a reverse prayer position (Figure 5.1). Proprioception screening of wrist and fingers, and reflex testing of the biceps, triceps and brachioradialis tendons were performed.

Strength was quantified by manual muscle testing of shoulder flexion and abduction, elbow flexion and extension, wrist flexion and extension, radial and ulnar deviation, finger extension, finger abduction and thumb abduction. Each subject performed three trials of power grasping using the Jamar dynamometer grip test at the

second setting. Each subject also performed three trials each of pinch testing of lateral, three jaw chuck and tip pinches.

Sensory nerve conduction studies were done using the ulnar nerve on the ipsilateral side as the control. A physiatrist or physiatry resident performed the physical examination and sensory nerve conduction studies. A standardized data sheet was used to record the physical examination results.

Magnetic Resonance Imaging Examination

Following the physical examinations, the examiner prepared each subject for the first magnetic resonance imaging (MRI) examination of the dominant forearm. Precise positioning and repositioning of the subject's right arm in the MRI magnet is vital for accurate comparative measurements of diameter, area and signal intensity of the tissue under study. Prior to the first imaging session, the investigator used an indelible marker to place a crosshatch on the surface landmarks denoting the lateral epicondyle and the approximate center of the forearm muscle bulk to assure accurate positioning for each imaging session. The dorsum of the carpal tunnel was outlined using an 'H' that was drawn on the skin with the parallel legs of the 'H' across the distal radius and ulna and bases of the metacarpals with the cross bar in the longitudinal center of the wrist. The markings were visible when the subject's arm was placed in either the extremity or wrist coil. The cross hatch was used to indicate the "zero point" for imaging within the magnet in a procedure called "land marking."

Imaging Position

A General Electric Signa 1.5 Tesla magnet and small extremity coil for the forearm muscle bulk and elbow were used to image each subject's right forearm. The examiner positioned each subject in the magnetic resonance imaging magnet in a modified swimmer's position with the arm outstretched in shoulder flexion, elbow extension, with the hand prone within the small extremity coil. The crosshatch mark on the approximate center of the muscle bulk was used to center the forearm in the extremity coil and "land mark" the forearm in the magnet core. Dual echo T2 weighted spin echo images with different TE's (TR 1500/TE 60; TR 1500/TE 30) were obtained from the proximal radial head through the musculotendinous junctions of the forearm flexors. TE, or echo time, is the time in milliseconds between the radio frequency perturbation pulse and the greatest induced signal. Each subject was then repositioned for imaging of the elbow.

The mark on the lateral epicondyle was used to "landmark" each elbow within the extremity coil. The elbow images were fast spin echo (FSE) (TR 1500 TE 80 and 15, echo train length 8), FSE with fat saturation (TR 1500 TE 80 and 15 ETL 8), and gradient echo (TR 700/TE 21, flip angle 40, Nex 2).

Each subject was then repositioned in side lying for the wrist images. The wrist was placed in a small wrist coil with the wrist and hand supported in a neutral position, wrist at 30°, fingers extended, by a thermal plastic resting pan splint (Figure 4.1). Fast spin echo (TR 2000/ TE 16.0; TR 2000/TE 80.0 ETL 8, 512 x 256 Nex 2), fast spin echo with fat saturation (TR2000/TE15, 512 x 256 Nex 2) and gradient echo (TR700/TE 21.0 flip angle 40, 512 x 256) images were obtained. Total image collection took one hour.

Typing as the Exercise Exposure

After the baseline MRI examinations were completed, the subjects then typed for 3 hours at a rate of approximately 50 words per minute. They were allowed one 15-minute break mid way in the typing session. Each subject was provided with a workstation that was adjusted for comfort and correct ergonomic position. Subjects were encouraged to type as rapidly as they were able, and to continue until they were informed of their break or the time to stop for the day. Typing material was not controlled, so each typist either provided their own material, or they were provided with a book or magazine to use.

Imaging After Typing

A second set of images was collected with the above protocol after the subjects completed three hours of typing. Muscle bulk images were begun less than 10 minutes after typing was discontinued, and collection of these images took approximately 6 minutes. As metabolites of muscle contraction are reabsorbed, particularly calcium and sodium, free water and unbound hydrogen that increased in the muscle tissues during eccentric contraction diminish in the tissue and return to a resting level. This causes T2 changes to begin to resolve between 20 and 30 minutes after discontinuation of the exercise exposure [19, 57, 68]. Subjects needed to be moved quickly from typing into the imaging position in the magnet for muscle studies.

Every attempt was made to duplicate the earlier imaging positions using surface markings. Images from these studies were used to assess shape and size changes, making it essential to precisely repeat the angle of imaging, slice content, and location of

important landmarks. When analyzing the images, examiners made use of bony landmarks.

Rest Period and Related Imaging

Subjects were dismissed as each completed the post exercise imaging session, and instructed to avoid repetitive tasks for 5 hours, then return for 3 hours of observed inactivity to complete an 8-hour rest period. Television was provided during the observed rest period in an attempt to lower the metabolic rate to simulate sleep. The third and final set of images of each subject was then obtained after the rest period reported at 12 hours.

Data Collection

Three radiologists and the author, each of whom were blinded to the exercise status and subjects' identity, analyzed images of the elbow, forearm and wrist compartment constituents. Measurements of the area and shape of the median and ulnar nerves, signal intensity, and fluid within the compartments of the wrist were made using axial images at each of the following imaging positions:

Elbow: 1. Proximal to the medial epicondyle

2. Distal to the medial epicondyle

Muscle bulk from elbow joint to teno-muscular junction

Wrist: 1. Proximal to the flexor retinaculum

2. At the level of the Pisiform

3. At the level of the Hook of the Hamate

4. At the level of the base of the metacarpals.

Many investigators have used MRI examinations to identify actively exercising muscle [19, 21, 22, 24, 57, 68] and characteristics of repetitive stress injuries at these levels [6-8, 15, 36, 47, 52, 55, 61, 64, 69](for further review and definitions of these imaging positions, please refer to the anatomical summaries in Chapter II, pages 27 - 41).

Hypothesis Development

Three hypotheses were tested in this study using different quantification techniques. A review of each hypothesis precedes the explanation of method of data analysis to clarify which methods are used for each hypothesis.

Hypothesis 1: Calculated T2 of the Forearm Muscles can be used to identify muscles more active in typing.

Two investigators graphically delineated each muscle of interest on an axial image by tracing an area of the muscle belly. Software on a UNIX system (X-vessel developed by Ronald A. Meyer at Michigan State University) applied the formula "T2= $\Delta TE / \ln (S1_1 / S1_2)$," to calculate T2 values where ΔTE is equal to the difference in TE between two images, $S1_1$ is equal to the TE in the first image, $S1_2$ is equal to the TE in the second image (Figure 3.7). Muscles contracting concentrically (not isometrically) have been demonstrated to show an increase in T2 relaxation time following the exercise exposure. On T2 weighted images, tissue with high unbound hydrogen or water content is brighter than tissue with high fat content. A mean T2 was established for each identified muscle by averaging the Calculated T2s taken along its full length. The values were analyzed for values at Baseline, After typing, and Post Rest. An increase in Calculated T2

following typing was expected. This was consistent with other studies where an increase in Calculated T2 has been observed in exercising muscle. Statistical significance was determined using a Repeated Measures ANOVA (Figure 4.6)(See Chapter IV, pages 63-66).

Hypothesis 2: The median and ulnar nerves change shape within the wrist compartments with exposure to typing.

Interpretation of images of the wrist structures demanded high resolution. Fast spin echo and fast spin echo with fat saturation images were used (TR 2000/TE 16.0 and TR 2000/TE 80 ETL 8, field of view 10x10, matrix 512 x 256/ Nex 2) to provide adequate visualization of the small anatomical structures in the wrist. Voxel volume was decreased to improve resolution. The field of view (FOV) was 10 x 10, matrix size 512 x 256/NEX 2, and this resulted in a pixel size of .008 mm squared (10mm/512 pixels by 10mm/256 pixels), 1 mm slice thickness. Gradient echo (TR 700 TE 21.0 flip angle 40; FOV 10 x 10, matrix 512 x 256, 2 NEX) allowed very clear differentiation between nerves and vessels (See Chapter IV and Chapter V, Pages 65-66, 83-86).

The chosen imaging techniques provided adequate resolution for identification of most structures. Magnification was used for identification of the median nerve and the ulnar neural vascular bundle at the wrist. Tethering of the nerve, nerve entrapment or invasion of a nerve by fibroblasts and connective tissue proximal to the transverse carpal ligament has been described in surgical and MRI literature [71, 73, 85]. Where evidence of entrapment was noted in this study, identification of the nerve fascicles separate from connective tissue structures was difficult, as was visualization of clear neural borders. In many of the images of the median and/or ulnar nerves of the symptomatic subjects,

evidence of some impingement on the median and/or ulnar nerves was apparent, making surface to area and T2 signal intensity calculations difficult.

The radiologists categorized the median and ulnar nerves as oval, flat or triangular in images taken at Baseline (the first image of the day), After typing (following the 3 hour typing session), and Post rest (at the end of the day, following the 8 hour rest period). These data were analyzed using Rank Sum, which is an analysis of the number of images placed in each category. Images taken at each state of exposure, Baseline, After typing and Post rest, were then compared using a Repeated Measure ANOVA to determine statistical significance of the shape changes. Surface to area (S/A) ratios were measured by delineating the outline of the median and ulnar nerves in images proximal to the transverse carpal ligament, at the pisiform, hook of the hamate, and at the base of the metacarpals. The investigator graphically delineated the outline of the nerves; then surface to area ratios were calculated internally by X-vessel software designed by Ronald A. Meyer, Ph.D. from Michigan State University on a computer using the UNIX operating system. This served as an objective verification of the subjective shape changes determined by the investigators. The ratios were analyzed using a repeated measures ANOVA.

The investigators delineated the areas of the nerves at each level by tracing the nerves with the computer mouse using the GE Advantage Windows workstation (AWS) or the X-vessel program. The area was then calculated by the AWS or X-vessel and recorded into an Excel file. Results were graphed and analyzed using Repeated Measures ANOVA to determine statistical significance. T2 signal intensity of the median nerve was determined by the method described for muscle calculated T2 (above) on the UNIX

system. Results were graphed with Excel and analyzed with correlation studies and repeated measures ANOVA. The graphs are labled "Baseline, After typing and Post rest," which corresponds to Hours of 0, 3 and 12. The "0" hour is equal to Baseline, "3" is following 3 hours of typing, and "12" is following one hour of imaging, and eight hours of rest.

Hypothesis 3: Changes in area, shape and T2 signal intensity of nerve and muscle will be different in asymptomatic vs. symptomatic subjects.

Both asymptomatic and symptomatic subjects were exposed to the same examinations, exercise and rest protocols. After data collection was complete, investigators (blinded to exercise status and diagnosis) quantified shape, area, T2 signal intensity, fluid content of the compartments and joints of interest. All of these measurements were recorded on identical work sheets and analyzed using repeated measures ANOVA's. Comparisons between and within groups were completed using Pearson Correlation with significance determined in 2-tailed tests. Trends were identified and graphed using Excel.

Human subjects

Physical and magnetic resonance imaging examination techniques used in this study are all standard clinical examinations. They expose the subject to minimal risk if all precautions are followed. The University Committee on Research Involving Human Subjects (UCRIHS) at Michigan State University approved all methods of examination and recruitment of subjects prior to data collection. All subjects signed informed consent forms approved by UCRIHS prior to participation in the program.

CHAPTER IV

MAGNETIC RESONANCE IMAGING ASSESSMENT OF COMPARTMENT CHANGES IN FOREARM AND WRIST FOLLOWING EXPOSURE TO TYPING

Gail Shafer-Crane OTR, CHT, Ronald Meyer, PhD, Marcy Schlinger, DO, D. Lee Bennett, MD, Kevin Robinson, DO, James Rechtien, PhD, DO

ABSTRACT

Dimensional, positional and fluid content changes of soft tissues of the forearm and wrist as a response to typing were analyzed in this study using magnetic resonance imaging. Axial images were taken at the mid-forearm, proximal to the transverse carpal ligament, at the longitudinal level of the pisiform, hamate, and base of the metacarpals levels. The intent was to contrast muscles more and less active through magnetic resonance imaging (MRI) examinations, and note changes in morphology of the median nerve at the wrist related to exposure to typing. Asymptomatic female professional typists (n=6) underwent three MRI examinations of the dominant forearm and wrist at baseline, after three hours of typing, and after eight hours of rest. Three investigators blinded to the subjects' exercise status analyzed forearm muscle and wrist compartment images with respect to T2 signal intensity and nerve morphology. Compartmental constituent fluid and shape changes were correlated with typing. Forearm flexors were more active in typing than extensors and thumb muscles (P=.0016). Progressive variations in T2 as well as size and shape of the median nerve highly correlated to typing. MRI analysis following exercise (typing) in this study revealed significant changes in both muscles and nerves, suggesting a relationship between exposure to typing and these findings.

INTRODUCTION

Computer data entry, hence typing, has been linked with repetitive stress injuries (RSI) of the upper extremity [9, 13]. The mechanism of this relationship is poorly understood. RSI is an all-encompassing term that includes disorders of nerves, muscles, tendons, and their surrounding connective tissue. It is not a diagnosis, but a variety of syndromes that have a proposed commonality of etiology. In the current study, investigators studied muscles and nerves as they changed with exposure to typing. Soft tissue compartmental constituents, synovium, tendons and their sheathes, joint spaces, and the muscles activated in typing were assessed for fluid content, shape changes, and other visible and quantifiable changes.

One cardinal symptom of some repetitive stress injuries is the patient's report of delayed or nocturnal onset of pain and paresthesias [50, 55]. These complaints are common in both median and ulnar neuropathy. Delayed onset muscle soreness (DOMS) has been documented as a common symptom in tendinopathy, tendinitis, and epicondylitis [79]. The patient may continue to participate in the injurious activity because of delayed onset of symptoms [62, 64].

The current investigation of the phenomenon of delayed onset of symptoms used MRI to examine soft tissue changes in the forearm muscles and wrist compartments of asymptomatic subjects with an exposure to typing followed by prolonged rest. Fluid content as well as shape and positional changes of the median and ulnar nerves with exposure to prolonged vocational speed typing followed by prolonged rest were also analyzed.

Identification of muscles that become active in typing

Typing is an activity that is becoming more and more common in everyday life. It is also closely linked with repetitive stress injuries [65]. The muscles that are considered more active in typing are assumed to be the finger and thumb flexors, flexor digitorum superficialis (FDS), flexor digitorum profundus (FDP), and flexor pollicis longus (FPL). Muscles considered to be supportive, or participating with an isometric contraction, and therefore less likely to have a short term increase in T2 relaxation time during typing, were the finger extensors, extensor digitorum (ED), and wrist stabilizers, flexor carpi radialis (FCR), flexor carpi ulnaris (FCU), extensor carpi radialis longus and brevis (ECRL, ECRB) and extensor carpi ulnaris (ECU). (T2 is the time in milliseconds between the radio frequency pulse and the decay of longitudinal magnetization. This allows calculation of unbound water content in the tissue.) These assumptions were challenged when these muscles were analyzed using MRI.

Studies have been published that use magnetic resonance imaging to identify the individual muscles of the forearm involved in pure exercise [20, 23]. Protocols to distinguish active from inactive muscles are well established [19-21, 23, 42, 68]. However, these prior studies use pure exercise, e.g.: squeezing a dynamometer repeatedly, whereas the current study uses a functional activity, typing, as its exercise exposure.

Changes in median and ulnar nerve shape in response to typing

In this study MRI examination was used to determine sequential changes in shape of the median nerve in volunteers who typed at a vocational rate of approximately 50 words per minute. Many investigators have shown shape and positional changes during postural changes at the wrist [71, 86]. The current study documented subtle shape changes with the imaging position held constant. It is now fairly well accepted that changes in shape are the nerve's normal protective response to changes in intracompartmental forces [30].

Studies related to typing have concentrated upon the effect of intracarpal tunnel pressures on the median nerve [43, 44, 72, 86]. Cadaveric and in vivo studies have demonstrated statistically significant intracarpal tunnel pressure increases related to typing and application of fingertip pressure [43, 44, 71, 72, 86]. It is postulated in the current study that these pressure changes will cause changes in the shape of the median nerve that will be observed with MRI examination.

Observation of the ulnar nerve will be included in this study to assess its value as a control. The ulnar nerve is considered by clinicians to be minimally affected by changes in pressure within the carpal tunnel, and is used as a control for sensory nerve conduction studies of the median nerve at the wrist.

The literature also describes changes in shape of the median nerve as it traverses the wrist beneath the transverse carpal ligament (TCL) [5, 8, 16, 28, 36, 47, 49, 55, 56]. The most significant findings seemed to describe the effect of neural tethering [49] and TCL pressure increases which impact the median nerve proximal to the TCL. Unless

otherwise stated, the results discussed here will refer to changes in images proximal to the TCL.

OBJECTIVES

Identification of Muscles Dominant in Typing

Identification of muscles more active in typing through documentation of short term increased T2 relaxation time as an exercise response was undertaken in this study. Compression neuropathies of the forearm are currently highly prevalent, and appear to have a direct relationship to the impact of muscle activity. The median and ulnar nerves are encased in the long wrist and finger flexor muscles of the forearm, and the radial nerve courses through the extensor muscle compartment. The tendons of the finger flexors surround the median nerve within the carpal tunnel. It is this very close physical proximity that suggests a relationship between muscle activity and an effect on the median nerve. It may be valuable to identify muscles active in typing that may be in close proximity to the median nerve.

Quantification of volume and T2 relaxation time changes of wrist and forearm compartmental constituents with exposure to typing

One cardinal sign of carpal tunnel syndrome or ulnar neuropathy is delayed onset of pain and/or paresthesias in the fingers supplied with sensation by the median or ulnar nerve. Many investigators have described these symptoms as the result of a cycle of ischemia and reperfusion of the nerves dependent upon compartmental pressure increases from position or exercise [44, 63, 71, 72, 86]. The design of this study allowed

investigators to observe the constituents of compartments of the elbow, forearm and wrist at three stages of activity; Baseline (prior to activity), After typing (following 3 hours of typing at 50 words per minute) and Post rest (following 8 hours of rest).

Materials and Methods

Population

Asymptomatic female professional typist volunteers (n=6), ages 21 – 52, mean age 38 were recruited. One subject volunteered to act as both a typing subject and a non-typing control. Volunteers were interviewed by telephone prior to participation to determine medical and work history. Individuals were excluded if they had a positive medical history for any injury to the dominant upper extremity, any metabolic disorder including diabetes, or were currently pregnant or nursing. All volunteers were required to be conditioned typists. This was defined to be individuals who routinely typed continuously for a minimum of four hours. Each volunteer signed the informed consent documents approved by the University Committee on Research Involving Human Subjects of Michigan State University. The right arm was identified as the dominant upper extremity in all subjects.

Study Protocol

On the day of the examinations, each subject reported for testing early in the morning, after being instructed to limit activity prior to the examination. Physical characteristics of the right arm of each subject were noted through the process of physical examination and 3 MRI examinations, which were performed: prior to typing (Baseline),

after three hours of vocational speed typing (After Typing), and following eight hours of rest (Post Rest). Initially, a physical examination was performed on the right arm of each subject, which included sensory nerve conduction studies, proprioception testing, strength and range of motion screening tests, and provocative tests (Phalen's and Tinel's tests). The physical examination was not used to eliminate any subjects from this study, but was used to provide comparative information regarding their performance on the physical examination and the MRI examinations. The physical examinations and sensory nerve conduction studies were all within normal limits for all subjects in this study. All subjects indicated they were without pain or paresthesias at each of the three examinations conducted during this study.

Typing protocol

Uniform, ergonomic workstations were provided for the typing/exercise exposure. Subjects were allowed to bring their own typing or use non-standardized typing material provided by the investigators. Each subject was provided with an adjustable chair with elbow rests, "natural" style keyboard, wrist rest and copy stand. Each workstation was adjusted for position and comfort for each subject. The subjects were then directed to type at a vocational rate (50 words per minute) for three hours, with one 15-minute break half way through the typing time. Subjects used the same word processing software to type un-standardized material. Keystrokes were counted through the word count feature.

MRI examinations were repeated immediately following the three-hour typing time period, "After Typing". Because exercise induced muscle T2 changes resolve within 30 – 60 minutes, the After Typing images were initiated within ten minutes of the

cessation of typing. The final MRI examination was completed after the subjects had completed 8 hours of rest, "Post Rest." The last three hours of rest were observed. All subjects watched television during the observed rest period in an attempt to decrease the subjects' metabolic rate and elicit delayed onset symptoms, which may have been brought on during sleep.

Magnetic Resonance Imaging Protocol

Precise duplication of the MRI imaging positions was required for comparison of changes in shape and size of the structures under study. Prior to the first images of the day being taken, surface landmarks of the carpal tunnel, forearm extensor muscle bulk and lateral epicondyle were marked on the skin with an indelible marker to facilitate consistent repositioning of the subject within the MRI equipment. The right forearm of each subject was positioned in a small extremity coil; then the subject was placed in the General Electric Signa 1.5 Tesla magnet with the arm extended overhead in the "swimmer's position" for the forearm muscle images taken every centimeter (dual echo axial T2 weighted spin echo images with different TE's: T2 TR 1500, TE 30 and 60, NEX 1); imaging duration 21 minutes.

The subject was then repositioned for imaging of the wrist. The right wrist of each subject was positioned in a resting hand splint made to fit in the wrist coil (Figure 4.1) in an unstressed position (wrist at 25 degrees of extension and fingers in full extension). Images of the wrist and forearm compartments were collected after moving the subject to side lying with the volar forearm opposite the subject's face. T2 weighted fast spin echo (TR 2000/TE 15&80, NEX 2, echo train length 8), fast spin echo with fat saturation (TR

2000/TE 21, NEX 2, echo train length 8) and gradient echo (TR700/TE 21, NEX 2) imaging methods were used to image the wrist compartments. Slices were one millimeter thick. The full imaging session required approximately 45-60 minutes.

Method of Analysis

Analysis of Muscle

Two investigators, blinded to the subjects' identity and exercise status, graphically delineated a portion of the muscle bellies of the flexor pollicis longus (FPL), abductor pollicis longus (APL), extensor pollicis longus (EPL), extensor digitorum (ED), flexor digitorum profundus (FDP), flexor digitorum superficialis (FDS), flexor carpi radialis (FCR), flexor carpi ulnaris (FCU), extensor carpi ulnaris (ECU), and extensor carpi radialis longus (ECRL) in imaging slices throughout the length of the forearm (Figure 4.2). T2 relaxation time for each muscle, which depends in part on intracellular fluid content of the muscles, was quantified. An average "Calculated T2" in milliseconds was determined for each muscle in each subject. The calculated T2s, reported in Results, represent the average of the calculated T2s from each image throughout the length of each muscle.

The average calculated T2 values for all muscles listed in this study were calculated from the images taken at three different times of the day. These times were: Early morning (Baseline), mid-day, (After Typing) and evening, (Post Rest). Subjects were instructed to avoid typing activities prior to the Baseline images, and between the After typing and Post rest images. A control subject participated in all examinations, but was instructed to remain inactive during the typing exposure. The results of the control

subject will be reported as "After Typing" to coincide with the typing subjects examinations.

Two investigators blinded to the subjects' identities and exercise status used a UNIX computer system to delineate images of each muscle under study (Figure 4.2). Two simultaneous fast spin echo T2 weighted images with 2 TE's (echo time which represents the interval between the radio frequency pulse and the maximum induced signal) were used to calculate T2 in the muscles (TR 1500, TE 30 and 80 NEX 1). Software on a UNIX system (x-vessel developed by Ronald A. Meyer at Michigan State University) used the formula "$T2= \underline{\Delta TE} / \ln (S1_1 / S1_2)$," to calculate T2 values where ΔTE is equal to the difference in TE between two images, $S1_1$ is equal to the TE in the first image, $S1_2$ is equal to the TE in the second image. Statistical significance of the data was analyzed using repeated measures ANOVA.

Analysis of T2 Relaxation time of the Median and Ulnar Nerves

Changes in T2 relaxation times of the median and ulnar nerves at the wrist were determined using the same formula as for muscle T2. However, images of the nerves were delineated at four imaging levels at the wrist: 1. Proximal to the transverse carpal ligament, 2. Pisiform, 3.Hook of the hamate, 4.Base of the Metacarpals. As the effect of intracarpal tunnel pressure may vary at each of these anatomical segments, it was considered appropriate to measure the T2 of the median and ulnar nerves at each imaging level as they progressed through the compartments instead of using an average T2 over the length of each nerve at the wrist.

Compartmental Analysis

Three radiologists blinded to the subjects' identity and exercise status, analyzed images selected at each of the four imaging levels listed above. They evaluated forearm and wrist compartment constituents for changes in fluid content, shape, and size. Investigators used the criteria defined by Mesgarzdeh, et. al. for categorization of the shape of the median and ulnar nerves as well as definition of bowing of the transverse carpal ligament [54-56]. Each nerve was categorized as flat (ratio of the major over the minor axis >3:1), oval (ratio approximately 1:1) or triangular (a visible point was noted). Bowing of the transverse carpal ligament was measured using the GE Advantage Windows workstation to first measure the length of a straight line between the points of medial and lateral attachments of the transverse carpal ligament (TCL), then measure the distance of a second line drawn perpendicular to the first at the widest point between the line and the inside, or deep edge, of the TCL. Bowing of the TCL was considered present if less than ½ of the TCL was straight [55].

Shape and size of the median and ulnar nerves were further quantified through the use of surface to area ratios, where the investigator graphically delineated the nerve and used the x-vessel software to compute the surface to area ratio. T2 of the median and ulnar nerves was also quantified on the axial images of the wrist (Figures 4.3, 4.4). These images were selected for analysis to correspond to bony landmarks along the length of the wrist. Images corresponded with an axial image proximal to the transverse carpal ligament, at the pisiform, at the hook of the hamate and at the base of the metacarpals.

RESULTS

Two methods of analysis were used in this study, one to contrast active from inactive muscle using T2 Relaxation times, and the other was used to compare and contrast the fluid content of the median and ulnar nerves (T2) at Baseline, After Typing, and Post Rest. One control subject, who did not type but otherwise participated in all examinations, was used to illustrate the effects of typing on the muscles and nerves of typing subjects. The results of the muscle analysis will be presented first, followed by the results of the nerve analysis.

Muscles Identified as Being Active in Typing

Muscles active in typing were found in the flexor/pronator group, including wrist flexors ($p=0.0016$). In typing subjects the flexor digitorum superficialis (FDS), flexor digitorum profundus (FDP), flexor carpi ulnaris (FCU), and flexor carpi radialis (FCR) T2 relaxation times increased between Baseline and After Typing, and decreased between After Typing and Post Rest. The T2 relaxation times of the extensor digitorum (ED), extensor pollicis longus (EPL), and abductor pollicis longus (APL) remained the same throughout the exposure to typing, then either increased with rest, or decreased to Baseline levels or below (Figure 4.5).

The T2 values of the finger and wrist flexor muscles increased significantly with typing and decreased more significantly after rest. The greatest difference between active and inactive muscles was the T2 value decrease between After Typing and Post Rest (Figure 4.6). Statistical significance was determined with a repeated measures ANOVA.

Response of muscle in the control subject

In the control subject's flexor muscle (FDP, FDS, FCU, and FCR) After Typing values, which in the case of the control would represent a three-hour interval without typing, decreased from Baseline, then remained level (Figure 4.7). In the muscles that were not active in typing (ED, EPL, and APL), the control value followed a similar pattern to the muscles of the subjects active in typing. The T2 of the muscles varied slightly, and seemed to randomly increase or decrease with the passage of time (Figure 4.8). Typing subject's ECU, ECR, ED, APL, and EPL seemed to randomly increase or decrease between Baseline and After Typing, between After Typing and Post Rest, and between Baseline and After Rest.

Differences Between Active and Inactive Muscles

If we graphically contrast the extensor digitorum and flexor digitorum profundus, a muscle very active in typing, the pattern of T2 increase is apparent (Figure 4.9, 4.10). The changes in T2 relaxation time of the FDP muscles are consistent, as opposed to the T2 relaxation times of ED muscles which remain essentially constant.

The identification of active muscles was based on the statistically significant T2 relaxation time changes between Baseline and After Typing, between After Typing and Post Rest, and a comparison between the non-typing control and typing subjects. It was also noted that T2 relaxation times were often lower Post Rest compared to Baseline in the majority of muscles found to be active in typing.

Shape and T2 Relaxation time Responses in the Control Subject's Median and Ulnar Nerves

Changes in shape of the median and ulnar nerves were subtle; however, they were more evident in the visible categorizations (Flat, Oval or Triangular) made by the radiologists (p=0.053) than in the surface to area ratios. Surface to area ratios (s/a) are calculated by delineating the circumference (surface) then dividing this into the area. If a shape changes, the s/a is expected to change as well. If the shape of the nerve were round, a change in shape would correspond to a change in area, therefore there would be a change in the surface to area ratio (s/a). Because the shape of the median and ulnar nerves is elliptical, that shape may vary subtly without a corresponding s/a ratio change [48].

The changes between Baseline, After typing and Post Rest in the control subject's T2 relaxation time values of the median and ulnar nerves were minimal. There was a small increase in the median nerve, and a small decrease in the ulnar nerve on the "After Typing" examination, compared to Baseline, on the axial images proximal to the TCL (Figure 4.11).

Comparison Between Typing subjects and control

Changes in shape of the median nerve, between Baseline and After typing and Post Rest, of typing subjects were compared with those of the non-typing control using the surface to area ratios (Figure 4.12). The changes were subtle, and lacked statistical significance. Statistical significance was noted, however, in the radiologists' assessment

of shapes at Baseline, After Typing and Post Rest (Figure 4.13) at the imaging level. This apparent discrepancy is addressed in the Discussion.

T2 changes in both the median and ulnar nerves between Baseline, After Typing and Post Rest where more apparent when compared to control (Figure 4.14). These changes, while not statistically significant, were highly correlated with typing using Pearson's correlation table (Figure 4.15). The range of T2 changes were wider in images of the median nerves than in images of the ulnar nerve. When contrasted with the T2s of the control subject, the T2s of the ulnar nerves of the typing subjects were, for the most part, equivalent to the control T2s of both the median and ulnar nerves (Figure 4.16).

DISCUSSION

This study was used to identify active muscles, and quantify some changes in the median and ulnar nerves at the wrist, using a vocational activity considered to be high risk for causing repetitive stress injuries. Use of the vocational activity of typing as the exercise exposure introduces the potential for application of this protocol to study the effects of other high-risk vocational activities. Methods well established in science to study the effects of exercise on both muscles and nerves have been used in this clinical application.

Delayed onset muscle soreness and delayed or nocturnal onset of paresthesias is a cardinal symptom of repetitive stress injury. While this study analyzes the effects of typing on an asymptomatic cohort, the information gathered following prolonged rest provides information on the normal response to activity following a significant recovery period.

Muscles Identified as Being Active in Typing

Techniques that have been well established to identify muscles more active than others in exercise were shown to be effective in this study. Muscles identified as being active in typing in this study were limited to the flexor/pronator compartment of the forearm. Included were the two wrist flexors, flexor carpi ulnaris and flexor carpi radialis. It was expected that these muscles, because they are thought to be acting to stabilize the wrist, would not show significant T2 changes during typing. The antagonists, the extensor carpi radialis longus and brevis as well as the extensor carpi ulnaris, were not shortening during typing, which would have caused an increase in T2. No long wrist or finger extensors, long thumb flexors or long thumb extensors were identified as being as active in typing as the muscles in the flexor group. It was expected that flexor pollicis longus would have shown a significant T2 increase with typing, because this is the muscle thought to be active in pressing the space bar. The results suggests that the FCR, a wrist flexor, may be more involved in depressing keys requiring the thumb, than previously thought.

Impact of Forearm Flexor Muscle Contraction on the Median and Ulnar Nerves

The median and ulnar nerves innervate the flexor/pronator group of muscles. The flexor muscles encase neurovascular bundles that provide the conduits for the median and ulnar nerves as they travel through the forearm. The forearm flexor muscle Random Calculated T2 values increased significantly following exposure to vocational speed typing (50wpm) for three hours. The tendons and bellies of these muscles are closely

associated with the median nerve within the carpal tunnel, and may be associated with the increases in mechanical pressures within the carpal tunnel during typing noted in earlier studies [43, 86].

Changes in Nerve Morphology Related to Typing

A relationship between delayed onset symptoms of paresthesias and pain related to repetitive stress injuries and ischemia/reperfusion of the median nerve has been supported in recent studies [63, 78, 86]. It may be surmised that intracarpal tunnel pressure variation that is sufficient to cause alterations in the shape of the median nerve, which are related to muscle activity, may also be sufficient to impair perfusion of the perineural circulation, which in the region of the wrist is dependent on longitudinal branches from various arteries in the vicinity. Investigators in previous studies using MRI have demonstrated changes in shape of the median nerve related to changes in position of the wrist during imaging, and surmise that this change in shape is a result of changes in intracarpal tunnel pressure [44, 71, 86].

Shape Comparisons Between Baseline, After Typing and Post Rest in Typing Subjects and the Control

In the current study, the shape of the median nerve in subjects exposed to typing was seen to respond to activity levels when the imaging position was held constant. Subtle changes in the shape of the median nerve are visible in each stage of activity and rest. The ulnar nerve was not noted to change shape significantly in the same images. The shapes of the median and ulnar nerves of the non-typing control subject were found to

remain fairly constant. The axial magnetic resonance images were made prior to activity (Baseline), following three hours of vocational speed typing (After typing), then after sufficient rest to approximate sleep (Post Rest).

Changes in Median Nerve T2 Apparently Related to Intracarpal Tunnel Pressure

The most common RSI is carpal tunnel syndrome, or median nerve compression at the wrist. For that reason, this study emphasized analysis of the median nerve, and the carpal tunnel. Organization of the axons of the median nerve is similar to other peripheral nerves, in that the sensory fibers (C6-C7 origin) are generally located more externally, and the motor axons (C8-T1 origin) are more central [51]. Carpal tunnel syndrome is often diagnosed through a medical history positive for nocturnal or delayed onset of paresthesias. Delayed onset paresthesias seem to be caused by transient impairment of the intraneural circulation that resolves within hours after normalization of intra-compartmental pressure [17, 46].

In this study, typing appears to impact the fluid content of the median nerve of asymptomatic subjects. When compared to the asymptomatic control subject more significant changes in T2 relaxation times of the median nerve were noted in the asymptomatic typing subjects. The ulnar nerve was also affected less than the median in all but one subject (Figure 4.16).

The Use of a Specific, High Risk Vocational Task, Typing, for This Study

There are longitudinal studies where MRI has been used to document changes in forearm and wrist compartments of subjects who have been diagnosed with compressive

disorders of the forearm peripheral nerves, or were exposed to repetitive vocational tasks [67]. In those studies, increased pressure sufficient to impair perineural circulation was noted in studies using pure exercise, e.g. repetitive grasping, lifting against resistance [46]. Others have shown the effects of typing on increasing intracarpal tunnel pressure, but did not use MRI, or record the recovery of the nerve following rest the same day as was done in this study [71, 72, 86].

Exposure to typing is thought to have a cumulative effect. An increased knowledge of the dimensional and extracellular fluid content changes of soft tissues as a response to repetitive activity followed by rest as assessed in this study, may provide insight regarding the onset and progression of forearm peripheral nerve compression injuries.

CONCLUSION

In summary, this study has shown the feasibility of using T2 relaxation time analysis to document muscles active in vocational activities. The identification of muscles that are more active than their antagonists may be helpful in design, and determination of efficacy, of ergonomic equipment and treatment techniques. Of particular interest is the discovery that wrist flexors are more active in typing than thumb muscles.

Furthermore, this study has shown a correlation between typing and changes in the T2 of muscle and the median and ulnar nerves. The ulnar nerve, minimally affected by these changes, is supported as an effective control for the median nerve in electrodiagnostic studies.

Future studies will assess muscle and nerve T2 relaxation time changes, and shape changes of the median and ulnar nerves with typing in symptomatic subjects. It will also be of interest to image subjects exposed to other vocational activities that are defined as high risk for carpal tunnel syndrome or other repetitive stress injuries.

CHAPTER V

Quantification of Shape and T2 Relaxation Time in the Median and Ulnar Nerves of Asymptomatic vs. Symptomatic Female Volunteers Exposed to Vocational Speed typing and Prolonged Rest

Gail Shafer-Crane, Ronald Meyer, Marcy Schlinger, Kevin Robinson, Joseph Pernicone

ABSTRACT

Introduction: A cardinal symptom of repetitive stress injuries (RSI) is nocturnal or delayed onset muscle soreness and/or paresthesias. This may occur when perineural capillaries of the median and ulnar nerves at the wrist are collapsed by increased pressure in the compartments of the wrist, followed by reperfusion of the nerves when the pressure resolves. Using magnetic resonance imaging, the length of T2 relaxation time has been related to perineural circulation. Changes in shape of the median nerve have been linked with an RSI. These shape changes may be related to changes in intracompartmental pressure.

Objectives: The objectives of the study were to use MRI to: (1) observe the median and ulnar nerves, at rest, after typing and after prolonged rest as they traverse the wrist; (2) demonstrate changes related to typing and prolonged rest in median and ulnar nerve morphology at the wrist; (3) compare and contrast observations of the median and ulnar nerves at the wrist between symptomatic and asymptomatic subjects.

Methods: Thirteen professional, female typists between the ages of 21 and 52, mean age 44, were placed in symptomatic or asymptomatic categories by medical history. Each subject was examined with MRI at Baseline, following three hours of vocational speed typing (average 50 words per minute) and following prolonged rest. Images were

examined for changes in shape and T2 relaxation time by four investigators blinded to the exercise status and identity of the subjects.

Results/Discussion: The investigators delineated the circumference of the median and ulnar nerves, and then calculated the surface to area ratios. A visual categorization of the shape of the median on images defined it as flat, oval, or triangular. The images taken following typing were found to have significant changes related to typing in the normal cohort ($p=0.053$) but not the symptomatic group ($p=0.69$). Changes in size followed the same pattern. The changes in the asymptomatic cohort were significant ($p=0.03$), but not in the symptomatic cohort (0.87). T2 changes for the median nerve of symptomatic subjects tended to decrease below baseline then recover, while T2 relaxation times of asymptomatic subjects tended to increase then return to baseline values.

Conclusions: The median and ulnar nerves respond to typing and prolonged rest with dynamic changes as a normal response to activity. The nerves of symptomatic subjects were less likely to respond to activity by changes in shape or size. T2 relaxation times of both asymptomatic and symptomatic subjects were correlated to typing.

INTRODUCTION

Repetitive stress injury (RSI) is a broad term for a category of disorders that are related to prolonged, repetitive activity. It is theorized that repetitious activities may cause microtrauma that accumulates in soft tissue causing stereotypical symptoms. There are at least 3 types of RSI: 1. Neuropathy; 2. Inflammation of muscle or tendon; 3. Synovitis or inflammation of the synovial membranes of the tendon sheath, joint capsule or bursa. In this study, the RSI of primary interest is peripheral neuropathy of the median nerve at the wrist. The neuropathies are generally thought to have one of two origins; either mechanical compression of the nerve within a compartment or circulatory changes to the nerves [44, 47, 78, 84].

Investigators in this study explored short-term effects of typing in asymptomatic and symptomatic subjects in a single day. It focused on ischemia and reperfusion of the median and ulnar nerves as evidenced by T2 relaxation time in the median and ulnar nerves at the wrist. Changes in the shape of the nerves were documented as related to typing in both the asymptomatic and symptomatic cohort.

Median and Ulnar Nerve Pathologies

Pathologies of the median and ulnar nerves at the wrist are described below. Two such pathologies are carpal tunnel syndrome and Guyon's canal syndrome. The pathology of highest significance is carpal tunnel syndrome, or median nerve compression at the wrist, beneath the transverse carpal ligament. The inclusion of the term "syndrome" in their descriptions indicates that these are not true diagnostic terms, but a description of a collection of symptoms.

Median neuropathy/carpal tunnel syndrome

Median neuropathy at the wrist is synonymous with carpal tunnel syndrome (CTS). Compression of the median nerve at the wrist may be caused by mechanical compression or impingement of the perineural circulation.

The carpal tunnel is a bony trough bridged by the non-extensible transverse carpal ligament (TCL). Flexor tendons of the fingers and thumb as well as the median nerve pass through this tunnel. The TCL also acts as the pulley mechanism for the flexor tendons [10, 43, 71, 72]. The median nerve is typically located just deep to the TCL, between the tendons of the flexor pollicis longus and flexor digitorum superficialis. In this location, it is vulnerable to point contact pressure during wrist flexion from the pulley action of the flexor tendons [44]. The median nerve is further vulnerable to compression from fractures or dislocations of the carpal bones, edema or excess fluid in the tendon sheaths, and invasion of the carpal tunnel by anomalous muscle development [55, 56].

CTS is often identified through complaints of pain or paresthesia in the area of sensory supply by the median nerve, which includes the palmar aspect of the thumb, index and middle fingers, as well as the lateral half of the ring finger. The pathway for this symptomatology is not well understood. It is theorized that compartmental compression sufficient to collapse perineural capillaries may cause transient neural ischemia [63, 86]. The collapse of these capillaries interrupts oxygenation of the nerve fibers (transient neural ischemia), causing a reversible physiological block of neural

transmission [46, 66]. When the compression is resolved, gradual return of sensory nerve function is marked by paresthesias.

Sensory nerve conduction studies are used to further diagnose CTS. The ulnar nerve of the same hand is used as a control when assessing for a sensory nerve conduction velocity slowing in the median nerve [14]. A number of studies show slowing of nerve conduction can occur when the circulation of the nerve is impaired by compression, then recovers quickly following resolution of the compression [17].

The median nerve is a mixed nerve, providing both sensory and motor nerve supply to the hand. Sensory fascicles tend to be located directly beneath the contact point of the TCL during wrist flexion, and are therefore thought to be more susceptible to damage from increased intracarpal tunnel pressure [51]. It follows that sensory changes of pain and paresthesia are the first noted symptoms identified in CTS. Atrophy of the thumb flexor muscles is a finding in advanced or chronic CTS. As the motor fascicle is more often located toward the radial side from the center of the nerve, where it is less vulnerable to contact pressure from the TCL [51].

Ulnar Neuropathy/Guyon's Canal Syndrome

Ulnar neuropathy at the wrist is much less prevalent than carpal tunnel syndrome. The ulnar nerve at the wrist passes superficial to the TCL with the ulnar artery, just deep to the pisohamate (volar-carpal) ligament [60]. Increases in pressure in this compartment are linked to ulnar neuropathy at Guyon's canal. In some cases, surgical release of the TCL has had a secondary benefit of reduction of intracompartmental pressure of Guyon's canal as well as reduction of pressure within the carpal tunnel [1]. The ulnar nerve is

commonly entrapped at the entrance of Guyon's canal in this syndrome [87]. Clinical signs include numbness or hypesthesia, pain or paresthesias on the ulnar side of the hand and in the ring and small fingers. Weakness of abduction of the fingers caused by weakness of the interosseous muscles is another symptom [60].

Perineural circulation

Peripheral nerves are organized in fascicles surrounded by connective tissue. This tissue encompasses a longitudinal capillary system that supplies the nerve axons. Many of the nerve fascicles are imbedded in myelin sheaths. In part, these sheaths are made up of Schwann cells. Spaces between the cells produce the Nodes of Ranvier. These nodes are responsible for speeding the conduction of action potentials, and their efficacy is dependent on spatial relationships between nodes. It has been theorized that there is sufficient pressure within the compartments of the wrist to impact the conduction of the action potential by displacing the Nodes of Ranvier. This seems unlikely in CTS. In animal models, damage to the myelin sufficient to displace the Nodes of Ranvier required 1000 mm Hg [17, 46]. Typing was shown to increase carpal tunnel pressure to approximately 45 mm Hg, sufficient to impact perineural circulation but not displace myelin [72].

In addition to the myelin sheath, layers of connective tissue separate the neural bundles. The epineurium (the outer layer of the nerve), perineurium (the layer that surrounds each fascicle), and the endoneurium (the layer that surrounds each axon), are interlaced with a network of longitudinal and interconnecting capillaries throughout the length of the nerve [27, 84]. These in turn are supplied by arteries that maintain close

proximity to the nerve as it traverses the compartments of the arm, forearm and wrist. In the case of the ulnar nerve, the nourishing artery is the ulnar artery in the forearm and wrist. In the case of the median nerve, which has no accompanying artery in the forearm or wrist, it depends on small branches from several arteries including the ulnar, radial and anterior interosseous arteries which may not be in very close proximity to the nerve. It is this capillary plexus of the median or ulnar nerves that is susceptible to either congestion or ischemia caused by increased intracompartmental pressure [84, 86]. It is further noted that surgical release of the median nerve has been shown to reverse ischemia measured by Doppler flowmetry [78].

It has been demonstrated in several studies that changes in position of the wrist and such activities as typing cause sufficient increases in intracarpal tunnel pressure to collapse the perineural capillaries of the median nerve within the carpal tunnel [43, 44, 63, 86]. Intermittent collapse of these capillaries may be sufficient to reduce or block axonal transport, but if of short duration will not cause axonal atrophy [11, 14, 46, 63].

DIAGNOSTIC TESTS

Physical examination of a patient suspected of having a repetitive stress injury may include imaging, strength testing, electrodiagnostic studies, and neurological testing to assess pathology in the physical structures and function of the nerves. Emphasis has been placed on provocative testing (see below) because of the ease of use in physical examination, the volume of clinical information involving provocative testing, and the reliance upon this method by clinicians for decades [52, 55].

Provocative testing

Provocative testing is targeted reproduction of paresthesias or pain in the distribution of the nerve tested by mechanical means. One method used to test the median nerve is Phalen's test, or sign. The backs of the hands are placed together in a "reverse prayer position" acutely flexing the wrists and holding that position for a minute or longer (Figure 5.1). The subject will complain of paresthesias within one minute of assuming this posture in a positive test. It is theorized that this is the result of increased intracarpal tunnel pressure, which collapses the perineural circulation of the median nerve [55, 83, 84]. Phalen's sign is often positive in individuals who do not have a median neuropathy, and therefore cannot be used independently to diagnose CTS.

Another test is Tinel's sign, which is the reproduction of parethesias when the examiner taps on the subject's skin along the course of the nerve being tested. A Tinel's sign is positive when the subject reports pain or paresthesias radiating out from the site of percussion on the surface along the course of a nerve. It is often related to regeneration of the nerve following degenerative changes, or irritation of the nerve [14, 46].

Provocative testing produces inconsistent results. Both Phalen's sign (Figure 5.1), and Tinel's Sign are associated with both false positives and false negatives [14].

Diagnosis Using Imaging

Magnetic Resonance Imaging (MRI) and ultrasonography studies have been used to enumerate characteristics consistent in patients with CTS. Bowing of the transverse carpal ligament, increased signal intensity of the median nerve, swelling of the median nerve proximal to the transverse carpal ligament, inflammation of the synovial sheaths

within the carpal tunnel, and flattening of the median nerve at the pisiform and hook of the hamate are often used to diagnose CTS [30, 47, 55].

T2 weighted spin echo and fast spin echo images have been used in other studies to quantify fluid changes in peripheral nerves. Gradient echo images provide excellent contrast between tissue types. T2 weighted images provide information on fluid content within the tissue. Tissue that has a higher fluid content will appear brighter than tissue with less fluid. T2 relaxation time is measured in milliseconds. Compression of a peripheral nerve has been shown to cause an increase in the T2 relaxation time of the nerve [32].

Tethering of a peripheral nerve is also one of the characteristics that can be disclosed by imaging. Connective tissue invades the perineurium, causing the nerve to be tethered to the surrounding compartmental structures. In CTS, the median nerve may be tethered proximal to the transverse carpal ligament [40, 47, 52].

OBJECTIVES

This study was undertaken to use a high risk, vocational activity (typing) to demonstrate changes in median and ulnar nerve morphology at the wrist in subjects. The characteristics selected for quantification were shape and fluid content of the nerves. Axial T2 weighted images of the right forearms were assessed for T2 relaxation time changes of the median and ulnar nerves with the expectation that the T2 relaxation time would increase with typing, and decrease with rest. In addition, it was expected that nerve shape would visibly change and the area would increase with the exposure to typing. T2 weighted and gradient echo images were used to analyze changes in shape and size. It

was further expected that there would be a quantifiable difference between symptomatic and asymptomatic subjects in both shape, size, and T2 relaxation time changes related to typing.

METHODS

Subjects

Subjects were female, professional typists aged 21 to 52, mean age 44 years, whose job required a minimum of four hours of continuous typing at a rate of 50 words per minute or higher. Each subject was placed in either the asymptomatic or symptomatic cohort following a telephone interview to determine medical history. No one was accepted as a subject who had a history of metabolic disorder, current pregnancy or injury to the dominant arm.

Six asymptomatic subjects and seven symptomatic subjects were recruited. Medical histories of two individuals in the symptomatic cohort were positive for a diagnosis of carpal tunnel syndrome. Four subjects in the symptomatic cohort had a positive medical history for a diagnosis of lateral epicondylitis and one was positive for tenosynovitis. One subject in the asymptomatic cohort, age 44, and one subject in the symptomatic cohort, age 51, volunteered to serve as both non-typing controls and typing subjects. These control subjects were tested on two days, once as a typing subject, once as a control. On each day they underwent the full physical examination and all MRI examinations. Each volunteer completed a medical history and "The Levine Scale of Carpal Tunnel Syndrome Severity" [50]. All were right handed.

All subjects signed consent forms approved by the Michigan State University Committee on Research Involving Human Subjects (UCRIHS).

Examination procedure

Each subject was given a physical examination that tested muscle strength, proprieoception, and reflexes of the right arm as well as sensory nerve conduction of the median and ulnar nerves at the wrist. Either a physiatrist or physiatry resident performed all physical examinations. Subjects were then examined with MRI at Baseline (before typing), following three hours of vocational speed typing, and following eight hours of rest, the last three hours observed. Subjects watched television for the three hours of observed rest to lower their metabolic rates in an effort to elicit delayed onset symptoms associated with sleep.

Magnetic Resonance Imaging Examinations

All MRI examinations were performed using a 1.5 Tesla General Electric Signa Magnetic Resonance Imager. Spin echo (TR1500,TE 36 and 60 NEX 1), fast spin echo (TR 2000, TE 15 and 80 NEX 2, echo train length 8), and fast spin echo with fat saturation (TR2000/ TE 21 NEX 2 echo train length 8), and gradient echo (TR 700, TE 21 NEX 2) images were obtained. Axial images of the forearm were used in all data collection. (Please refer to the MRI glossary of terms for an explanation of TR, TE, etc.)

Data Collection

Three radiologists and a third investigator blinded to the subjects and their exercise status analyzed the images (Figure 5.2). Visible categorization of the shape of the median nerve just proximal to the transverse carpal ligament, at the level of the pisiform and the hook of the hamate identified the nerves as either oval, flat or triangular.

The examiner delineated the area of interest in either a nerve or muscle, then using X-vessel software for the UNIX computer, developed by Ronald A. Meyer at Michigan State University, was able to calculate T2 relaxation time by averaging the T2 relaxation times between simultaneously collected T2 weighted images with different TE's. The X-vessel formula is: $T2=\Delta TE/\ln (SI_1/SI_2)$, where T2 refers to the calculated value of T2 relaxation time; ΔTE refers to the difference between the echo times in milliseconds; ln is the natural log; SI_1 is the T2 relaxation time in milliseconds in the first image; and SI_2 is the T2 relaxation time in milliseconds in the second image.

Surface to area ratios were performed to provide additional information regarding nerve shape change. An investigator graphically delineated the circumference of the nerves under study. The X-vessel software was used in conjunction with a UNIX operating system to calculate the surface to area ratios.

Methods of Analysis

Results were compared using Repeated Measures ANOVA. The results of each of the investigators were analyzed separately and results were then compared. If there were

disparate results each examiner was asked to review their data for accuracy and repeatability, which resolved most disparities.

RESULTS

Morphology of the median and ulnar nerves with exposure to typing at Baseline

The shape of the median nerve is different at each imaging level (Figure 5.3, 5.4). The median nerve is expected to be oval proximal to the transverse carpal ligament in the asymptomatic subject [54]. Our study demonstrates variability of the shape of the median nerve, but for the most part, the median nerve was oval at the TCL in asymptomatic subjects. Symptomatic subjects' median nerves were sometimes very flat, making them difficult to differentiate from the TCL, or rounded suggesting edema (Figure 5.5).

Statistically significant changes in the shape of the median nerve were noted when a comparison was made between Baseline and After Typing, and between After Typing and Post Rest images of the median nerves of asymptomatic subjects ($p=0.053$). Surface to area ratios of asymptomatic subjects did not show significant changes ($p=0.64$).

Images of the ulnar nerves of both symptomatic and asymptomatic subjects were nearly all oval. Surface to area ratios and the radiologists' categorizations were in agreement. No statistically significant shape changes were noted in the ulnar nerve with exposure to typing or following rest, or between symptomatic and asymptomatic subjects. The ulnar nerve remained, for the most part, elliptical in shape.

Median nerves of symptomatic subjects had anomalous morphology

Tethering of the median nerve proximal to the transverse carpal ligament was observed in two ways. The median nerve was seen to be edematous, surrounded by connective tissue, which appeared to be tethering the nerve proximal to the TCL (Figure 5.6). In the second type, the nerve is flattened against the TCL (Figure 5.7). The borders of the nerve can barely be discerned. While this nerve is visible with a border that can be delineated, obliteration of the median nerve by connective tissue proximal to the TCL associated with long-standing carpal tunnel syndrome has been described in other studies [47].

Shape of the Median Nerve as it Traverses the Wrist

The shape of the median nerve is subject to the pressures it encounters proximal to the TCL, and as it traverses the wrist. The imaging levels of this study provide views of the nerve at each of three levels (Figure 5.3, 5.4). Compression beneath the TCL from the bony carpal walls, anomalous muscle within the carpal tunnel, and forces from the flexor tendons become obvious at each level.

Comparison of Changes in T2 relaxation times of the median and ulnar nerves of the Controls

The T2 relaxation time of both the asymptomatic and symptomatic control subjects' median nerves did not vary significantly between Baseline and after three hours. The T2 relaxation time value then decreased to below Baseline. The ulnar nerve of the control subjects demonstrated a slight drop in the T2 relaxation time between Baseline

and 3 hours later (After Typing). Between this observation and the After Rest, the T2 relaxation time remained essentially unchanged. T2 relaxation time values decreased in the median (Figure 5.8) and ulnar (Figure 5.9) nerves in both the symptomatic and asymptomatic controls when comparing Baseline to Post Rest. Please note, that although control subjects did not type, in the graphs control results are labeled "After typing". This allows a comparison at that time interval with the subjects who were typing.

Symptomatic Subjects Report Pain With Typing

All of the symptomatic subjects reported at least a pain level of one on a scale from zero to ten (Figure 5.10). The two subjects who had been diagnosed with carpal tunnel syndrome prior to this study reported delayed onset pain with prolonged rest, as did the subject who acted as both a non-typing control (Subject 13) and a typing subject (Subject 16).

Comparison of Changes in T2 relaxation times of the median and ulnar nerves, Symptomatic vs. Asymptomatic Subjects

T2 relaxation times of the asymptomatic subjects had a tendency to increase with the exposure to typing, then decreased to Baseline levels. T2 relaxation time values of the symptomatic subjects either increased very slightly, or decreased between Baseline and After Typing (Figure 5.11). Between After Typing and Post Rest, T2 relaxation time values of the median and ulnar nerves of the asymptomatic subjects returned approximately to Baseline, while the T2 relaxation times of Symptomatic subjects'

median nerve in all cases but one, increased to above Baseline values (Figure 5.12). Tables in Figures 5.13, 5.14, 5.15, and 5.16 include the values depicted in the graphs.

As shown in Figure 5.17, the average T2 relaxation times of the median and ulnar nerve of all symptomatic subjects maintained a higher range of values than all but one of the asymptomatic subjects. The exact interpretation of these findings is unclear.

DISCUSSION

There is a correlation in changes and shape of the median nerve with typing

The median nerve was seen to change shape significantly in the asymptomatic subjects with exposure to typing. This appears to be a response to activity. The shape changes noted in the median nerves of symptomatic subjects, while still undergoing some subtle shape changes when exposed to typing, were less significant than the shape changes seen in the asymptomatic subjects.

The shapes of the median nerves of symptomatic subjects were often swollen, very flat, nearly obliterated by connective tissue, or were subjected to tethering in images taken proximal to the TCL in images taken at Baseline. These findings agree with many others, that the median nerve is often misshapen in symptomatic subjects at rest [47, 49, 55, 56]. This study shows a tendency for these median nerves to respond less robustly to typing by changing shape.

T2 Relaxation Time Values Respond differently in Controls vs. Typing Subjects

As was expected, the T2 relaxation times in non-typing control subjects varied less than in subjects engaged in typing. This may be related to dilatation of perineural capillaries as an exercise response. It is interesting to note that the average T2 relaxation

times of both the median and ulnar nerves of asymptomatic subjects were seen to be higher than those of the symptomatic subjects.

A pattern of ischemia of the nerves brought on by impaired perineural circulation followed by reperfusion is discussed in the literature. It would follow that delayed onset symptoms, either delayed onset muscle soreness (DOMS) or delayed/nocturnal onset paresthesias may be closely linked to this phenomenon. A change in neural T2 relaxation time was affected by typing in this study. Those T2 relaxation time changes may be evidence of the cycle of ischemia and reperfusion. If symptomatic individuals have less robust perineural circulation than asymptomatic individuals, they may be more sensitive to pressure changes suggested in this study.

As shown in Figure 5.17, the average T2 relaxation times of the median and ulnar nerves of symptomatic subjects maintained a higher range than those of the asymptomatic subjects. Higher T2 relaxation time is used as a diagnostic sign of neural inflammation, and is diagnostic in carpal tunnel syndrome. It was of interest that while this cohort was not homogenous in diagnosis, only two subjects were diagnosed with CTS, all symptomatic subjects' average T2 relaxation times in both the median and ulnar nerves were higher than those of asymptomatic subjects.

CONCLUSIONS

MRI studies of functional activity, typing, has been shown to be efficacious. It is valuable to study subjects performing a functional activity in order to quantify the effects of the activity. Facsimiles of the activity have value in establishing the protocols for scientific analysis. However, the use of the actual, functional activity has the benefit of

direct observation over conjecture. Further investigation into the effects of other high-risk vocational tasks on shape, size and T2 relaxation time changes would provide additional information on this subject.

In this study, both the median and ulnar nerves showed T2 relaxation time changes related to typing, while changes in shape were less apparent. Results should be substantiated by a larger study, with higher numbers of both asymptomatic and symptomatic subjects, and with symptomatic subjects with greater homogeneity of diagnosis.

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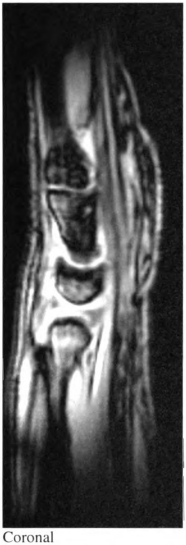
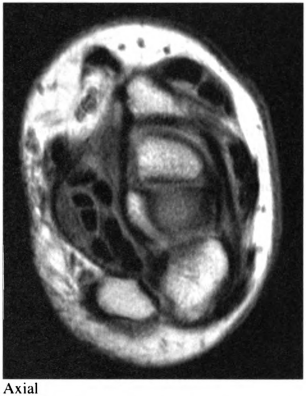


Coronal



Axial

Figure 2.1: Anatomical terms, sagittal, coronal, axial are ways to describe "slices" of images. The sagittal image on the left is taken longitudinally and used to locate the area that will be imaged in the study. This "Localizer" image is 90 degrees from the axis of the images that will be used. The axial image on the right provides excellent detail and sufficient resolution for quantification of size, shape and fluid content of tissues in the image.

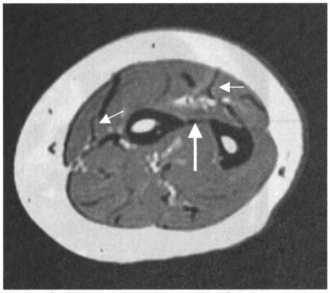


Figure 2. 2: Fascial compartments can be seen in this axial image of forearm muscles. The interosseous membrane appears as a dark line, which divides the image top to bottom (heavy white arrow). The extensor compartment is in the upper third of the image, the flexor/pronator compartment is in the lower two-thirds of the image. Boundaries between muscles (light white arrows) are also visible.

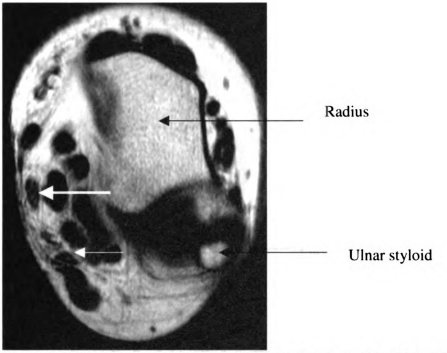


Figure 2.3: The most proximal of the imaging levels used in this study, this image is "Proximal to the Transverse Carpal Ligament." The radius and ulnar styloid are visible at this level, but not the lunate. The median nerve (heavy white arrow) and ulnar nerve (light white arrow) are easily identified.

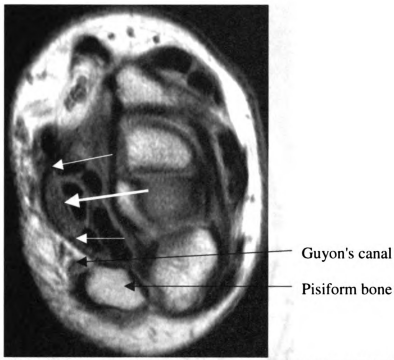


Figure 2.4: Level of the pisiform bone. The transverse carpal ligament (light white arrows) can be seen as a dark line enclosing the contents of the carpal tunnel. The median nerve (heavy white arrow) can be identified just beneath the TCL. Guyon's canal is a triangular space just outside the carpal tunnel.

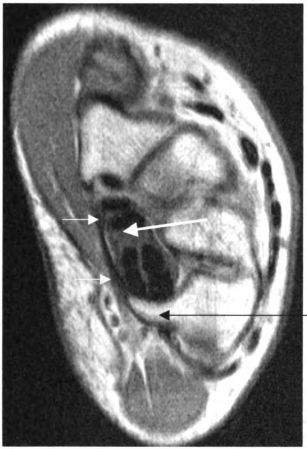


Figure 2.5: Level of the hook of the hamate is well within the carpal tunnel. The transverse carpal ligament (light arrows) appears as a dark border to the carpal tunnel. The median nerve (heavy white arrow) is just deep to the TCL, surrounded by flexor tendons.

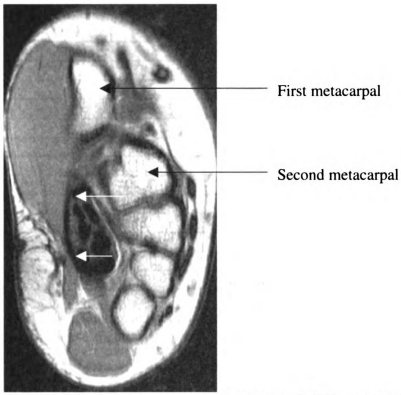


Figure 2.6: Level of the base of the metacarpals. The metacarpals form an arch beginning with the first metacarpal (of the thumb). The transverse carpal ligament (light white arrows) can still be seen as a dark border of the carpal tunnel.

Study Subjects by Age and Diagnosis

Subject Number	Age	Diagnosis
1	38	None
2	51	None
3	46	None
4	21	None
5	46	None
6	21	None
9	31	Carpal Tunnel Syndrome
10	52	Lateral Epicondylitis
11	38	Lateral Epicondylitis
12	44	Lateral Epicondylitis
13	40	Tenosynovitis
14	51	Lateral Epicondylitis
18	52	Carpal Tunnel Syndrome

Figure 3.1: This table lists all of the subjects with age and diagnosis. Asymptomatic subjects have diagnoses listed as "None."

Subject Name: _____
Subject number: 00_xxxx

Date _____

PROLONGED TYPING/MRI RESEARCH STUDY
QUESTIONNAIRE

Please indicate if you have ever had the symptoms of, or have ever been told you have the following by circling the correct response, if yes, describe.

Heart disease	YES	NO	_____
High blood pressure	YES	NO	_____
Stroke	YES	NO	_____
Diabetes	YES	NO	_____
Rheumatoid arthritis	YES	NO	_____
Osteo arthritis	YES	NO	_____
Lupus	YES	NO	_____
Fibromyalgia	YES	NO	_____
Carpal Tunnel Syndrome	YES	NO	_____
Lateral Epicondylitis	YES	NO	_____
Fracture of arm, forearm or wrist	YES	NO	_____
Surgery	YES	NO	_____
Implants of any kind	YES	NO	_____
Could you be pregnant now?	YES	NO	_____
Do you use caffeine?	YES	NO	How much_____
Do you use nicotine?	YES	NO	How much_____

List medicines you use daily or as needed:

Indicate how many hours you routinely type at one time/in one day 1-3 4-6 8-10
DATE OF BIRTH_____
MEDICAL RELEASE

I GIVE MY CONSENT FOR Michigan State University MRI RESEARCH TEAM MEMBERS TO RELEASE INFORMATION REGARDING ANY DIAGNOSITIC INFORMATION TO THE PHYSICIAN LISTED BELOW IN THE UNLIKELY EVENT THE RADIOLOGIST DISCOVERS AN ABNORMALITY IN MY RESEARCH MRI EXAMINATION.

PHYSICIAN NAME _____

ADDRESS_____PHONE NUMBER_____

I AM VOLUNTEERING TO PARTICIPATE IN THIS RESEARCH STUDY. I HAVE READ AND ACCEPTED THE TERMS OF THE INFORMED CONSENT. I GIVE MY CONSENT FOR THE MRI RESEARCH TEAM TO USE THE INFORMATION OBTAINED THROUGH THE REPETITIVE STRESS INJURY MRI PROJECT THAT PERTAINS TO ME FOR RESEARCH, PUBLICATION AND FURTHER STUDY. I UNDERSTAND MY NAME WILL NOT BE USED, HOWEVER DEMOGRAPHIC INFORMATION AND THE RESULTS OF ANY RELATED TESTS MAY BE USED FOR THIS RESEARCH PROJECT, AND FOR FUTURE PROJECTS OF THIS NATURE. MY NAME AND OTHER IDENTIFYING INFORMATION WILL BE HELD AS CONFIDENTIAL INFORMATION, AND NOT RELEASED WITHOUT MY SPECIFIC INFORMED CONSENT.

PARTICIPANT'S SIGNATURE _____

Figure 3.2

RSI/TYPING RESEARCH STUDY INFORMED CONSENT

You have been asked to volunteer in a research study involving the use of a Magnetic Resonance Imaging (MRI) examination. The purpose of this examination is to study what occurs in the tissues of the forearm and wrist when exposed to prolonged typing and during rest. Because many symptoms, especially numbness, tingling and pain, occur at night, a portion of this study will involve nighttime tests. You have been selected because you are either diagnosed with or experience symptoms of a repetitive stress injury in your forearms or wrists, and continue to work with a primary work requirement of typing.

Magnetic Resonance Imaging requires the use of a very large permanent magnet made in the shape of a large tube with a movable table on tracks that carries the person into the center of the imaging magnet. **It is imperative that the subject of these examinations avoids wearing or carrying any metal objects that may be magnetic during the test.** As a participant in this study, you will be asked to lie face down, then on your side on the imaging table with your dominant arm over your head inside a smaller "extremity coil" for about thirty minutes for each test. Use of a positioning splint helps position your forearm and wrist comfortably inside the extremity coil. There will be three examinations, one before you begin typing, one immediately following typing and one at night. If you request one, we will schedule a visit to the MRI area, in order for you to see the magnet and experience the experimental position inside the magnet. When you agree to participate, you will be given several questionnaires including a general health questionnaire, the Magnetic Resonance Imaging questionnaire, and a questionnaire to determine your level of symptoms of repetitive stress injury.

If selected for the study, you will be asked to participate in a physical examination of your arms. This will include strength testing, sensory testing, range of motion, nerve conduction studies, and MRI examination the morning of the experiment. You will then report for your normal work duties. Immediately following vocational typing of at least three hours, you will be given a second MRI examination. You will be asked to return between 6 and 8 pm that evening for a period of absolute rest followed by a final MRI examination. You will be compensated $60.00 for participation as a subject in this study.

We hope that if you agree to participate in the experiments, you will complete all requirements of the study. However, should you decide not to complete any portion of the experiments, there will be no attempt to force you to continue, and there will be no penalty for stopping your participation at any time, for any reason.

It is not expected that there is any potential for harm in this study. However, it is necessary that you understand that Michigan State University and the faculty and students participating in this project do not compensate for injuries incurred as a result of your participation in this research. The questionnaire is provided to screen volunteers with health risks that are inappropriate for this study.

I _____agree to take part in this project as described above.

Signature Date

Witness Date

Figure 3.3

LEVINE CARPAL TUNNEL SYNDROME SYMPTOM SEVERITY SCALE

TABLE I

SUBJECT NUMBER _____ DATE _____

The Following questions refer to your symptoms for a typical twenty-four-hour period during the past two weeks (Circle one answer to each question).

How severe is the hand or wrist pain that you have at night?

1.) I do not have hand or wrist pain at night.
2.) Mild pain
3.) Moderate pain
4.) Severe pain
5.) Very severe pain

How often did hand or wrist pain wake you up during a typical night in the past two weeks?

1.) Never
2.) Once
3.) Two or three times
4.) Four or five times
5.) More than five times

Do you typically have pain in your hand or wrist during the daytime?

1.) I never have pain during the day
2.) I have mild pain during the day
3.) I have moderate pain during the day
4.) I have severe pain during the day
5.) I have very severe pain during the day

How often do you have hand or wrist pain during the daytime?

1.) Never
2.) Once or twice a day
3.) Three to five times a day
4.) More than five times a day
5.) The pain is constant

How long, on average, does an episode of pain last during the daytime?

1.) I never get pain during the day

2.) Less than 10 minutes

3.) 10 to 60 minutes

4.) Greater than 60 minutes

5.) The pain is constant throughout the day

Do you have numbness (loss of sensation) in you hand?

1.) No

2.) I have mild numbness

3.) I have moderate numbness

4.) I have severe numbness

5.) I have very severe numbness

Do you have weakness in your hand or wrist?

1.) No weakness

2.) Mild weakness

3.) Moderate weakness

4.) I have severe numbness

5.) I have very severe numbness

Do you have tingling sensations in your hand?

1.) No tingling

2.) Mild tingling

3.) Moderate tingling

4.) Severe tingling

5.) Very severe tingling

How severe is numbness (loss of sensation) or tingling at night?

1.) I have no numbness or tingling at night

2.) Mild

3.) Moderate

4.) Severe

5.) Very severe

How often did hand numbness or tingling wake you up during the past two weeks?

1.) Never

2.) Once

3.) Two or three times

4.) Four to five times

5.) More than five times

Do you have difficulty with the grasping and use of small objects such as keys or pens?

1.) No difficulty

2.) Mild difficulty

3.) Moderate difficulty

4.) Severe difficulty

5.) Very severe difficulty

SUBJECT NUMBER:_____ DATE:_____

Figure 3.4

LEVINE FUNCTIONAL STATUS SCALE
TABLE II

On a typical day the past two weeks have hand and wrist symptoms caused you to have any difficulty doing the activities listed below? Please circle one number that best describes you ability to do the activity.

Activity	No difficulty	Mild Difficulty	Moderate Difficulty	Severe Difficulty	Cannot Do at All Due to Hand and Wrist Symptoms
Writing	1	2	3	4	5
Buttoning of clothes	1	2	3	4	5
Holding a book while reading	1	2	3	4	5
Gripping of a telephone handle	1	2	3	4	5
Opening of jars	1	2	3	4	5
Household chores	1	2	3	4	5
Carrying of grocery bags	1	2	3	4	5
Bathing and dressing	1	2	3	4	5

Figure 3.5

PHYSICAL EXAMINATION TYPING/RSI RESEARCH STUDY

Subject Number: _____ Date of examination: _____

Date of Birth _____ Time of examination: _____

Examiner_____

Hand Tested: Right Left
Dominant hand: Right Left
Completion of questionnaire: note all questions answered yes, and explain:
_____

Subject indicates she routinely types four hours at a time: YES NO

	Right	Left
Phalen's test: Indicate positive or negative	_____	_____
Proprioception: Index finger	_____	_____
	Normal/abn	Normal/abn

Reflexes:

Location	Scale 0-4/4 Right	Scale 0-4/4 Left	Normal/Abnormal
Biceps			
Triceps			
Brachioradialis			

Manual muscle tests:

Muscle	Strength Right 1-5/5	Strength Left 1-5/5	Normal/Impaired
Deltoid	/5	/5	
Biceps	/5	/5	
Triceps	/5	/5	
Wrist extension	/5	/5	
Wrist flexion	/5	/5	
Interosseous	/5	/5	
Extensor indicus	/5	/5	
Abductor Pollicus Brevis	/5	/5	

Semmes Weinstein Monofilament Sensory Test

Nerve	Right	Left	Normal/Abnormal
Radial – Thumb			
Median- Index f.			
Ulnar – Small f.			
Nerve root 6			
Nerve root 7			
Nerve root 8			

PHYSICAL EXAMINATION TYPING/RSI RESEARCH STUDY
Page 2 of 2

Grasp and pinch strength in pounds: Right Left
(three trials)

	Right Trial 1	Right Trial 2	Right Trial 3	Left Trial 1	Left Trial 2	Left Trial 3
Mass grasp						
Lateral pinch						
Three jaw chuck						
Tip pinch						

Nerve conduction study

Right	**Nerve**	**Stimulation/ Record**	**D.L MSEC**	**AMP Microvolt**	**Dist. cm**	**Normal/ Abnormal**
	Median		/	/	**14/6**	
	Ulnar				**14/6**	

Figure 3.6: This physical examination for provided a standardized method of recording results.

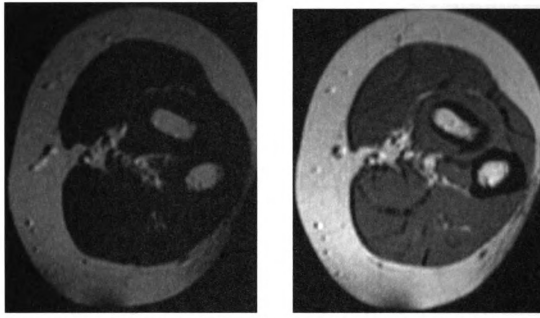


Figure 3.7: Dual T2 weighted images used to establish Calculated average T2 for individual muscles.

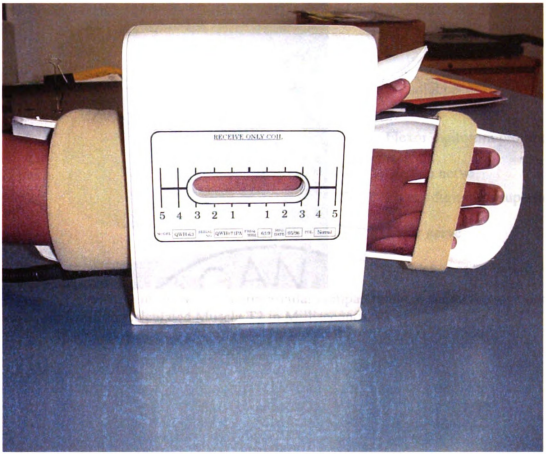


Figure 4.1: Position of wrist and hand using thermoplastic splint within the wrist coil

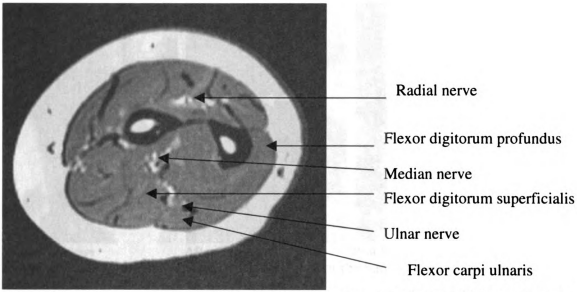
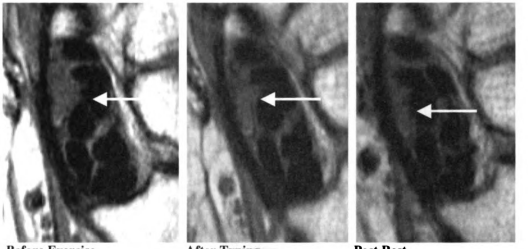
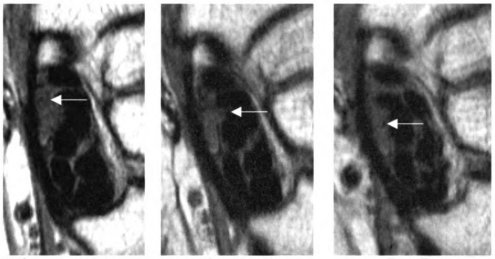


Figure 4.2: Forearm muscles and neurovascular compartments in an axial image used to calculate Random Calculated Muscle T2 in Milliseconds.



Before Exercise **After Typing** **Post Rest**

Figure 4.3: Carpal tunnel of Subject 1 at the hook of the hamate. The arrow indicates the median nerve.



Before Exercise **After Typing** **Post Rest**

Figure 4.4: Carpal tunnel at the hook of the hamate of Subject 2, arrow indicates the median nerve. Note the change from triangular/flat to triangular to oval.

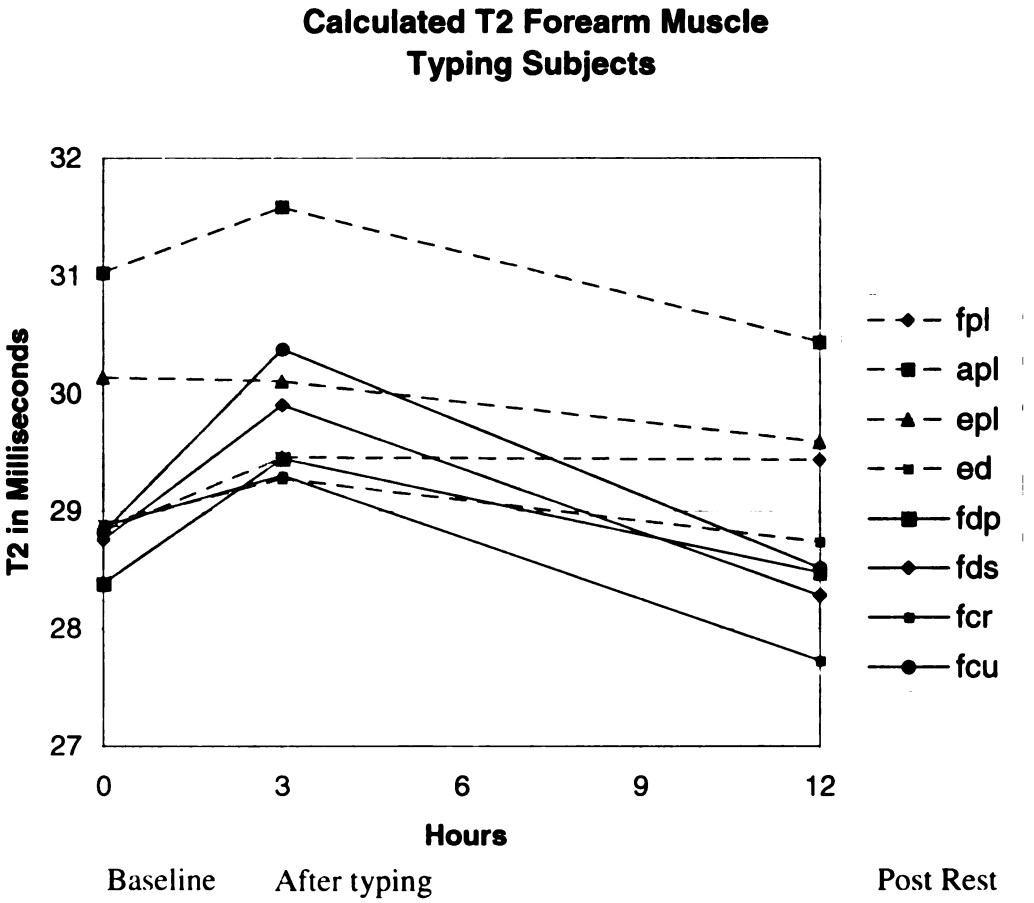


Figure 4.5: Averaged Calculated T2 of forearm muscles of all typing subjects demonstrates the increase in T2 relaxation time immediately following typing in the more active muscles contrasted with the flat or less acute increase in T2 of the less active muscles.

Random Calculated T2 Forearm Muscle	Baseline	After typing	Post Rest	P value
Flexor pollicis longus (FPL)	28.82	29.45	29.43	0.51
Abductor Pollicis Longus (APL)	31.02	31.58	30.43	0.34
Extensor Pollicis Longus (EPL)	30.13	30.10	29.58	0.51
Extensor Digitorum (ED)	28.89	29.27	28.74	0.76
Flexor Digitorum Profundus (FDP)	28.38	29.44	28.48	0.02
Flexor Digitorum Superficialis (FDS)	28.76	29.90	28.28	0.01
Flexor Carpi Radialis (FCR)	28.87	29.30	27.73	0.02
Flexor Carpi Ulnaris (FCU)	28.82	30.38	28.51	0.01
Extensor Carpi Radialis Longus (ECRL)	30.07	28.79	29.07	0.10
Extensor Carpi Ulnaris (ECU)	30.62	26.00	30.11	0.10

Figure 4.6: Forearm muscle Random Calculated T2 in milliseconds with corresponding significance level.

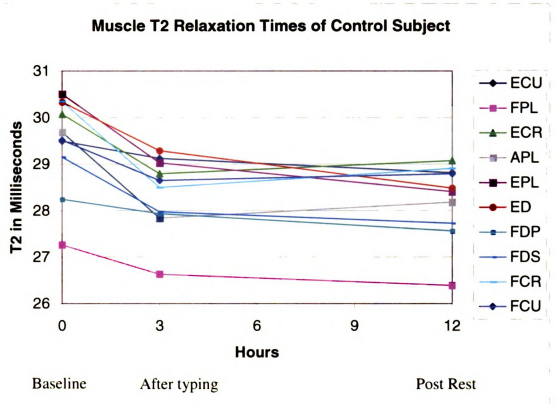


Figure 4.7: The T2 relaxation time in milliseconds of the non-typing control is depicted in this graph. Note that the T2 decreases or remains flat in all muscles analyzed here. The control subject did not type, and therefore her muscles would not be expected to demonstrate an increase in T2 After Typing. The Post Rest T2s are as expected as well.

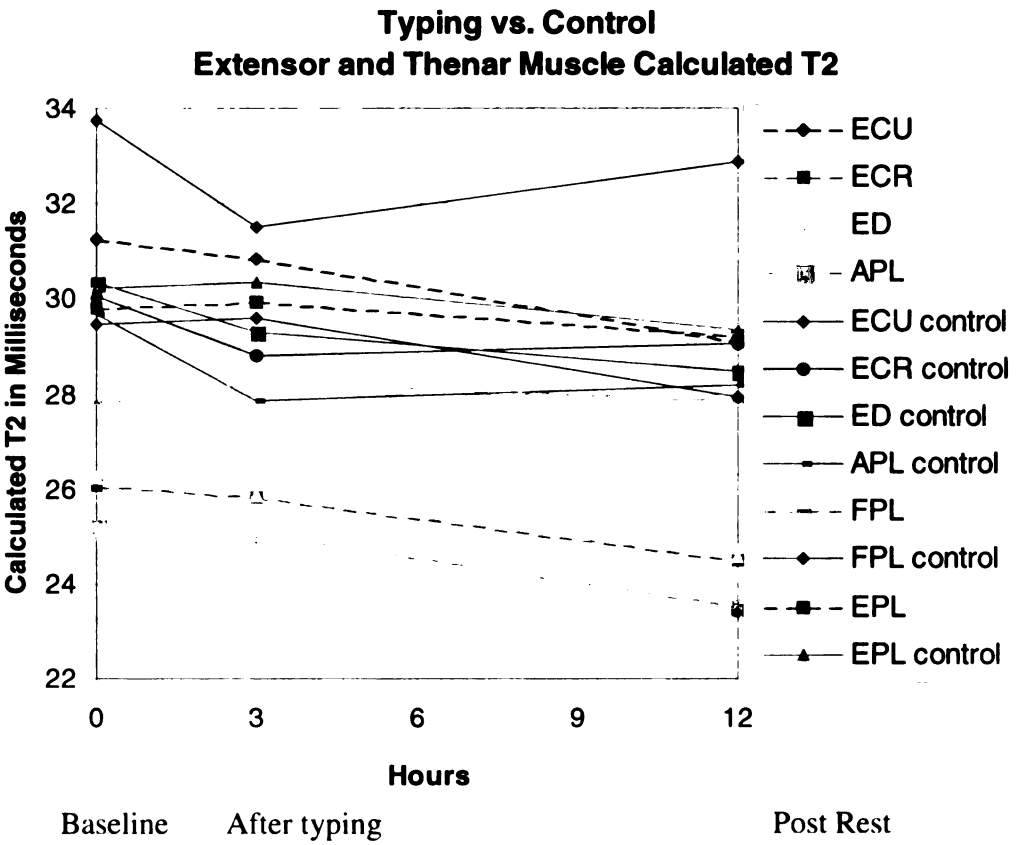


Figure 4.8: Comparison of the extensor and thenar muscle groups calculated muscle T2 of the control subject with typing subjects showing no significant change in T2 with passage of time (control solid line) or typing (broken line).

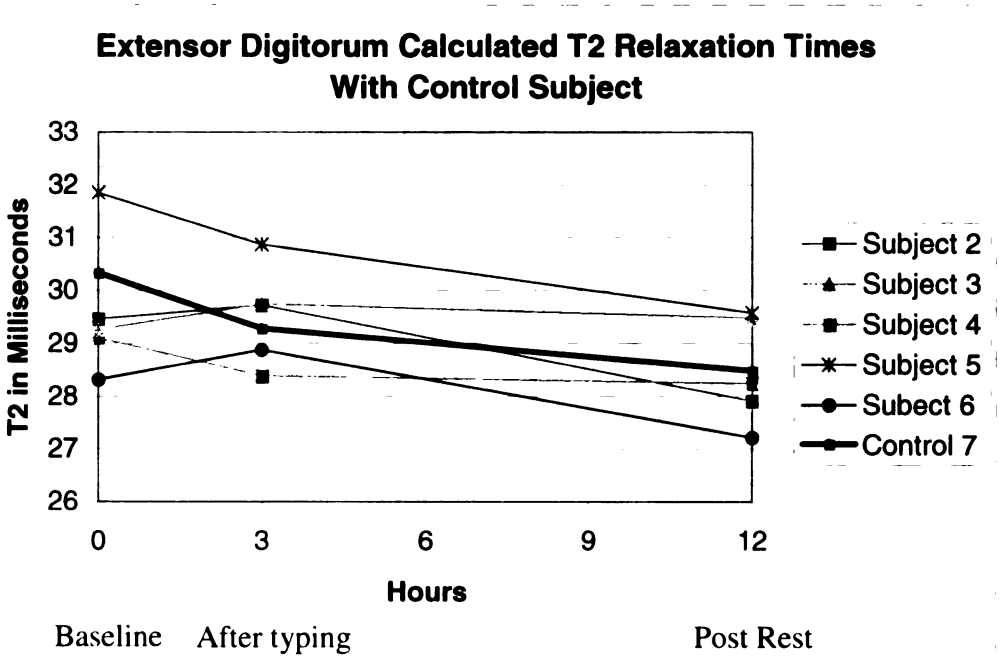
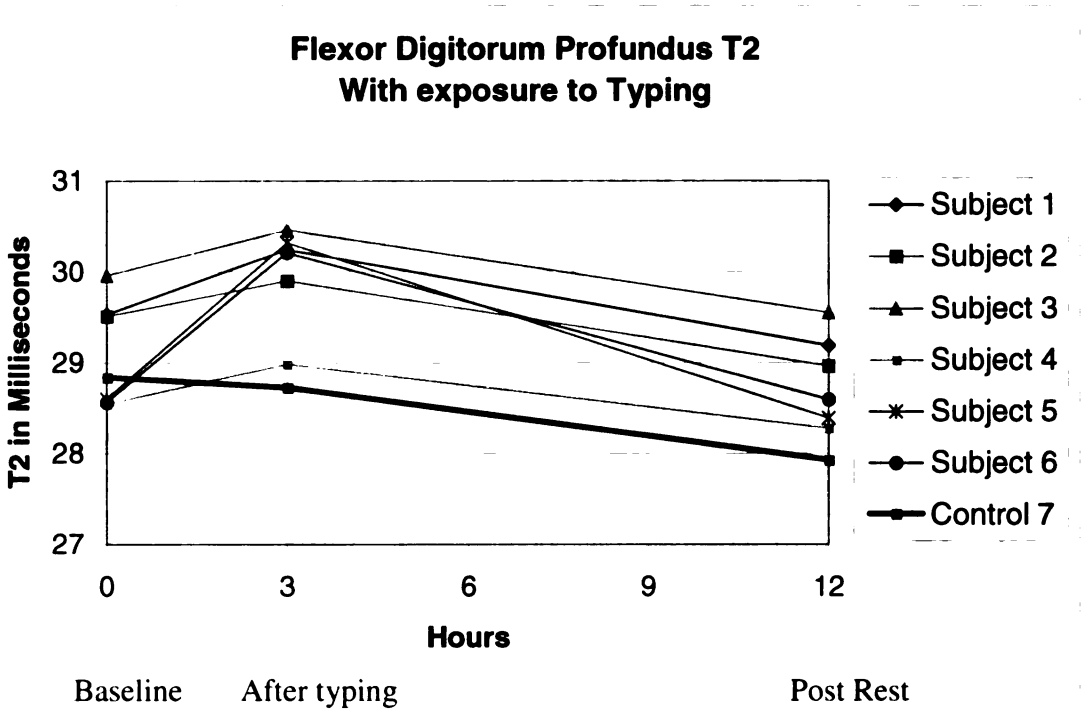


Figure 4.9: Scatterplot of Calculated T2s of Extensor Digitorum all study subjects including the non-typing control.



4.10: Scatterplot of Calculated T2 of Flexor Digitorum. Compared to the previous graph, the consistent increase in the T2 Relaxation times of the active muscles compared to the Control is significant. This demonstrates the pattern of T2 increases with exercise, decrease with rest in an active muscle.

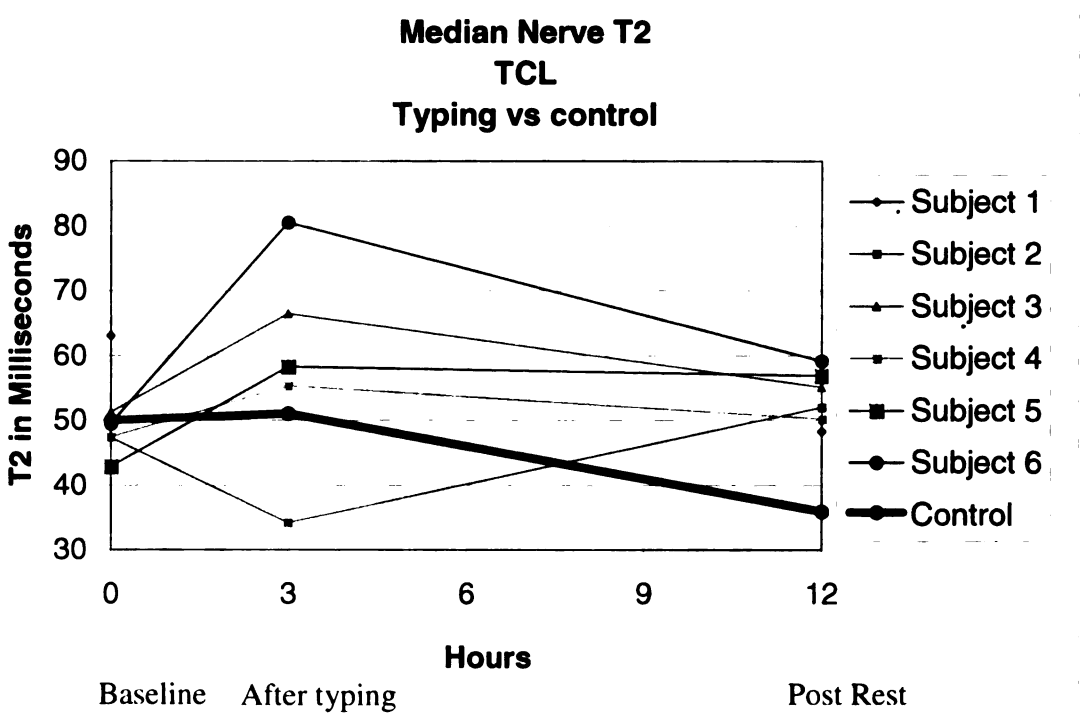


Figure 4.11: Graphic representation of the pattern of T2 changes in the median nerve with exposure to typing.

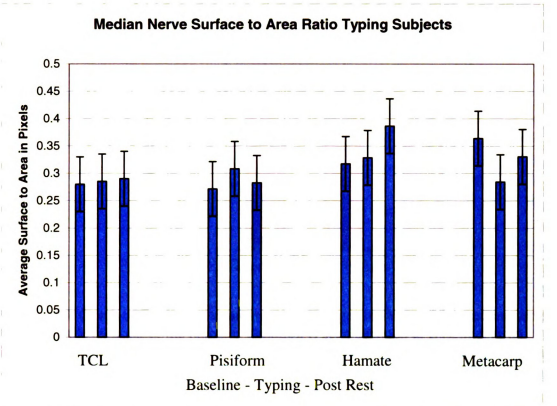


Figure 4.12: This chart graphically depicts the surface to area ratios at each of the four imaging levels. The bar to the left represents "Baseline," the center bar represents "After typing," and the right bar represents "Post Rest." Variation at the hook of the hamate and metacarpal level, while more noticeable, still do not approach statistical significance.

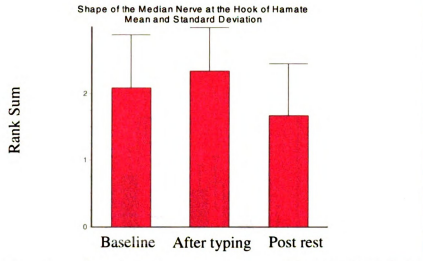


Figure 4.13: Graph of Rank Sum comparing the changes in shape of the median nerve at the imaging level hook of the hamate. Variation is seen between at Baseline, After Typing and Post Rest. This imaging level was chosen because it is beneath the TCL and is suggestive of compression from both the TCL and flexor tendons within the carpal tunnel.

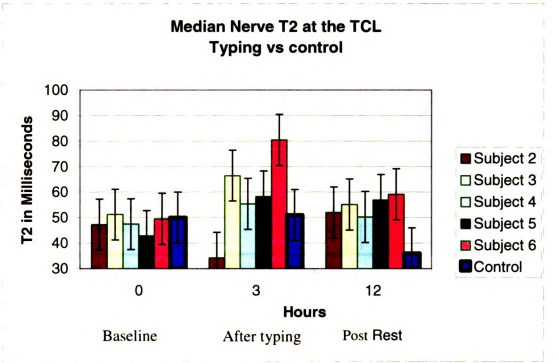


Figure 4.14: This histogram compares T2s of the median nerve of each subject with error bars. While the trends are apparent, the lack of statistical significance is graphically demonstrated.

Asymptomatic Cohort Median Nerve Level of TCL

Correlations

		BASELINE	TYPING	REST
BASELINE	Pearson Correlation	1.000	.879*	.832
	Sig. (2-tailed)	.	.050	.080
	N	5	5	5
TYPING	Pearson Correlation	.879*	1.000	.478
	Sig. (2-tailed)	.050	.	.416
	N	5	5	5
REST	Pearson Correlation	.832	.478	1.000
	Sig. (2-tailed)	.080	.416	.
	N	5	5	5

*. Correlation is significant at the 0.05 level (2-tailed).

Figure 4.15: This Pearson Correlation Table illustrates the significant correlation between changes in the calculated T2 of the median nerve of typing subjects.

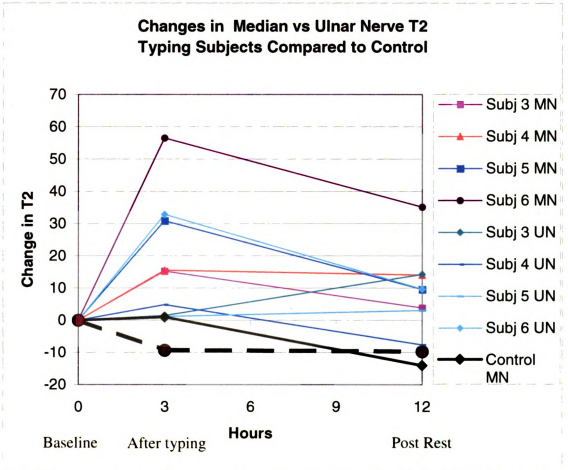


Figure 4.16: This graph demonstrates the range of T2 Relaxation time variation in the median nerves of typing subjects compared to the narrower range of the T2 values of both the ulnar nerves of typing subjects and the median and ulnar nerves of the non-typing control subjects.

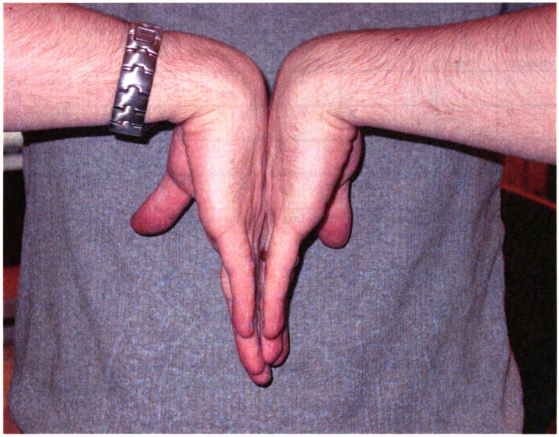
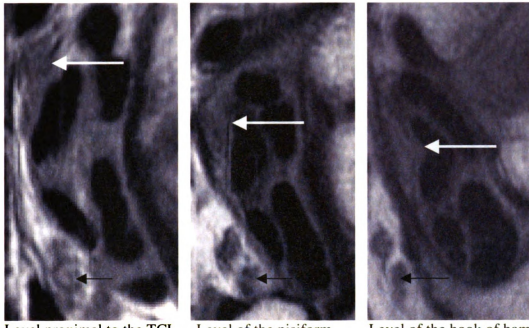


Figure 5.1: Phalen's test requires the subject to place the backs of the hands together with the wrists acutely flexed. This increases carpal tunnel pressure, and often elicits complaints of paresthesias or pain in the thumb, index, long and ring fingers in less than one minute.

Investigator	Surface to Area	Calculated T2	Asymptomatic Cohort	Symptomatic Cohort	Visible shape of the nerve	Visible T2 signal intensity
Radiologist LB			X		X	X
Radiologist KR		X	X	X	X	X
Radiologist JP				X	X	X
Author	X	X	X	X	X	X

Figure 5.2: Images analyzed were axial T2 and gradient echo images of the forearm of each of the subjects.



Level proximal to the TCL Level of the pisiform Level of the hook of hamate

Figure 5.3: This asymptomatic subject's median nerve is somewhat flattened at each level. It changes shape subtlety at each of the imaging levels. The ulnar nerve (black arrow) remains oval or rounded at each of the imaging levels. These images are of the same subject taken at baseline.

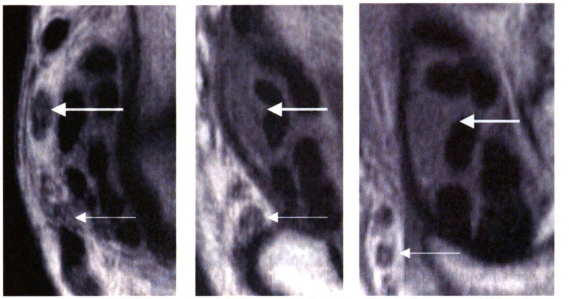
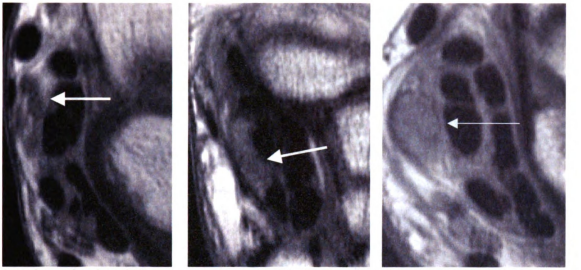
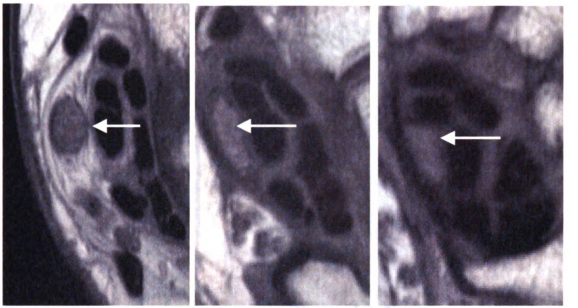


Figure 5.4: This asymptomatic subject's median nerve (heavy white arrow) is oval. It widens and flattens at the TCL, but remains essentially oval. A distinct point becomes apparent at the hook of the hamate. The ulnar nerve remains oval (light white arrow). Note the change in shape of the carpal tunnel at the different imaging levels.



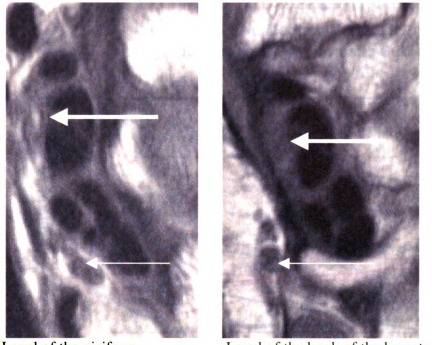
Level proximal to TCL Level proximal to TCL Level of pisiform bone

Figure 5.5: These images of the median nerves of symptomatic subjects just proximal to the transverse carpal ligament and at the level of the pisiform illustrate the two deformities of the median nerve most reported in the literature, flattening (heavy white arrow) and edema (right image, white arrow).



Level proximal to TCL Level of pisiform bone Level of hook of amate

Figure 5.6: Fast Spin Echo T2 images at the imaging levels: Proximal to transverse carpal ligament, Level of Pisiform, and Hook of Hamate, magnified x 3. The white arrow indicates the Median nerve. This is a symptomatic subject, diagnosis carpal tunnel syndrome. Note size of median nerve and presence of thickened connective tissue surrounding the median and ulnar nerves proximal to the TCL. This connective tissue "tether" disappears at the pisiform level, and the size of the median nerve diminishes as it passes through the carpal tunnel denoting swelling of the median nerve prior to entry into the carpal tunnel. The signal intensity of the median nerve visibly increases from TCL to pisiform, and from pisiform to hamate.



Level of the pisiform Level of the hook of the hamate

Figure 5.7: Note the dramatic flattening of the median nerve (large arrow) in an image of a symptomatic subject at the level of the pisiform, left, and hook of the hamate, right. The ulnar nerve (small arrow) is ovoid, suggesting minimal compression of the ulnar nerve.

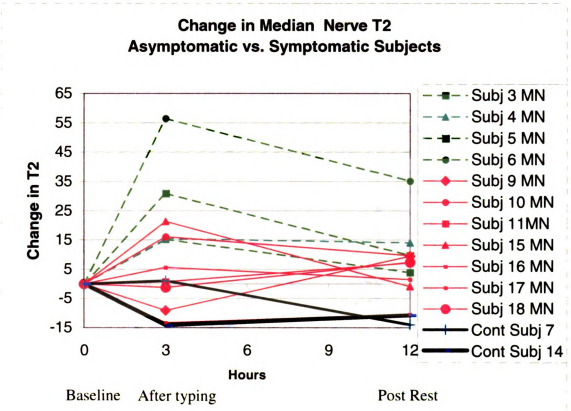


Figure 5.8: T2 relaxation time changes in the median nerve when the subject was exposed to typing. This scatterplot depicts symptomatic subjects (solid) tend to have minimally increased or decreased T2 after typing, while asymptomatic subjects (broken) tend to have increased T2 SI. Following the prolonged rest period, T2s of several of the symptomatic subjects increased slightly above Baseline levels. Heavy, solid lines indicate controls. Changes in T2 are defined as the calculated T2 at each time period minus the T2 relaxation time at Baseline.

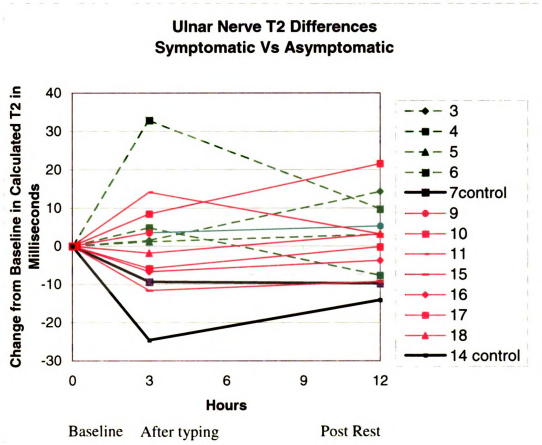


Figure 5.9: Less variation in T2 is noted in this graph of ulnar nerves of all subjects. T2 of control subjects (Black lines) remains below Baseline, while the majority of typing subjects' T2s (Dashed line) increase to above Baseline in the Post Rest interval. Symptomatic subjects' ulnar nerve T2s both increase and decrease below Baseline levels After Typing. Changes in T2 are defined as the calculated T2 at each time period minus the T2 relaxation time at Baseline.

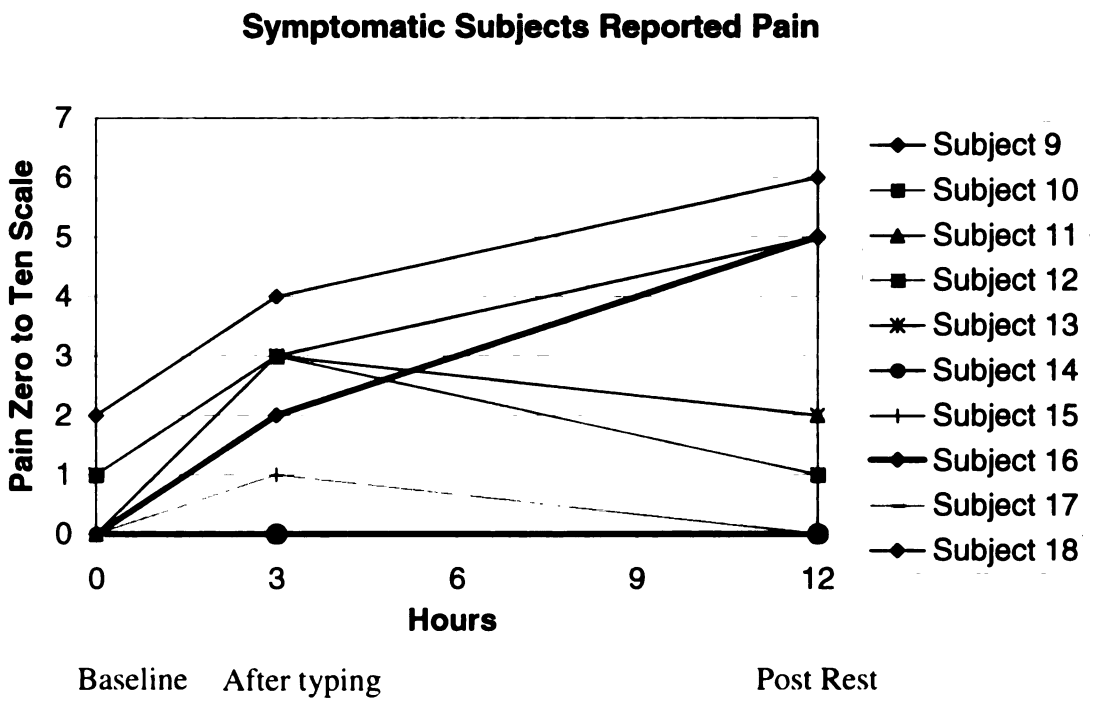


Figure 5.10: Subjects 9 and 18 were diagnosed with carpal tunnel syndrome prior to this study. The heavy black line represents the subject who acted both as a typing subject and control. Her reported pain was zero while acting as a non-typing control, and demonstrated delayed onset of pain after rest.

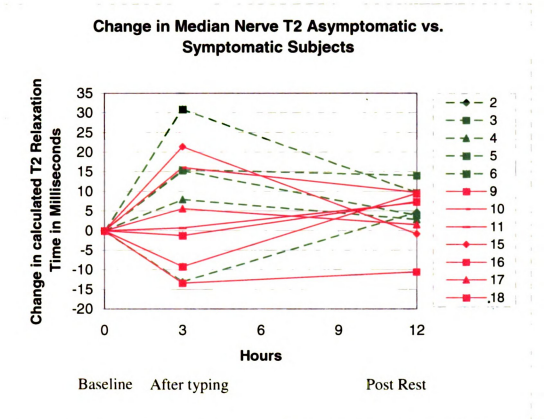


Figure 5.11: Asymptomatic subjects (dashed lines) increased T2 relaxation times, while symptomatic subjects (solid lines) were more likely to decrease T2's or remain unchanged. Changes in T2 are defined as the calculated T2 at each time period minus the T2 relaxation time at Baseline.

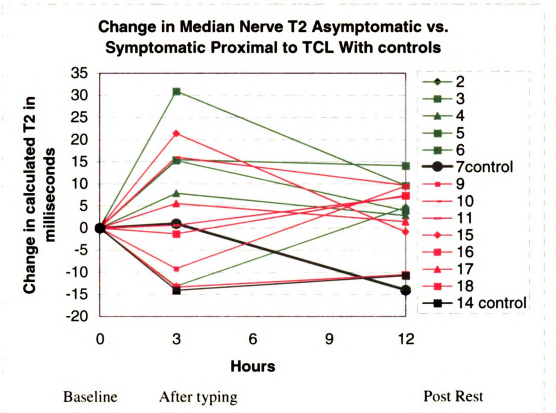


Figure 5.12: Median nerve T2 relaxation time trends are noted in this scatter plot. The median nerves of symptomatic subjects (red lines) tend to vary less than those of asymptomatic subjects (green lines). Several T2 relaxation times remain fairly constant After Typing, then increase above Baseline, while others decrease After Typing, then recover to a value above Baseline. Only one asymptomatic subject's T2 relaxation time decreases After Typing. Changes lack statistical significance. Changes in T2 are defined as the calculated T2 at each time period minus the T2 relaxation time at Baseline.

Median Nerve Average T2s: Asymptomatic Subjects	Baseline	After typing	Post Rest
Proximal to TCL	39.73	49.15	45.59
Pisiform	39.57	42.38	43.23
Hook of Hamate	41.92	46.63	42.13
Metacarpal heads	38.79	37.57	43.09

Figure 5.13: Average T2s of the asymptomatic subjects' median nerve at the four imaging levels. Changes are not statistically significant using a repeated measures ANOVA (p=0.14).

Ulnar Nerve: Asymptomatic Subjects	Baseline	After typing	Post Rest
Proximal to TCL	48.56	45.61	52.31
Pisiform	47.45	39.71	47.96
Hook of Hamate	47.65	38.86	48.68

Figure 5.14: T2 values of the Ulnar nerve were not available at the metacarpal heads. The ulnar nerve branches before it reaches this imaging level.

Median Nerve: Symptomatic Subjects	Baseline	After typing	Post Rest
Proximal to TCL	50.17	53.02	55.15
Pisiform	50.25	48.26	48.22
Hook of Hamate	49.42	49.15	51.67
Metacarpal heads	53.24	51.84	52.98

Figure 5.15: The T2 value changes were not statistically significant at After Rest (p=0.56).

Ulnar Nerve: Symptomatic Subjects	Baseline	After typing	Post Rest
Proximal to TCL	55.2	58.15	50.25
Pisiform	54.05	54.88	55
Hook of Hamate	51.2	49.97	58.87

Figure 5.16: No statistical significance was noted After Rest in symptomatic subjects' average T2s of the ulnar nerve (p=0.17).

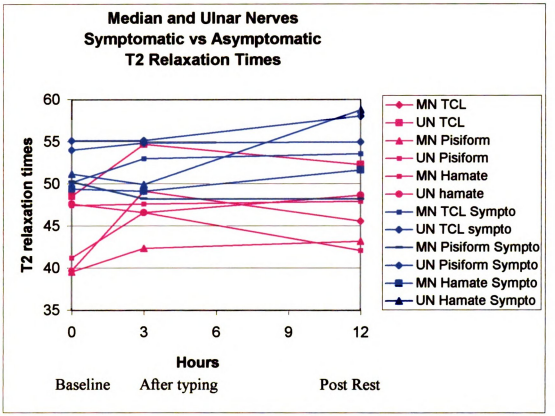


Figure 5.17: For the most part, asymptomatic subjects' average T2s maintained a lower average T2 than those of symptomatic subjects. The one exception is the average of the ulnar nerve at the transverse carpal ligament of one of the asymptomatic subjects.