THE EFFECT OF FORCE, POSTURE, AND REPETITIVE WRIST MOTION ON INTRANEURAL BLOOD FLOW IN THE MEDIAN NERVE
THE EFFECT OF FORCE, POSTURE, AND REPETITIVE WRIST MOTION ON INTRANEURAL BLOOD FLOW IN THE MEDIAN NERVE

By

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TITLE: The Effect of Force, Posture, and Repetitive Wrist Motion on Intraneural Blood Flow in the Median Nerve

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Many epidemiological studies have named pinching, deviated wrist postures, and repetitive motion as ergonomic risk factors in the development of carpal tunnel syndrome (CTS). Evidence suggests that hypervascularization of the median nerve and increased intraneural blood flow proximal to the carpal tunnel result in response to ergonomic risk factors (finger pressing and deviated wrist postures). The purposes of this study were to 1) determine the effect of a pinch posture, with and without force exerted by the finger, thumb, or both and 2) determine the effect of repetitive wrist flexion and extension on intraneural blood flow velocity in the median nerve proximal to the carpal tunnel. Eleven healthy and eleven CTS symptomatic individuals participated in this study and completed three components: 15 pinch posture force trials, 3 repetitive wrist motion trials, and 3 static wrist posture trials. Intraneural blood flow was measured using pulse wave Doppler during each trial. Main effects of pinch posture force \((F_{4,80} = 21.397, p < 0.001)\) and wrist posture \((F_{2,40} = 14.545, p < 0.001)\) were observed. Trials where force was applied by the finger \((2.21 \text{ cm/s})\), thumb \((2.22 \text{ cm/s})\) or both \((2.34 \text{ cm/s})\) produced higher intraneural blood flow velocities than trials with no force \((1.79 \text{ cm/s})\) or relaxed hand \((1.89 \text{ cm/s})\). Trials performed in flexion \((2.24 \text{ cm/s})\) were greater than neutral \((2.06 \text{ cm/s})\) and extension \((1.97 \text{ cm/s})\). No interactions or main effects of time were found in response to repetitive wrist motion. These results suggest that at low force levels \((6 \text{ N})\) it’s not how the force is applied but rather that the force is being applied that has an effect on the median nerve. Additionally these results suggest that the contribution of repetitive motion to the development of CTS may not be directly to the median nerve.
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Chapter 1: Introduction

Carpal tunnel syndrome (CTS) is a clinical syndrome involving compression of the median nerve within the carpal tunnel. CTS is the most commonly reported peripheral neuropathy affecting 5% of the working population and 1% of the general population (Concannon et al, 1997). Many epidemiological studies have assessed the prevalence, incidence, and associated risks of CTS. The prevalence of CTS is high in jobs with highly repetitive motions, deviated wrist postures, and forceful pinching (Silverstein et al, 1987, Viikari-Juntura and Silverstein, 1999; Van Rijn et al, 2009). Further, combining these risk factors increases the risk of developing CTS (Silverstein et al, 1987). To ultimately prevent or reduce the incidence of CTS, it is important to go beyond correlational relationships to understand the physiological mechanisms of CTS.

The median nerve is a highly vascularized structure and is dependent on its blood supply. Median nerve blood supply can be altered by compressive pressures as low as 20 mmHg (Rydevik et al, 1981; Lundborg et al, 1983). The median nerve may be compressed by structures within the tunnel or by an increase in hydrostatic pressure (known as carpal tunnel pressure or CTP). Elevated CTP has been associated with altered nerve function by collapsing the capillaries within the nerve (Gelberman et al, 1981; Lundborg et al, 1982) leading to altered blood flow and symptoms associated with CTS (pain, tingling, numbness, decreased sensation in fingers innervated by the median nerve, and thenar muscle weakness/atrophy). Differences in resting CTP have been found between healthy individuals and those with CTS. Healthy individuals typically have CTP
below 10 mmHg, while those with CTS have measured pressures of 30 mmHg in neutral wrist and hand postures (Gelberman et al, 1981, Seradge et al, 1985; Luchetti et al, 1989). When pressures of 30 mmHg have been induced in healthy individuals, symptoms of CTS develop (Lundborg et al, 1982), suggesting 30 mmHg as a threshold for functioning of the median nerve (Keir et al, 2007). Occupational risk factors such as repetitive motion, deviated wrist postures, pinching, and finger pressing place the median nerve at risk by elevating CTP (Keir et al, 1997; Keir et al, 1998; Rempel et al, 1998; Clark et al, 2004).

Extensive research has analyzed the effects of wrist posture and finger force on CTP. In healthy individuals, wrist deviation of 50° has been shown to elevate CTP to 35-60 mmHg in extension and 18-35 mmHg in flexion (Werner et al, 1997; Keir et al, 1997; Keir et al, 1998). In individuals with CTS, pressure levels have been observed up to 90 mmHg with wrist flexion and 110 mmHg with extension (Gelberman et al, 1981). CTP is also elevated by finger-pulp presses (Rempel et al, 1997; Keir et al, 1998b) and pinching (Keir et al, 1998b; McGorry et al, 2014). Further, the application of force in wrist flexion and even more in wrist extension elevates CTP to a greater extent (Luchetti et al, 1998).

Pinch grip has received attention due its relationship to CTS in epidemiology studies (Silverstein et al, 1987). Based on these epidemiological findings, Keir et al (1998b) found significantly higher CTP when pinching than with fingertip pressing with equal force requirements. As well, the thenar muscles have also received attention due to their involvement with pinching but also their effect on the shape of the carpal tunnel. Shen and Li (2013) found that thenar muscle activation pulls on the transverse carpal ligament, opening the carpal tunnel. As this would suggest pinching is a positive action,
alternative mechanisms must be occurring from within the tunnel to result in elevated CTP.

CTS has been shown to be a vascular issue in which altered nerve function occurs as a result of compression, leading to ischemia in the capillaries that feed the median nerve (Lundborg et al, 1982). CTP has been used as an indicator of nerve compression, with higher pressures associated with retarded blood flow, however CTP is an indirect measure of blood flow changes within the nerve. Measurement of intraneural blood flow, using ultrasound, has provided insight into the vascular mechanisms involved with the median nerve (Mallouhi et al, 2004; Joy et al, 2011; Evans et al, 2012a; Evans et al, 2012b; Wilson, 2013). Intraneural blood flow has been examined in neutral wrist and relaxed hand postures to evaluate connections between vascular flow and CTS diagnoses (Mallouhi et al, 2004; Joy et al, 2011; Evans et al, 2012a; Evans et al, 2012b). Wilson (2013) used ultrasound to evaluate the effects of occupational risk factors (fingertip pressing and wrist posture) on intraneural blood flow. It was found that the fingertip force and wrist posture independently increased intraneural blood flow. Thus it is necessary to examine the effect pinching may have on intraneural blood flow as well.

Repetitive motion of the fingers and wrist is common in the workplace and has been identified as an ergonomic risk factor for the development of CTS (Silverstein, 1986). More specifically, a measured increase in CTP has been found in occupations (i.e. those involving typing) with repetitive use of the fingers in deviated wrist postures (Rempel et al, 2008). However the direct effect of repetitive wrist motion on CTP has not been examined extensively. One study showed an increase in CTP after one minute of
passive wrist motion in CTS individuals (Szabo and Chidgey, 1989). Seradge et al (1995) tried to replicate these findings with active motion, however they were unable to confirm the previous results. Much of the research involving repetitive motion has focused on the flexor tendons and subsynovial connective tissue. Frictional work between longitudinal movement of the tendons, subsynovial connective tissue (Kociolek et al, 2015), and the median nerve has been measured in cadavers and in vivo (Zhao et al, 2010). Flexor tendons were moved through the tunnel and increased levels of friction between the tissues were measured at higher levels of induced (with a catheter) CTP. This demonstrated that persistent friction through tissue motion and elevated CTP could lead to the development of CTS (Zhao et al, 2010). However minimal work has examined the direct effects of repetitive motion on the median nerve itself.

Individuals with CTS have been seen to have a more vascular median nerve than healthy wrists (Mallouhi et al, 2004; Joy et al, 2011). Previous studies have used ultrasound to examine median nerve intraneural blood flow in the hopes of understanding the physiological mechanisms associated with the development of CTS. This study will examine intraneural blood flow using the components of a pinch grip (third finger and thumb) using ultrasound. As well, the effects of repetitive wrist motion will be explored.
Chapter 2: Review of the Literature

2.1 Anatomy of the Carpal Tunnel

The carpal tunnel is a small region of the wrist that is bordered by the carpal bones and the transverse carpal ligament (TCL) (Figure 1). In the carpal tunnel there are 4 flexor digitorum superficialis tendons, 4 flexor digitorum profundus tendons, the flexor pollicis longus tendon, the median nerve, and surrounding synovium and subsynovial connective tissue (SSCT). In healthy wrists, the SSCT connects to and aids in the movement of tendons and the median nerve. It is hypothesized that the SSCT helps protect structure of the carpal tunnel and its contents by acting as a sliding guide (Guimberteau, 2001). The median nerve traverses the carpal tunnel and branches into the recurrent and palmar digital nerves. The recurrent branch of the median nerve lies distal to the carpal tunnel and contains sensory nerve fibres for the first three and a half digits and motor nerve fibres for the thenar muscles (opponens pollicis, abductor pollicis brevis and flexor pollicis brevis).
**2.1.1 Carpal Tunnel Dimensions**

Carpal tunnel dimensions have been shown to change with wrist posture. In 14 healthy individuals, Skie et al (1990) found that the cross sectional area at the distal carpal tunnel (hook of the hamate) changed as a function of wrist posture. Wrist flexion resulted in the smallest area (1.36 cm²) followed by a neutral (1.52 cm²) and extended wrist (1.75 cm²) (Skie et al, 1990). Yoshioka et al (1993) also found an increased carpal tunnel area in wrist extension and decreased area in flexion at the distal carpal tunnel however, this was not consistently the case along the length of the tunnel (Yoshioka et al, 1993; Bower et al, 2006). In response to wrist flexion and extension, the carpal tunnel area decreased at the level of the pisiform, contrary to results found at the hook of the hamate. To address the inconsistencies seen with carpal tunnel area, the volume of the carpal tunnel in response to wrist deviation has been assessed (Bower et al, 2006 with...
Mogk and Keir, 2008). A correction factor was used to correct for parallax errors in deviated wrist postures resulting in the smallest carpal tunnel area in wrist flexion and, contrary to previous work, largest in a neutral wrist rather than extended wrist. The correction factor significantly reduced the volume in both flexed and extended wrist postures with the smallest volume in wrist extension (Bower et al, 2006). Mogk and Keir (2008) found that extension decreased the cross sectional area of the tunnel when the cross section was made perpendicular to the carpal tunnel.

The shape of the carpal tunnel is also affected by the thenar muscles which originate on the transverse carpal ligament (TCL). The TCL spans from the scaphoid and trapezium on the radial side to the pisiform and hook of the hamate on the ulnar side (Garcia-Elias et al, 1992). Shen and Li (2013) examined the relationship between the thenar muscles and the TCL during a pinching task. When the thenar muscles are activated, as in pinching, they pull on the ligament. As pinch force increased, the carpal arch (the region in the carpal tunnel formed by the bowing of the TCL) narrowed and the area increased (Shen and Li, 2013). This effect depended on the magnitude of the pinching force as well as wrist posture. As pinching force increased from 0% to 100%, the carpal arch area increased from 22.2 mm to 27.3 mm, the height increased from 1.8 mm to 2.3 mm, and the width decreased from 23.9 mm to 23.1 mm (Shen and Li, 2013). Thus, activation of the thenar muscles appears to increase the carpal arch area. This suggests that pinching is beneficial for the median nerve, thus there must be alternative explanations to why pinching poses a risk to the median nerve.
2.1.2 Median Nerve Vasculature

The median nerve has a complex vascular system which includes blood supply from what are known as the extrinsic and intrinsic microvascular systems. The extrinsic system is comprised of segmentally arranged blood vessels that are derived from nearby arteries and veins (Lundborg, 1975). This system is coiled to prevent occlusion during movement (Figure 2) (Lundborg, 1975). The extrinsic vessels stem from nearby arteries and connect to the epineurium, they divide into ascending and descending branches, becoming the intrinsic system. These branches separate and reconnect throughout the nerve allowing blood to flow in multiple directions (Lundborg 1970). The intrinsic system includes the epineurial, perineurial, and endoneurial layers (Figure 2). The epineurium is largest and outermost layer of the nerve. Inside the epineurium, the perineurium forms multiple fascicles located throughout the epineurial space. Many axons within a fascicle make up the endoneurium. Over time, if occlusion occurs within the intrinsic system, the extrinsic system will compensate, likewise, the intrinsic system will compensate for an extrinsic occlusion (Lundborg, 1970). This occurs through the development of newer and larger intraneural blood vessel in response to continued occlusion. The tendons and SSCT also have an intricate vascular system supplied by the extrinsic system. The highly vascularized SSCT provides a means of blood supply to the flexor tendons (Guimberteau et al, 1993).
Figure 2. Anatomical structure of the median nerve showing the extrinsic system – connecting vessels from nearby arteries into the nerve allowing sliding of the nerve; and the intrinsic system - containing the epineurium, perineurium, and endoneurium (from Lundborg, 1988).
2.2 Factors Affecting the Median Nerve

In the carpal tunnel, compression of the median nerve may occur through increased carpal tunnel pressure (CTP) or local contact stress from other structures. Compression of the median nerve affects nerve function and conductivity by altering blood supply, reducing axonal transport (Rydevik et al, 1980; Dahlin et al, 1984), and producing physical damage to the nerve sheath (Figure 3) (Viikari-Juntura and Silverstein, 1999). Early research examined the effects of ischemia and mechanical compression on peripheral nerves. Pressures of 50-600 mmHg were applied with a cuff to isolated rabbit tibial and sciatic nerves from 15 minutes to 6 hours with injury outcome affected by the magnitude and duration of compression (Rydevik and Lundborg, 1977). Lower levels of compression (50 mmHg) for relatively short time periods (2 hours) caused damage to the epineurium (outer layer) of the nerve by increasing its permeability resulting in epineurial edema (Rydevik and Lundborg, 1977). Larger magnitudes of compression (600 mmHg) resulted in damage to endoneurial vessels leading to endoneurial edema (Rydevik and Lundborg, 1977). In a rabbit model, Lundborg (1970) found a breakdown of the perineurium after eight hours of ischemia resulting in endoneurial edema with increased endoneurial pressure. Compression induced ischemia alters the functioning of the walls of the nerve thus affecting fluid penetration and flow. The preserved nature of the endoneurium, at high pressures for extended periods of time, suggests the perineurium is highly resistant to compression, thus acts like a barrier to protect the endoneurium (Lundborg et al, 1973).
The effect of lower pressures on nerve function has also been examined. Using a rat model, Powell and Myers, (1986) observed Schwann cell degeneration and demyelination after compression of 20-30 mmHg for two hours (Figure 3). Viikari-Juntura and Silverstein (1999) proposed a cascade of nerve breakdown in which the first signs of pathology begin at pressures of 20-30 mmHg. First, a decrease in epineurial venous flow has been observed in response to compression. At pressures of 60-80 mmHg, decreased capillary flow occurs and thus increased permeability of fluid. Over time, if pressures are not reduced the perineurium permeability is altered allowing for endoneurial edema. If edema is not reduced or eliminated, Schwann cells are affected leading to their destruction through demyelination and remyelination. Demyelination affects the functioning of the nerve and results in symptoms seen in many neuropathies (Powell and Myers, 1986; Viikari-Juntura and Silverstein, 1999) (Figure 3).
Figure 3. Proposed Pathomechanics of nerve damage (Viikari-Juntura and Silverstein, 1999). First signs of pathological changes occur at 20-30 mmHg by decreasing epineurial venous flow. At pressures of 60-80 mmHg, capillary flow decreases and permeability increases leading to endoneurial edema. Over time if edema persists the endoneurial pressure remains elevated which can lead to the destruction of Schwann cells, demyelination and eventually impaired nerve function. Contact stress can result in physical destruction of Schwann cells, with emphasis on the edges of impingement zone. Contact stress can lead to decreased axonal transport and even ischemia changes.

Investigations on animal nerves have suggested that, although nerve conduction velocity has been shown to return after the cessation of mechanical compression, full function of the nerve, as measured by action potential amplitude, does not return until blood flow is fully restored (Lundborg et al, 1982). Yayama et al (2010) further demonstrated this by applying force directly to rabbit sciatic nerves with a custom compressor. The compressor had two transducer clamps that were placed directly on the nerve and elevated to different levels of measured force. An applied force of 0.49 N equated to 51.8 mmHg. Compound nerve action potential amplitudes decreased from
100% to 0% at the same compressive force levels (0.44-0.53 N) that intraneural blood flow ceased. However, intraneural blood flow begun to retard around 0.3 N of force. This established the connection between the ability of a nerve to function and the necessity of blood flow in the nerve. With the cessation of blood flow in the nerve, the nerve is effectively unable to function.

These studies demonstrate the effect of compression on nerve vasculature and function in isolated animal nerves. However, this effect has yet to be explored in vivo. Hydrostatic pressure within the carpal tunnel as well as contact stress by adjacent tissues, place pressure on the median nerve. Carpal tunnel pressure (CTP) has been examined extensively as a mechanism of compression to the median nerve.

### 2.2.1 Carpal Tunnel Pressure

A marked difference in carpal tunnel pressure (CTP) has been consistently shown between healthy individuals and those with CTS. Typically, healthy individuals exhibit resting CTP below 10 mmHg (Lundborg, 1962; Gelberman et al, 1981; Szabo and Chidgey, 1989; Keir et al, 1997) while individuals with CTS have higher resting CTP in neutral postures (around 30 mmHg) (Luchetti et al, 1989; Luchetti et al, 1998; Gelberman et al, 1981; Seradge et al, 1995). Interestingly, by elevating CTP by applying external pressure of 30 mmHg to the palm of the hand, Lundborg et al (1982) produced CTS-like symptoms in healthy individuals. As well, Dahlin et al (1984) found near complete blockage of axonal transport when 30 mmHg was applied directly to a rabbit vagus nerve, suggesting that 30 mmHg is a threshold for nerve functioning (Lundborg et al, 1982).
Further research has shown that CTP also increases in response to occupational risk factors such as deviated wrist and hand postures, application of force, and repetitive wrist motion.

2.2.1.1 Wrist and Finger Posture

Deviated wrist and finger posture have also been shown to increase CTP. Compared to the neural wrist, CTP is elevated with wrist flexion, extension and ulnar and radial deviation. (Keir et al, 2007; Gelberman et al, 1981; Rojviroj et al, 1990; Keir et al, 1997; Werner et al, 1997). CTP of approximately 30 mmHg was produced with wrist extension of 40° and flexion of 45° (Keir et al, 1998; Keir et al, 2007).

Finger posture also alters CTP. Keir et al (1998), examined metacarpophalangeal (MCP) joint posture during wrist flexion/extension motions. Depending on the wrist angle, MCP joint posture increased CTP. With wrist extension (up to 50°), a fully extended MCP joint elevated CTP more than only 45° or 90° of MCP flexion (Keir et al, 1998). However, MCP posture did not have same effect on CTP in wrist flexion. The postulated explanation for increased CTP in wrist extension with extended fingers is the extrinsic finger flexor muscle bellies entering the proximal end of the carpal tunnel. With full finger extension, the muscle bellies are pulled distally, allowing the incursion. However this was seen to a lesser effect with the fingers were flexed (MCP joint angle of 45° and 90°) and to an even lesser extent with wrist flexion. Additionally, Cobb et al (1995) found that the lumbrical muscle bellies entered the distal end of the carpal tunnel during finger flexion, elevating CTP. This effect was stronger with higher degrees of finger flexion, which explains the elevated CTP when not in wrist or finger extension.
Luchetti et al (1998) also measured CTP, but in 6 postures: a relaxed hand and a gripping hand with 1) neutral wrist, 2) 45° wrist extension, and 3) 45° wrist flexion. CTP in the gripped hand posture was consistently higher than the relaxed hand for all wrist postures with highest CTP in extension. This further supports that in wrist extension, extrinsic flexor muscle belly incursion into the carpal tunnel plays a role in CTP elevation, while in wrist flexion, lumbrical incursion into the distal carpal tunnel plays a role in CTP elevation. McGorry et al (2014) further examined type of grip through finger posture and the effect on CTP. Three grip types (relaxed hand, power grip, and pulp pinch) with resisted and non-resisted wrist motion were examined. Important to note, is that there was no grip force applied, only force through the wrist. The authors found that the no grip posture (relaxed hand) produced the lowest CTP. Surprisingly, the pinch grip posture produced the highest overall CTP, even more so than a power grip posture, especially when moving into wrist extension motion, suggesting a mechanism by which pinching becomes a risk factor in the development of CTS.

2.2.1.2 Loading of the Fingers

Finger loading via gripping, pinching, pressing, and tendon loading (in cadavers), has been shown to increase CTP (Seradge et al, 1995; Rempel et al, 1997; Keir et al, 1997; Keir et al, 1998b; Luchetti et al, 1998; Rempel et al, 2008). In full extension, statically loading the third finger elevated CTP to 37-145 mmHg from a resting level of 10-48 mmHg (Seradge et al, 1995). Further, small fingertip forces of 1-12 N, are also sufficient to elevate CTP from 20 mmHg resting to 58 mmHg at 12 N of force,
independent of deviated wrist and hand postures (Rempel et al, 1997; 2008). Using cadavers, Keir et al (1997) loaded the finger flexor tendons, palmaris longus, and flexor pollicis longus, each with a 1 kg mass, while measuring CTP through wrist flexion/extension. Loading palmaris longus and the finger flexors increased CTP significantly, independent of wrist posture. However loading flexor pollicis longus did not significantly elevate CTP. Keir et al (1998b) also found that pinching (which requires the use of the flexor pollicis longus) produced a larger increase in CTP than fingertip pressing. Pinching has been shown to elevate CTP significantly more than fingertip pressing with equal force requirements up to 15 N (Figure 4) (Keir et al, 1998b). Keir and colleagues (1998b) postulated that since the thumb is required in a pinch and the flexor pollicis longus tendon resulted in no increase in CTP, the thenar muscles must play a role in this difference (although they did not postulate with that role might be). With a significant increase in CTP with pinching forces less than 15 N, it is feasible that performing pinching tasks places an individual at an increased risk of developing CTS.
Figure 4. Carpal tunnel pressure (mmHg) for pinch and fingertip press (mean with Standard deviation). Pinch grip is approximately twice as high as fingertip pressing for force levels up to 15 N (Keir et al, 1998)

2.2.1.3 Repetitive Wrist Motion

Evidence that repetitive wrist motion increases CTP is equivocal. Repetitive flexion/extension of the wrist has been shown to increase CTP (Szabo and Chidgey, 1989). Mean CTP was approximately 11 mmHg prior to the motion in the mild/moderate CTS group. Immediately following one minute of passive motion, the mean CTP of the mild/moderate CTS group was elevated to about 26 mmHg and remained elevated for ten minutes after the motion ceased. The authors referred to this phenomenon as a “pump up” effect (Szabo and Chidgey, 1989). Seradge et al (1995) attempted to create a similar effect by having participants fully flex and extend their fingers and wrist at 0.5 Hz for one minute but did not find an increase in CTP in healthy controls or CTS individuals. Interestingly the “pump up” effect observed by Szabo and Chidgey (1989) was not observed in either the severe CTS or healthy groups. It is possible that, in the severe CTS group, the damage to the carpal tunnel was too extensive and the swelling of the tissues in the tunnel was gone and more fibrotic and shrunken tissues had begun to form. In a recent study of intraneural blood flow, a parabolic relationship of intraneural blood flow velocities was observed in mild moderate and severe CTS individuals with slower blood flow observed in mild and severe CTS individuals whereas individuals with moderate CTS tended to have higher velocities by (Evans et al, 2014). This suggests a point at which the tissues in the carpal tunnel progressed beyond these acute pathological responses.
2.2.1.4 Contact Stress

Keir et al (1997) examined two types of pressure enforced on the median nerve in the carpal tunnel. Using a catheter to measure hydrostatic pressure (CTP) and a bulb transducer to measure contact stress, Keir and colleagues measured the effect of tendon load and wrist posture. While highest CTP have been observed in wrist extension, the bulb transducer measured highest pressure in wrist flexion. The flexor tendons move palmarly during wrist flexion and can place contact stress on the median nerve. Additionally, the median nerve may also press against the transverse carpal ligament creating another source of contact stress (Smith et al, 1977). Keir et al (1997) deduced that CTP nor contact stress are sufficient in solely explaining the insult to the median nerve.

2.2.2 Median Nerve Motion

Longitudinal motion of the median nerve has been measured in response to MCP joint motion (Erel et al, 2003; Ugbolue et al, 2005) and full finger motion (Hough et al, 2007; Korstanje et al, 2012; Lopes et al, 2011). Median nerve excursion ranged from 2.6 to 12.5 mm in controls and 2.2 to 10.2 mm in CTS groups respectively (Erel et al, 2003; Hough et al, 2007; Ugbolue et al, 2005; Lopes et al, 2011). Erel et al (2003) found no significant differences in the longitudinal motion of the median nerve between groups, however there was a significant reduction in transverse motion in the affected hand.
compared to the unaffected hand of the CTS individuals. The authors postulated that longitudinal motion of the median nerve likely does not contribute to the development of CTS. However, a reduction in transverse median nerve motion, in the event of finger motion, could place the median nerve at risk for the development of CTS by not allowing it to move out from between the flexor tendons and transverse carpal ligament.

Van Doesburg et al (2012b) examined the transverse motion of the flexor tendons of the index and middle finger, as well as the FPL, in relation to the transverse motion of the median nerve during differential finger motion in CTS and healthy volunteers. They found that the median nerve had different motion patterns during flexion and extension of the index, middle, and thumb in CTS individuals than did healthy individuals. One possible explanation for this is the fibrosis of the SSCT in the carpal tunnel. Ettema et al (2007) measured the relative motion of the SSCT with the third FDS tendon during finger flexion and extension in CTS patients and healthy cadaver hands. They found that the SSCT moved with the tendon in CTS wrists but independently and smoothly in cadaver wrists. This suggests that fibrosis of the SSCT may alter, and even prevent, the motion of the tendons and median nerve independently in the carpal tunnel (Ettema et al, 2007). Fibrosis of the SSCT has been seen to alter relative motion of flexor tendons and SSCT during longitudinal motion suggesting that, although median nerve longitudinal motion may not play a contributing role in the development of CTS, longitudinal motion, although natural, may lead to adaptations of other tissues.

Longitudinal motion of the flexor tendons in deviated wrist postures have been found to increase gliding resistance between the flexor tendons and SSCT in cadavers and
healthy individuals (Zhao et al, 2007; Kociolek and Keir, 2015; Tat et al, 2015). Yoshii et al (2009), found that friction increased between the flexor digitorum superficialis tendon and SSCT but also between the tendon and median nerve. Experimentally elevated CTP in 8 cadaveric wrists resulted in increased frictional force to move the flexor tendons in the carpal tunnel (Zhao et al, 2010). Pressures of 60 mmHg and greater significantly increased frictional force from 0.075 N to 0.14 N. The authors suggest that with increased frictional force, it is more difficult to move the flexor tendons. Higher resistance on the flexor tendons through the tunnel could result in higher shear forces between the flexor tendons, SSCT, and median nerve (Zhao et al, 2010).

The median nerve also displayed different motion patterns in response to wrist flexion compared to wrist extension in healthy individuals. Wang et al (2013) tracked the median nerve in response to wrist flexion and extension in healthy individuals and found that with wrist flexion the median nerve, in healthy individuals, moves “out of the way” of the flexor tendons, which move palmarly. However in a wrist with CTS, decreases median nerve transverse motion, possibly due to SSCT fibrosis and stiffness (Ettema et al, 2004; Oh et al, 2006), may prevent this motion and result in the flexor tendons compressing the median nerve against the transverse carpal ligament (Wang et al, 2013).

2.2.3 Median Nerve Changes with Carpal Tunnel Syndrome

Adaptations in the dimensions, vasculature, and functioning of the median nerve have been observed in individuals with CTS. Measures of nerve shape such as circularity, perimeter, and cross sectional area have been used to assess the median nerve
(Wang et al, 2014a, b; van Doesburg et al 2012a; Ghasemi-Esfe et al, 2010). Using ultrasound, van Doesburg et al (2012a) found decreased circularity, larger perimeter, and larger cross sectional area in CTS median nerves compared to healthy controls. Studies by Joy et al (2011), Ghasemi-Esfe et al (2010), and Wang et al (2014b) also observed larger nerve cross sectional area in CTS individuals compared to healthy controls.

Changes in finger and wrist postures have also shown to produce changes in the size and shape of the median nerve (Wang et al, 2104b).

Wang et al (2014b) assessed the effect of wrist movement and finger postures on median nerve deformation using nerve cross sectional area, perimeter and circularity. Circularity of 1 meant the nerve was perfectly round and any value great or less than 1 indicated a deviation from the circle (Wang et al, 2014b). Twenty wrists of 13 CTS individuals and 20 wrists of 10 healthy individuals moved from neutral to maximal wrist flexion and from neutral to maximal wrist extension for three cycles with flexed and extended fingers. Median nerve circularity in CTS individuals decreased in wrist flexion with fingers flexed (circularity deformation ratio from resting to flexion = 1.25 ± 0.28) and wrist flexion with fingers extended (1.23 ± 0.16) significantly less than healthy individuals (1.57 ± 0.36 and 1.49 ± 0.38 respectively). The shape of the median nerve has implications for blood flow within the nerve. A more engorged, or swollen nerve may have excess fluid (edema) present, impeding blood flow within the nerve (Joy et al, 2011). In contrast to this, a more engorged, or swollen nerve could also be explained by an increase in the size and number of blood vessels (hypervascularization) in the median nerve (Mallouhi et al, 2004). The difference in these two explanations depends primarily
on the time difference. The process of hypervascularization would occur over a prolonged period of time in which the nerve would have time to adapt and develop the blood vessels within it. Thus the development of hypervascularization is to help with a lack of blood flow distal to the impingement and thus, upon observation, the nerve appears swollen and engorged.

Mallouhi et al (2006) examined a variety of measures and tried to relate them to the presence of CTS using grey scale and colour Doppler ultrasound. Nerve edema, swelling (cross sectional area), nerve flattening, bowing of the flexor retinaculum, and nerve hypervascularization were compared for sensitivity, specificity, accuracy, and positive and negative predictability of CTS. Nerve edema is the presence of fluid in the nerve. Presence of edema was examined qualitatively, by a sonographer, when a more hypoechoic nerve was viewed with ultrasound compared to a healthy nerve which presence as bundles of fascicles (hypoechoic regions) surrounded by epineurial connective tissue (hyperechoic regions). Swelling was considered present when a cross sectional area of the median nerve was greater than 0.11 cm². Nerve flattening was defined as an increase in the nerve’s major axis with a major to minor axis flating ratio of at least 3. Bowing of the flexor retinaculum was determined by an increase in the palmar apex of the ligament of at least 2 mm measured between the hamate and trapezium. Nerve hypervascularization was characterized by the presence of excess vascular structures not seen in a healthy nerve. Their presence was determined by an expert sonographer (Mallouhi et al, 2004). Using a logistic regression, nerve hypervascularization was the only measure to independently predict the presence of CTS.
as confirmed by nerve conduction studies (Mallouhi et al, 2004). The exact mechanism behind hypervascularization proximal to the carpal tunnel is not fully understood. Ischemia has been shown to occur at a site of chronic nerve compression leading to edema and increased nerve cross sectional area proximal to the site of compression (Rydevik and Lundborg, 1977; Rydevik et al, 1981). Thus, hypervascularization proximally could be due to ischemia distally (Lundborg et al, 1982; Joy et al, 2011). Mohammadi et al (2012) found a significant correlation between hypervascularization and severity of CTS as well as between hypervascularization and cross sectional area of the nerve. This suggests that it is important to examine the cross sectional area of the median nerve as well as the presence of vascular changes from a healthy nerve as an indicator of CTS development.

The presence of hypervascularization proximal to the carpal tunnel has been described qualitatively, as a significant predictor of CTS (Mallouhi et al 2004) and recently has been measured as increases in intraneural blood flow. Joy et al (2011) found increased intraneural blood flow in both highly likely and indeterminate groups with higher velocities in the highly likely CTS group (mean 13.3 ± 8.2 cm/s) than the indeterminate CTS group (mean 8.5 ± 4.5 cm/s). Furthermore, intraneural blood flow showed the high sensitivity for testing for highly likely CTS diagnosis (83%) along with nerve conduction studies (83%). In testing for indeterminate CTS, intraneural blood flow had a higher sensitivity (73%) compared to nerve conduction studies (47%) (Joy et al, 2011). Thus measuring intraneural blood flow using ultrasound is a viable tool to assess CTS risk.
Evans et al (2012a) examined whether ultrasound could be used to measure differences in intraneural blood flow waveforms between CTS and healthy individuals. Further they examined how intraneural blood flow measures related to three provocative CTS tests (Tinel’s test, Durkan’s test, and Phalen’s maneuver). Tinel’s test is performed by tapping or percussing over the carpal tunnel to elicit symptoms of CTS (Tinel, 1915). Durkin’s test is a modified version of Tinel’s test. Constant pressure is placed over the carpal tunnel for 30 seconds to elicit symptoms of CTS (Durkan, 1991). Lastly, Phalen’s test is performed by placing the subject’s hands at 90° of flexion for one minute to elicit symptoms (Phalen, 1972). Intraneural blood flow was measured at the proximal wrist crease, mid-tunnel, and distal wrist crease. No differences were observed in the blood flow velocities with a relaxed and neutral hand and wrist. However, blood flow increased in the mid-tunnel and decreased at the proximal wrist crease when exposed to multiple provocative CTS tests (Evans et al, 2012a). This suggests that not only is increased intraneural blood flow present in CTS individuals but it is also altered in response to acute changes in posture and force placed on the carpal tunnel.

Recently, acute changes to intraneural blood flow were observed when the median nerve was exposed to non-neutral wrist postures and fingertip loading in both healthy controls and individuals with CTS symptoms (Wilson, 2013). It is understood that a decrease in blood flow at the level of the carpal tunnel, via increase CTP or mechanical compression, creates a state of hyperemia, or increased blood flow, proximal to the carpal tunnel. This is believed to be a compensatory response to the lack of blood flow distally. Wilson (2013) used colour and pulse wave Doppler ultrasound to image intraneural blood
flow at the proximal wrist crease in flexed and extended wrist postures, with and without fingertip force. The pulse wave Doppler window (1 mm) was placed over the median nerve to measure intraneural blood flow (Figure 5). Pulsatile (Figure 5A) and non-pulsatile flow (Figure 5B) was observed in individuals with CTS symptoms and controls. The application of fingertip force (6 N) and more deviated wrist postures (15° and 30° flexion and 30° extension) resulted in increased intraneural blood flow (Figure 6) (Wilson, 2013). The effect of wrist posture was stronger in flexion than in extension. A significant increase was only seen at 30° of extension where increases were seen at 15° of flexion suggesting wrist flexion has more of an effect on intraneural blood flow. Wilson (2013) did not show a significant statistical difference between CTS symptomatic (3.34 cm/s) and healthy control groups (3.03 cm/s) (Wilson, 2013), however other work has noted increased flow in CTS individuals (Joy et al, 2011). Joy et al (2011) measured intraneural blood flow in 29 highly-likely CTS hands with a mean velocity of 13.3 ± 8.2 cm/s and 25 indeterminate CTS hands with a mean velocity of 8.5 ± 4.5 cm/s which were both significantly greater than the control group with a mean velocity of 1.9 ± 2.8 cm/s. A large difference in velocities between studies is likely due to the population sample. Wilson (2013) did not have individuals with severe or clinically diagnosed cases of CTS. Wilson (2013) was also limited because the deviated wrist postures and applied force both elicited symptoms of CTS and presented discomfort in many individuals with CTS or severe symptoms. Wilson (2013) had a subset of participants return to test for reliability. No significant differences were observed in intraneural blood flow velocity
from week 1 to week 2. The reliability of using ultrasound to measure intraneural blood flow was found to be high.
2.3 Diagnostic Techniques

Clinical diagnoses of CTS are typically confirmed with electrodiagnostic testing also known as nerve conduction studies. Despite being the current gold standard, nerve
conductive studies have been known to deliver both false positives and negatives (Werner and Andary, 2002). Thus supplementary and alternative measures have been used and developed to aid in diagnosing CTS. Various provocative tests (i.e. Phalen’s test) and symptom hand diagrams, which provide a score of symptom severity as well as location and type of symptoms experienced (Katz Hand Diagram and Levine’s Carpal Tunnel Questionnaire), have proved useful (Katz and Stirrat, 1990; Levine et al, 1993).

Provocative and clinical tests act to elicit symptoms associated with the condition. Phalen’s test places the subject in full wrist flexion for one minute. If symptoms of CTS develop, such as pain, tingling, and numbness in the thumb and/or the index, third, and half of the fourth fingers, the test is considered positive (Phalen, 1972; Georgiew, 2007). The Katz Hand Diagram is used to locate specific signs and symptoms of CTS as well as where they were located (Dale et al, 2008). Levine’s Carpal Tunnel Syndrome Questionnaire assesses symptom severity and functional scale of symptoms in a typical 24 hour day in the previous two weeks (Levine et al, 1993). As well, these tools can be used to categorize individuals as healthy or CTS and categorize the CTS severity.
2.4 Summary

Occupational risk factors such as pinching, deviated wrist postures, and repetitive motion are associated with increased risk of the development of CTS at work. Thus further examination into the effects of pinching on CTP were conducted. Pinching produced a greater increase in CTP than fingertip pressing for equal force requirements. As well, pinching requires the use of the thenar muscles however, activation of the thenar muscles increased the carpal tunnel area. An increase in carpal tunnel area suggests a decrease in CTP. Thus the effect of pinching on the carpal tunnel is unclear and further investigation is warranted.

A larger median nerve, via edema or hypervascularization, has been observed in CTS individuals. Early work demonstrated the effects of compression on blood flow within the nerve. We now have the ability to use ultrasound to measure the blood flow within the median nerve. An investigation into intraneural blood flow velocity in response to pinching and finger and thumb pressing may provide insight into how pinching poses a risk to the median nerve. Studies have also linked highly repetitive work to the incidences of CTS cases. Thus, the median nerve intraneural blood flow may also be affected by repetitive wrist motion.
2.5 Purposes

1) To test the effect of a pinch grip on intraneural blood flow of the median nerve at the wrist using 3 wrist postures (0° 30° flexion, 30° extension) in healthy and CTS symptomatic individuals with and without force applied by the third finger, thumb, and a combination of both fingers (a pinch).

2) To determine the effect of repetitive wrist motion on intraneural blood flow in healthy and CTS symptomatic individuals.
   - Tested at wrist postures of 0° 30° flexion, 30° extension after the motion.

2.6 Hypotheses

1) Posture will independently increase intraneural blood flow.
   a) Wrist flexion and extension will increase blood flow relative to neutral
   b) A pinch posture will increase blood flow relative to a relaxed hand

2) Applying force will increase intraneural blood flow
   a) Pinching with force by both the third finger and thumb, will increase blood flow greater than the third finger pressing alone, which will be greater than thumb pressing alone

3) Repetitive wrist motion will increase intraneural blood flow after each three-minute block of motion.

4) CTS symptomatic individuals will have higher intraneural blood flow velocities compared to the healthy individuals in all conditions
Chapter 3: Methods

3.1 Participants

Eleven healthy (8 female, 3 male) and eleven CTS symptomatic (10 female, 1 male) individuals aged 20-55 years participated in this study. An attempt to age match by group was made (approximately the same mean age). Each participant filled out a questionnaire to screen for upper extremity musculoskeletal disorders (Appendix A). All participants were required to be free of arthritis of the wrist and/or hand, previous wrist surgery, Colles fracture, radial malunion, degenerative joint disease, gout, sarcoidosis, amyloidosis, hypothyroidism, and diabetes mellitus. All participants provided informed written consent prior to data collection. This study was approved by the Hamilton Integrated Research Ethics Board (Appendix D).

Participants were categorized into a “healthy” or “CTS symptomatic” group. Categorization was based on participant reported symptoms as well as through the use of a provocative test (Phalen’s test) and two questionnaires: Levine’s Carpal Tunnel Syndrome Questionnaire (Appendix B) and Katz Hand Diagram (Appendix C). A positive Phalen’s test and/or a score greater than zero on either questionnaire placed the participant in the CTS symptomatic group. Phalen’s test was conducted by placing the participant’s wrist in 90° of flexion for one minute. A positive test was indicated by the production of any pain, tingling, or numbness in the first 4 fingers. Levine’s Carpal Tunnel Syndrome Questionnaire has two components, the symptom severity scale and functional status. The symptom severity scale scores range from 0-4 with 0 (no
symptoms), 1 (mild), 2 (moderate), 3 (severe) and 4 (very severe). The functional status scores also range from 0-4. Interpretations are similar with 0 as ‘none’ and 4 as ‘severe’. Katz Hand Diagram required the participant to place symbols associated with different symptoms of CTS (pain, tingling, numbness, decreased sensation) on a diagram of the hand. Scores range from 0-3. Score interpretations include: 0 (unlikely), 1 (possible), 2 (probable), and 3 (classic) (Appendix C).

3.2 Experimental Setup and Data Collection

This study was comprised of three components all performed during one 2-hour collection: (1) a series of 15 pinch and finger force trials, (2) three repetitive wrist motion trials, and (3) static measurements of the median nerve. Trials were performed in the same order for each participant (pinching trials, followed by repetitive wrist motion trials, then cross section trials). However, the order of each of the conditions within each component were block randomized. All participants completed all three components.
Figure 7. Experimental Protocol. Healthy and CTS symptomatic groups completed three sections. First a series of 15 pinch and finger force trials, 5 measures in three wrist postures: extension (E), neutral (N), and flexion (F). Second, 3 repetitive motion trials, moving at 45 cycles per minute, starting and stopping in each of extension (E), neutral (N), and flexion (F). Third, 3 static measures of a cross section of the median nerve at the distal wrist crease. Each of the sections...
3.2.1 Pinching Trials

An apparatus was made to allow measurement of the force contribution of the middle finger and the thumb in a pinch grip while allowing different wrist postures. The experimental apparatus was adjusted to fit the anthropometrics of each participant prior to starting each component. Participants were seated with their right arm adducted and forearm fully supinated. The elbow was positioned at approximately 120° of extension. The forearm and hand were supported by two padded surfaces. The padded surface beneath the hand was positioned to support the hand in each of three wrist postures (0°, 30° flexion, 30° extension). The fixture axis of rotation aligned with the wrist centre of rotation between the two padded surfaces. The tips of the thumb and third finger were held in a pinching posture by two metal rings each secured to a uniaxial force transducer (MLP50, Transducer Techniques, Temecula, CA, USA) to measure the applied force exerted by the thumb and third finger independently (Figure 8).
Each participant performed 15 finger force trials (3 with a relaxed hand and 12 while applying force in a pinching posture). The trials consisted of three wrist postures (30° extension, neutral, and 30° flexion), with five conditions, four of which were in a pulp pinch posture. The trials included (i) relaxed hand (fingers not in rings, ii) pinch posture - no force, iii) pinch posture - 6 N thumb force, iv) pinch posture - 6 N force by third finger, and v) pinch posture - 6 N force applied by both the third finger and thumb.

Visual feedback for both the thumb and third finger forces were provided using a custom program (Labview 8.5, National Instruments, Texas, USA) and displayed on a monitor. Target lines were displayed on the screen for the participant. Two lines, one at
5.5 N and one at 6.5 N, presented the acceptable range of ± 0.5 N. Applied thumb and finger forces were also displayed to inform the participant how hard they were pressing. Forces were collected at 30 Hz.

Participants maintained the 6 N force for a minimum of 1 minute, and up to 3 minutes to allow the blood flow to reach steady state. From this trial, 5 measures of intraneural blood flow were obtained. The manner in which the measures were obtained was consistent with previous work by Wilson (2013), which was found to be reliable within and between groups (measures of both healthy and CTS symptomatic groups obtain 1 week apart). The participant was instructed to aim for the center of the force target lines (6 N). For the relaxed hand and no force pinch posture conditions, the force target lines were removed. A force of 6 N was chosen to remain consistent with previous literature but it was also the value seen to elicit CTP of 30 mmHg during a pinch, a possible threshold for CTS symptom development (Keir et al, 2007). This force level was not sufficient to elevate CTP to 30 mmHg during a finger press, however the forces to reach that level (~15 N) were too difficult to maintain.

The median nerve was imaged proximal to the carpal tunnel and intraneural blood flow was measured at the end of each pinching condition. The probe was held in position by a clamp which maintained a constant force on the wrist. Each condition was held for a minimum of 1 minute and up to 3 minutes to ensure steady flow and avoid placing the participant in any unnecessary discomfort. A minimum of two minutes of rest was provided.
Blood pressure was monitored and recorded during the collection of each trial to provide insight into whether blood pressure played a role in blood flow changes. Blood pressure was monitored on the left third finger (NexFin Continuous Non-invasive Blood Pressure Monitor, Bmeye Monitor Series (St.Louis, Missouri, U.S.A.) was used to monitor blood pressure on the left third finger throughout the study. Blood pressure was recorded at the same time as each of the intraneural blood flow measures.

3.2.2 Repetitive Wrist Motion

The same apparatus was used for the repetitive motion trials as the pinch force trials with the components of the apparatus for the pinch removed. The supinated forearm was placed in the apparatus, with the elbow at approximately 120° of extension, while the participants actively flexed and extended their wrist from 45° flexion to 45° extension with extended fingers, for three trials of three minutes (Figure 9). Padded surfaces indicated the end range of motion. Participants touched the pads in each direction to ensure consistent motion. Three trials were completed. Each trial started and stopped in one of three wrist postures: 0°, 30° flexion, 30° extension. Three postures were used to see if a posture played a role in measuring elevated pressure. Pilot work demonstrated that frequencies greater than 0.75 Hz and durations longer (tested to 5 minutes) were too strenuous for young healthy adults. Thus, a metronome was used to guide the participant at 45 cycles per minute (0.75 Hz) for 3 minutes. Wood wedges were used to position the wrist in the appropriate starting and ending wrist posture. Once the trial was initiated, the wood block was removed. Rest periods of at least 2 minutes were
provided between conditions to allow the tissues and blood flow to return to a rested state and to avoid fatigue. By this time, intraneural blood flow had returned to resting levels. Intraneural blood flow velocity was measured proximal to the carpal tunnel at the start and end of the 3 minute trial. The participant was instructed to hold still while the intraneural blood flow velocity was obtained. Blood pressure was measured on the left third finger throughout the trials at the same time as the intraneural blood flow velocity.

**Figure 9.** Repetitive wrist motion experimental setup for wrist flexion, neutral and extension start and end postures. Wood blocks to position participant wrist into start and stop positions for flexion (2), neutral (3), and extension (4). The end range of motion pad for extension (1) and end range of motion for flexion (5) are noted in the figure.

### 3.2.3 Static Measures of the Median Nerve

To examine cross sections of the median nerve between both groups (healthy and CTS symptomatic) and in response to wrist postures, participants were instructed to extend their fingers and hold three wrist postures (30° extension, 0°, and 30° flexion).
The ultrasound probe was positioned perpendicular to the wrist and transverse images of the carpal tunnel at the distal wrist crease was obtained in each wrist posture. Each posture was held until the investigator was able to obtain a clear image of the median nerve. The image was obtained with the ultrasound probe perpendicular to the participant’s forearm.

### 3.3 Ultrasound Measurement of Intraneural Blood Flow

Both longitudinal and transverse images of the median nerve were obtained in this study. To avoid altering intraneural blood flow, minimal pressure was placed on the wrist by the transducer. Longitudinal gray scale images of the median nerve were obtained using an ultrasound machine (Vivid Q, General Electric Healthcare, Milwaukee, WI) with a 12 MHz linear array transducer (12L, General Electric Healthcare). The ultrasound transducer was placed on the palmar surface of the wrist at the proximal wrist crease. Ultrasound gel was used as a contact medium between the transducer and the participant’s skin. A gel standoff pad (Aquaflex Gel Pad; Cone Instruments, Solon, OH) was used to increase the imaging depth of the nerve as the nerve is located 0.25-0.50 cm below the skin and the minimum focal point of the transducer is 0.50 cm (Wilson, 2013).

The upper extremity artery setting was used for intraneural blood flow imaging (Table 1). Pulse wave Doppler, collected in duplex mode, with spectral waveform and live grey scale imaging was used to obtain a waveform of the blood flow. Colour Doppler was used to qualitatively identify a region of blood flow within the median nerve (Wilson, 2013). However no longitudinal colour maps were observed for this study. The
pulsed wave Doppler gate (1 mm) was positioned over the median nerve until an intraneural blood flow signal was found. If a pulsatile signal was obtained, the peak systolic blood flow velocities were measured and averaged across five cardiac cycles. If no pulsatile signal was obtained, a non-directional, non-pulsatile signal was used. In both cases, 5 measures of intraneural blood flow velocity were obtained to ensure a consistent signal and reliable measure were obtained. Since non-pulsatile flow has no discernable peak systolic flow, measurements were taken based on the alignment of the ECG QRS complex of the radial artery with the pulse wave Doppler tracing of the median nerve. To ensure a stable signal was present, five seconds of steady state flow was required (Wilson, 2013). Electrocardiography (ECG) was used to measure heart rate during all conditions by placing electrodes on the clavicles and lower left rib (Wilson, 2013).

**Table 1. Optimized Ultrasound Parameters (Wilson, 2013)**

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<thead>
<tr>
<th>Parameter</th>
<th>Specification</th>
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<tr>
<td>Probe</td>
<td>12 MHz linear (12L)</td>
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<tr>
<td>Application</td>
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<td>Depth</td>
<td>3.0 cm</td>
</tr>
<tr>
<td>Frequency</td>
<td>12 MHz</td>
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<tr>
<td>Continuous Tissue Optimization (CTO)</td>
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<tr>
<td>CTO Gain</td>
<td>55-65</td>
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<tr>
<td>Pulse Repetition Frequency (PRF) / Scale Low</td>
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<tr>
<td>B-Mode Gain</td>
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<tr>
<td>Compound</td>
<td>ON</td>
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<tr>
<td>Power</td>
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</tr>
<tr>
<td>Colour/PW Frequency</td>
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</tr>
</tbody>
</table>
3.4 Data Analysis

3.4.1 Intraneural Blood Flow Velocity

Grey scale images were exported to the ultrasound post processing program for analysis (EchoPac, General Electric Healthcare, Easton Turnpike, Fairfield, USA). If pulsatile flow was observed, an average of five peak systolic velocities across three cardiac cycles was calculated. If pulsatile deflections were not observed, peak systolic velocities across a consistent 5 seconds of steady state was calculated. Using the estimated location of peak systolic blood flow from the radial artery QRS wave peak measure, the highest intraneural blood flow velocities were obtained across 5 cardiac cycles. The ECG signal was used to confirm a pulsatile signal in the Doppler tracing with the alignment of the pulsations with the cardiac cycles.

3.4.2 Static Measures of the Median Nerve

Transverse grey scale images of the carpal tunnel at the distal wrist crease were obtained in neutral, flexed and extended wrist postures (Figure 9). Images were analyzed using EchoPac (EchoPac, General Electric Healthcare, Easton Turnpike, Fairfield, USA). The median nerve cross sectional area and circumference were obtained using a tracing tool in the ultrasound post-processing program (EchoPac, General Electric Healthcare). The inner rim of the nerve was measured and rounded to the nearest 0.01 cm² for area and 0.01 cm for the circumference. From the area and circumference, the median nerve circularity was calculated using the formula:
\[ \text{circularity} = \frac{4\pi \text{area}}{\text{circumference}^2} \]

The median nerve width was measured as the widest point in the radial/ulnar direction. The height was the largest distance perpendicular to the width (Erel et al, 2003). Each of the median nerve cross sectional area/circumference inner rim trace, the median nerve height, and median nerve width were measured 3 times to ensure consistency and reliability.

Figure 10. Transverse cross section of the median nerve in a neutral wrist posture obtained with ultrasound image in b-mode. Radius and ulnar are noted on the image. The median nerve inner rim is traced. The ECG signal was not used in this measure.
3.5 Statistical Analysis

A 5 (grip) × 3 (wrist posture) × 2 (group) mixed measures ANOVA was used to test the effect of pinch grip (5 levels: relaxed hand, pinch posture with no force, thumb force, third finger force, and a pinch with both third finger and thumb force) and wrist posture (3 levels: 30° extension, 0° neutral, and 30° flexion) between healthy control and CTS symptomatic groups on peak intraneural blood flow velocity (cm/s). A 2 (time) × 3 (wrist posture) × 2 (group) repeated measures ANOVA was used to test the effect of repetitive wrist motion on intraneural blood flow after 3 minutes of motion with three different wrist posture starting and ending points (30° extension, 0° neutral, and 30° flexion). A 5 (grip) × 3 (wrist posture) × 2 (group) mixed measures ANOVA was used to test the effect of pinch grip and wrist posture between healthy control and CTS symptomatic groups on mean arterial pressure (mmHg). As well, a 2 (time) × 3 (wrist posture) × 2 (group) repeated measures ANOVA was used to test the effect of repetitive wrist motion on mean arterial pressure after 3 minutes of motion with three different wrist posture starting and ending points. Four 3 (wrist posture) × 2 (group) repeated measures ANOVAs were used to test the effect on (1) median nerve cross sectional area, (2) median nerve height, (3) median nerve width, and (4) Median nerve circularity. Tukey’s HSD was used to follow up all significant effects. Significance level was set to α < 0.05. All statistical analyses were performed using SPSS Statistics 20 (IBM Corporation, Armonk, NY, USA).
Chapter 4: Results

4.1 Clinical Tests (Symptoms)

Twenty two participants were placed in one of two groups (11 Healthy and 11 CTS Symptomatic). The CTS symptomatic group significantly correlated with a positive Phalen’s test, a higher Levine’s Symptom Severity Score, a higher Levine’s Functional Status Score, and a Katz Hand Diagram of greater than zero. Significant correlations were observed between each of the tests as well, which was to be expected as they are all related. All correlations are listed in Appendix E. Table 2 shows the participant age, sex, height, weight, and clinical tests (Phalen’s Test, Levine’s CTS Questionnaire, and Katz Hand Diagram).

Table 2. Participant details and clinical scores (mean with standard deviation).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Healthy (N=11)</th>
<th>CTS Symptomatic (N=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>33.9 (12.7)</td>
<td>35.8 (12.9)</td>
</tr>
<tr>
<td>Sex</td>
<td>8F, 3M</td>
<td>10F, 1M</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73.2 (14.6)</td>
<td>70.9 (20.7)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>169.4 (8.6)</td>
<td>165.4 (8.6)</td>
</tr>
<tr>
<td>RH Dominance</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>Levine's Symptom Severity Score</td>
<td>0 (0)</td>
<td>1.02 (0.84)</td>
</tr>
<tr>
<td>Levine's Functional Status Score</td>
<td>0 (0)</td>
<td>1.08 (1.27)</td>
</tr>
<tr>
<td>Phalen’s Test (+)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Katz Hand Diagram (&gt;0)</td>
<td>0</td>
<td>4</td>
</tr>
</tbody>
</table>
4.2 Effects of Pinching on Intraneural Blood Flow

No interactions were found. Main effects of grip type (F_{4,80} = 21.397, p < 0.001) (Figure 11) and wrist posture (F_{2,40} = 14.545, p < 0.001) (Figure 12) were observed. No significant interactions were observed. Intraneural blood flow velocities were higher at 30° flexion (2.24 ± 0.42 cm/s) than neutral (2.06 ± 0.45 cm/s) and 30° extension (1.97 ± 0.46 cm/s). Intraneural blood flow velocities during 6 N thumb press, 6 N finger press, and 6 N pinch were significantly greater than both a relaxed hand and 0 N pinch (Figure 11). No differences were observed between experimental groups (healthy and CTS symptomatic) (F_{1,20} = 2.932, p = 0.102).

![Figure 11](image_url)

*Figure 11. Intraneural blood flow velocity in 5 grip types: relaxed hand, pinch posture with no force, thumb force, finger force, and pinch force in healthy and CTS symptomatic participants. Asterisk (*) notes force conditions are significantly greater than no force conditions (p < 0.05).*
Figure 12. Intraneural blood flow velocity in 30° wrist extension, neutral, and 30° wrist flexion in healthy and CTS symptomatic participants. Main effect of wrist posture noted with (*). Flexion is greater than both neutral and extension (p < 0.05).

4.2.1 Force

Comparisons were performed to examine the finger and force exertions that were produced at the same force level. A main effect of transducer (third finger and thumb) was observed (F\textsubscript{1,19} = 46.068, p < 0.001). Table 3 shows the mean force in each condition (0 N pinch, 6 N thumb press, 6 N third finger press, and 6 N pinch) collapsed across all wrist postures. The third finger was significantly greater than the thumb during the 0 N pinch (italic) and during the 6 N pinch (bold and italic). During the thumb press, the thumb produced a lower force than the finger in the finger press (bold).
Table 3. Mean and standard deviation of force measured by thumb and third finger transducers for each of 4 conditions: 0 N Pinch, thumb press, third finger press, and 6 N pinch (both third finger and thumb press together)

<table>
<thead>
<tr>
<th></th>
<th>0 N Pinch</th>
<th>Thumb</th>
<th>Finger</th>
<th>6 N Pinch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thumb</td>
<td>0.12 ± 0.32</td>
<td>5.46 ± 1.19</td>
<td>-0.15 ± 0.61</td>
<td>5.42 ± 1.14</td>
</tr>
<tr>
<td>Finger</td>
<td>0.35 ± 0.33</td>
<td>0.16 ± 0.36</td>
<td>6.00 ± 1.04</td>
<td>6.07 ± 1.27</td>
</tr>
</tbody>
</table>

4.2.2 Mean Arterial Pressure (MAP)

A significant interaction of grip type by group on MAP was found (F_{4,80} = 2.805, p = 0.031) (Figure 12). Tukey’s HSD showed that in the relaxed hand and 0 N pinch conditions in the healthy group produced smaller MAP than the finger and thumb presses in the 6 N pinch condition. A significant wrist posture by grip type interaction was also observed (F_{8,160} = 2.639, p = 0.010) (Figure 13). The relaxed hand and 0 N pinch produced smaller MAP than the thumb press and 6 N pinch for the healthy participants. For the CTS symptomatic participants, the relaxed hand and 0 N pinch showed smaller MAP than the 6 N pinch conditions, however the relaxed hand also was smaller than the finger press MAP. MAP also varied with the digit applying force (finger or thumb) depending on wrist posture. Thumb press in extension produced higher MAP than thumb press in flexion while the finger press in flexion produced higher MAP than the finger press in extension.
Figure 13. Grip type by group interaction on mean arterial pressure (MAP). Healthy (black) and CTS symptomatic (grey) groups across each grip condition (relaxed, 0 N pinch, 6 N thumb press, 6 N third finger press, and 6 N pinch). 6 N pinch (**) in healthy group was significantly greater than the relaxed hand and 0 N pinch (*).

Figure 14. Wrist posture by grip type on mean arterial pressure. Wrist extension (black), neutral (grey), and flexion (stripes).
4.3 Effects of Repetitive Wrist Motion on Intraneural Blood Flow

There were no main effects of time ($F_{1,20} = 0.974, p = 0.335$) or wrist posture ($F_{2,40} = 0.419, p = 0.661$) observed. No significant interactions were found. Figure 14 shows intraneural blood flow velocities in each condition in healthy and CTS symptomatic participants. No significant differences were observed between groups ($F_{1,20} = 0.048, p = 0.828$).

4.3.1 Mean Arterial Pressure (MAP)

No significant interactions were observed in the mean arterial pressure in any of the repetitive wrist motion conditions. There were no significant main effects of wrist posture ($F_{2,38} = 0.439, p = 0.648$) nor of time ($F_{1,19} = 2.123, p = 0.161$). There was no difference between the experimental groups (Healthy and CTS Symptomatic) ($F_{1,19} = 0.008, p = 0.930$).
4.4 Median Nerve Cross Sectional Area and Circularity

No significant differences of median nerve cross sectional area (F\(_{1,20} = 0.829, p = 0.373\)) or circularity (F were observed between groups). Median nerve cross sectional area, width, and height were measured in a neutral, flexed and extended wrist. No significant differences were observed between wrist postures for cross sectional area (F\(_{2,40} = 0.986, p = 0.382\)), median nerve height (F\(_{2,40} = 0.942, p = 0.361\)), nor median nerve width (F\(_{2,40} = 2.094, p = 0.153\)). No interactions were found (Table 4). No significant differences in median nerve circularity were observed between groups (F\(_{1,19} = 1.972, p = 0.176\)) or between extended, neutral, or flexed wrist postures (F\(_{2,38} = 0.791, p = 0.461\)).

Figure 15. Intraneural blood flow velocity in 30° wrist extension, neutral, and 30° wrist flexion before motion began (minute 0) and after motion ceased (minute 3) (A) in healthy and (B) CTS symptomatic participants.
Table 4. Median nerve cross sectional area, height, width, and circularity for healthy and CTS symptomatic participants. Measurements were obtained in neutral 0°, 30° flexion, and 30° extension.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Healthy (N=11)</th>
<th>CTS Symptomatic (N=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median Nerve CSA (cm²)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extended Wrist</td>
<td>0.09 (0.02)</td>
<td>0.10 (0.03)</td>
</tr>
<tr>
<td>Neutral Wrist</td>
<td>0.09 (0.02)</td>
<td>0.10 (0.03)</td>
</tr>
<tr>
<td>Flexed Wrist</td>
<td>0.09 (0.03)</td>
<td>0.11 (0.04)</td>
</tr>
<tr>
<td><strong>Median Nerve Width (cm)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extended Wrist</td>
<td>0.57 (0.07)</td>
<td>0.56 (0.11)</td>
</tr>
<tr>
<td>Neutral Wrist</td>
<td>0.60 (0.06)</td>
<td>0.59 (0.10)</td>
</tr>
<tr>
<td>Flexed Wrist</td>
<td>0.57 (0.10)</td>
<td>0.61 (0.13)</td>
</tr>
<tr>
<td><strong>Median Nerve Height(cm)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extended Wrist</td>
<td>0.19 (0.03)</td>
<td>0.22 (0.03)</td>
</tr>
<tr>
<td>Neutral Wrist</td>
<td>0.18 (0.03)</td>
<td>0.21 (0.04)</td>
</tr>
<tr>
<td>Flexed Wrist</td>
<td>0.20 (0.05)</td>
<td>0.22 (0.09)</td>
</tr>
<tr>
<td><strong>Median Nerve Circularity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extended Wrist</td>
<td>0.58 (0.06)</td>
<td>0.66 (0.27)</td>
</tr>
<tr>
<td>Neutral Wrist</td>
<td>0.50 (0.08)</td>
<td>0.65 (0.17)</td>
</tr>
<tr>
<td>Flexed Wrist</td>
<td>0.56 (0.16)</td>
<td>0.62 (0.26)</td>
</tr>
</tbody>
</table>
Chapter 5: Discussion

The impetus for this study was to examine aspects of a pinch grip on intraneural blood flow in the median nerve given that the use of a pinch grip is a well-documented risk factor for CTS. This study built on recent research to examine intraneural blood flow by testing the components of the pinch grip, namely posture, finger force, thumb force, and the complete pinch grip. The first hypothesis was partially confirmed. Wrist posture, namely flexion, increased intraneural blood flow above a neutral wrist. However, an extended wrist did not. The pinch posture itself did not alter flow above a relaxed posture. We confirmed the second hypothesis that all force conditions would elevate intraneural blood flow above that found in a relaxed hand and 0 N pinch. The second component of the hypothesis, that the highest increases in flow would be observed in the 6 N pinch condition followed by the finger press and then the thumb press, was not confirmed. However, despite lack of significance, there was a pattern of increasing intraneural blood flow between the separate components of pinch (6 N thumb press and 6 N finger press) and the 6 N pinch in the CTS symptomatic group. The third hypothesis of my thesis was also not confirmed. No significant increases in intraneural blood flow were observed in response to repetitive wrist motion. Lastly, the final hypothesis was not met. There was no significant difference in intraneural blood flow between the healthy and CTS symptomatic groups.

The data from my thesis show that applying force, despite application, increases intraneural blood flow in the median nerve. This agrees with previous work by Wilson
(2013), who found that applying a finger force through the third finger elevated intraneural blood flow compared to a no-force condition. An unexpected finding was a lack of difference between the thumb and finger presses and the complete pinch. Research examining CTP has shown that pinching elevated CTP more than a finger press (Keir et al, 1998b). Elevated CTP essentially compresses the median nerve, and at levels of 30 mmHg begins to block off blood flow in the nerve (Keir et al, 2007; Lundborg et al, 1982). Decreasing the blood flow at the level of the carpal tunnel reduces blood flow distally (ischemia) resulting in an increase in blood flow proximally to compensate. Thus a larger increase in intraneural blood flow in response to a pinch was expected over that in response to a single digit press (thumb or finger). It is possible that the type of pinch used in this study (single finger to thumb pulp pinch) was not sufficient to elevate CTP enough to elicit an increase in intraneural blood flow significantly greater than a single finger press would. Keir et al (1998b) used a two finger-tip to thumb pinch which requires the use of an additional tendon. This may have played a role in the elevating of CTP more than a single tendon would have which suggests that intraneural blood flow may also have been elevated more if two fingers were used in the pinch.

Velocities observed in this study differed somewhat from previous reports. In Wilson (2013), velocities ranged from approximately 2.2 cm/s to 4.0 cm/s in the healthy and CTS symptomatic participants, whereas velocities during the pinch tasks in this study ranged from approximately 1.1 cm/s to 3.4 cm/s. The differences between Wilson (2013) and my thesis may be explained by the finger postures used. Wilson (2013) placed all fingers in an extended posture whereas this study only controlled the third finger (in a
pinch posture) and allowed the other fingers to sit where they felt natural (flexed to varying degrees in all cases). Keir et al (1998) showed that in wrist extension, the full extension of the fingers resulted in significantly higher CTP compared to MCP flexion of 45°. The relaxed posture of the other fingers in this thesis were near this 45° of MCP flexion. Therefore it is feasible that the manner in which Wilson (2013) and my thesis exerted force through the fingers (flat finger press vs. pinch grip posture) is responsible for the differences observed, especially in wrist extension, in blood flow velocities.

Another source of difference between the two studies was the use of a hand strap. Wilson (2013) placed a band across the palm to secure the participant’s hand to the fixture and maintain the posture. No strap was used in this study due to the posture required to perform the pinch posture. However, pilot work showed an increase in intraneural blood flow velocity of up to 0.5 cm/s, approximately 2.0 cm/s to 2.5 cm/s without and with the strap respectively. Cobb et al (1995b) examined the effect applied external force to different areas of the palm had on CTP. They found that force of only 1 kg was sufficient to elevate CTP significantly. Thus it is possible that the differences between Wilson (2013) and my thesis are partially explained by the use of a strap.

In other studies measuring intraneural blood flow, velocities ranged from 1.9 cm/s in healthy individuals to 13.3 cm/s in individuals who were labeled “highly likely” to have CTS (Joy et al, 2011) and 3.87 - 4.50 cm/s in asymptomatic controls and 3.34-4.54 cm/s in symptomatic patients (Evans et al, 2013). Both of these studies examined intraneural blood flow in a neutral wrist, however the difference in the values could be attributed to measurement location. Joy et al (2011) measured over the wrist crease
(similar to this study, specifically over the proximal wrist crease). Their healthy participant values (1.9 cm/s) were very similar to those seen in my study. However, velocities much higher were also measured. Joy et al (2011) had clinically diagnosed CTS individuals in which directional, pulsatile flow was measured. Vessels capable of producing a pulsatile signal are much larger and thus can produce higher velocities. Therefore the differences seen here between this study and Joy et al (2011) could be explained by different samples of participants. Evans et al (2013) measured directly over the carpal tunnel, which could explain the higher velocities observed in this study. Measuring over carpal tunnel could allow measurements of increased compensational flow as the ultrasound probe is closer to the impingement of the median nerve and thus increased hypervascularity could be present over this region. Changes in intraneural blood flow were previously observed in response to occupational risk factors (wrist posture and finger force) by Wilson (2013). This wrist location was chosen to remain consistent with the lab results but in addition, this location could not be used due to the wrist and hand postures of interest. A smooth and consistent coupling of the surface would not be possible.

This study showed that a 30° flexed wrist posture (2.24 cm/s) raised intraneural blood flow compared to a 0° neutral wrist posture (2.06 cm/s), which supports previous work by Wilson (2013). It was hypothesized that both flexion and extension would elevate intraneural blood flow relative to neutral, however unlike Wilson (2013), wrist extension did not raise blood flow relative to a neutral wrist. The main difference between the two studies was the finger posture, which as previously mentioned, could
have also accounted for the lack of increase in intraneural blood flow in wrist extension in my thesis.

To account for any possible differences, blood pressure was monitored throughout the whole study with measurements taken at the same time as blood flow measurements. Any significant differences found in the mean arterial pressure (MAP) measurements were found to be within normal fluctuations (Deveraux et al, 1983) and did not account for any changes seen in the blood flow. MAP was used rather than systolic and diastolic blood pressure as they showed the same trends, which held constant with the MAP measures.

Force was collected throughout the pinch component of the study to see if any differences occurred between the conditions and participants. A significant difference was observed between the third finger and thumb transducers. The third finger transducer consistently recorded higher forces than the thumb transducer. However this did not play a role in affecting the blood flow measurements because when analyzing the blood flow velocities of the thumb press, finger press, and 6 N pinch, there were no significant differences. If the higher force exerted by the third finger had affected flow, it would be expected that the blood flow velocities would also be higher.

Little work has explored the effects of repetitive wrist motion on the median nerve, thus this study aimed to examine the effect of repetitive wrist motion on intraneural blood flow in the median nerve. This was the first study to measure intraneural blood flow before and after a bout of repetitive wrist motion. Repetitive motion has been associated with the development of CTS as well as many other
musculoskeletal disorders. Previous work has examined different tissues in the carpal tunnel and their response to repetitive motion, however how the median nerve vasculature is affected remains unknown. Szabo and Chidgey (1989) observed elevated CTP after only 1 minute of passive wrist flexion and extension in both healthy and mild to moderate CTS individuals. In addition, the CTP remained elevated for up to 10 minutes. Seradge et al (1995) attempted to replicate these findings by having the participant actively move through wrist flexion and extension for one minute however no elevation in CTP was observed. This study aimed to measure intraneural blood flow after a bout of wrist motion, with the idea that flow would be elevated post motion in response to increase CTP in the tunnel. No change in flow was observed pre- to post-motion in either group in this study. There are many differences between this study and both Szabo and Chidgey (1989) and Seradge et al (1995). Szabo and Chidgey (1989) passively moved the wrist from flexion to extension whereas the participants in this study actively moved. In addition, both studies only moved the wrist for 1 minute, this study had participants move for 3 minutes to see if the duration was a factor not considered by Seradge et al (1995). However, the results of this study still suggest that repetitive wrist motion does not have an effect on intraneural blood flow. To account for any possible differences, this study took it one step further and measured blood pressure throughout the repetitive motion trials with measurements collected both pre- and post-motion. No significant changes in blood pressure were observed from the start to the end of the motion in any of the three wrist postures (flexion, neutral, or extension).
Repetitive motion has been examined extensively in relation to CTS, however tissues other than the median nerve have been the focus. Ettema et al (2006) found that changes in the SSCT occurred most severely in the layers closest to the tendon. As well, the gliding characteristics of the SSCT become altered in CTS individuals compared to healthy controls (Ettema et al, 2007). In light of these findings, Kociolek et al (2015) measured the frictional work between the tendon and SSCT in response to repetitive finger motion in different wrist postures. The authors found that repetitive forceful work increases the frictional work between the tissues in the carpal tunnel providing a plausible rational for the fibrosis of the SSCT and link to the development of CTS. Thus it is possible that the link between repetitive motion and CTS is not necessarily found in the median nerve but rather the neighbouring tissues. With the wrist moving through neutral and extension, while only spending a small portion of the time in flexion (posture shown to elevate intraneural blood flow), it is possible that repetitive motion does not have as large of an effect on blood in the nerve but rather it is the motion itself (sliding and causing friction of the tendons and SSCT) that results in the damage and factors leading to the development of CTS.

No statistical difference between the healthy control and CTS symptomatic groups was found on intraneural blood flow velocity. It was hypothesized that the CTS symptomatic group would display higher intraneural blood flow velocities due to suspected increased vascularity of the median nerve (Mohammadi et al, 2012; Wilson, 2013) compared to the healthy control group. It is possible that since the CTS symptomatic group contained individuals with only minor symptoms or who were only in
the early stages of the development of the disorder were not subject to the pathological changes necessary to observe this phenomenon (Joy et al 2011). In addition, the CTS symptomatic group was not required to have been clinically evaluated with the gold standard test nerve conduction studies (NCS). With individuals with more severe symptoms of CTS, it may be possible to see a larger difference in the intraneural blood flow (Joy et al, 2011; Mallouhi et al, 2006).

Median nerve cross sectional area (CSA) has been used as an indication of median nerve compression, CTS presence, and development. CSA has also been shown to have a positive relationship with intraneural blood flow (Joy et al, 2011; Wilson, 2013). However this study did not observe differences in the CSA of healthy and CTS symptomatic individuals nor did it correlate with intraneural blood flow. This is consistent with Joy et al (2011) in that no differences were observed between the normal and intermediate CTS group CSAs. It is possible that population differences may have resulted in these differences between studies. The transverse shape, or circularity of the median nerve was also calculated in an attempt to observe any differences between groups as well as between wrist postures. The CSA wasn’t different but the shape of that area could present a different story. A value of 1 represented a perfect circle. Mean circularity measures for the extended, neutral and flexed wrist were 0.58, 0.50, and 0.56 respectively in the healthy group and 0.66, 0.65, and 0.62 respectively in the CTS symptomatic group. Despite what appears to be a rounder median nerve in the CTS symptomatic group, there wasn’t a significant difference between the groups nor between wrist postures. This is in contrast to a study by Wang et al (2014) where a rounder nerve
was observed in CTS wrists compared to healthy wrists. In a study comparing the
circularity of the median nerve solely in healthy wrists, wrist flexion with flexed fingers
(similar to the posture assumed in this study) increased the circularity of the nerve relative
to neutral (Wang et al, 2013) whereas no change was observed in this study. This study
did not use clinically diagnosed CTS individuals and all participants had minor
symptoms. This could have contributed to a lack of severity observed. In addition, some
of the expected changes, such as increased circularity, could be attributed to changes that
occur over a longer period of time, such as hypervascularization.

This study has shown that the application of intraneural blood flow goes beyond
demonstrating differences between healthy and CTS symptomatic individuals.
Intraneural blood flow also presents a connection between occupational risk factors,
namely force and wrist flexion, and the acute changes they elicit on the median nerve.

5.1 Limitations

This study had individuals with very mild symptoms in the CTS symptomatic
group which may have contributed to the lack of difference in intraneural blood flow seen
between the two groups. Work by Wilson (2013) recommended further analysis on more
individuals with more severe symptoms of CTS however, pilot work showed that the
protocol caused too much discomfort for clinically diagnosed individuals.

This study measured intraneural blood flow using a longitudinal view of the
median nerve. Changing posture and applying force altered the position of the flexor
tendons and median nerve. The median nerve sliding longitudinally during changes of
wrist and finger posture, thus, the ultrasound probe was shifted between wrist posture conditions in order to attempt to measure a similar portion of the median nerve between wrist postures.
Chapter 6: Thesis Summary and Future Directions

6.1 Thesis Summary and Conclusions

This study used ultrasound pulse wave Doppler to measure intraneural blood flow in the median nerve in response to different pinching conditions as well as repetitive wrist motion. This study looked at the two components of a pinch grip (finger press and a thumb press) to examine how the pinch grip contributes to the development of CTS. This study confirmed that the presence of finger force increased the blood flow within the median nerve potentially contributing to the development of CTS. This study also showed that a flexed wrist posture increased flow in the median nerve more so than a neutral or extended wrist with a flexed finger posture (pinch). Repetitive wrist motion did not appear to affect intraneural blood flow. This study showed a link between intraneural blood flow velocity and the presence or absence of CTS symptoms as well as the application of two occupational risk factors, force and deviated wrist postures.

6.2 Future Directions

This study presented the first attempt at examining the intricacies of a pinch using ultrasound. Further examination into the application and level of force of the pinch grip is warranted. This study only used one force level, however a graded response may be present and thus the use of multiple force levels may provide insight into how or if intraneural blood flow is affected through a range of forces. The repetitive motion
component of this study did not show any significant differences in blood flow. However, duration and speed of wrist and finger motion and their effects (if any) on intraneural blood flow have yet to be explored.
Chapter 7: References


Tat, J and Wilson, K. (2015 [in press]). Pathological changes in the subsynovial connective tissue increase with severity of carpal tunnel syndrome symptoms. Submitted to *Clinical Biomechanics*.


Displacement in the Human Carpal Tunnel during Wrist Movements. *Ultrasound in Medicine & Biology, 40*(1), 53-61.


Appendix A: Participant Questionnaire

Title: The effect of repetitive motion on intraneural blood flow in the median nerve

Participant Identification
Name: _______________________ Date: _________________________
Age: _________________________

Handedness
1) Are you are you right-handed or left-handed or ambidextrous (use both hands equally)?
   right-handed ___  left-handed ___  ambidextrous ___

Health History
1) Have you ever had any of the following health conditions and/or treatment protocols performed on you currently and/or in the past? [please check all that apply]

   __ Diabetes mellitus
   __ Thyroid condition (e.g. hypothyroidism)
   __ Gout
   __ Amyloidosis
   __ Sarcoidosis
   __ Renal Failure (or hemodialysis)
   __ Degenerative joint disease
   __ Arthritis of the wrist/hand
   __ Corticosteroid injection
   __ Cervical radiculopathy
   __ Peripheral neuropathy
   __ Radial malunion
   __ Colles fracture
   __ Wrist/hand musculoskeletal disorder
   __ Flexor tendonopathy
   __ Carpal tunnel syndrome
   __ Ultrasound/laser/soft tissue treatment
   __ Wrist/hand surgery
   __ Pain/tingling/numbness of the hand

2) Are you currently on any medications that affect blood flow? Yes ___ No ___
   * If yes, please list:

   __________________________________________________________________________
   __________________________________________________________________________
   __________________________________________________________________________

Work History
1) Occupation: ________________________________________________________________
2) Hours at work per week: ____________________________________________________
3) Years at current job: ________________________________________________________
4) Typical tasks performed at work: ____________________________________________
   __________________________________________________________________________
   __________________________________________________________________________
   __________________________________________________________________________
5) Have you ever-experienced a wrist or hand injury? **Yes ____ No ____**
* If yes, please elaborate (type of injury, onset of injury, what do you attribute it to, how long have you have had the injury, symptoms, treatment of injury, time off work): ______
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________

**I verify that I have answered the above questions to the best of my knowledge. I understand that no confidential health information will be released without my written consent.**

Name of Participant (Print) ______ Signature ______ Date ______

Name of Research Investigator Obtaining Consent (Print) ______ Signature ______ Date ______
Appendix B: Levine’s Carpal Tunnel Syndrome Questionnaire

### CTS QUESTIONNAIRE

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).

**SEVERITY SCALE:** 0 = None or Never; 1 = Mild; 2 = Moderate; 3 = Severe; 4 = Very severe

<table>
<thead>
<tr>
<th>QUESTION</th>
<th>SEVERITY SCALE 0= NONE; 4=SEVERE</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. How severe is the hand or wrist pain that you have at night?</td>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2. How often did hand or wrist pain wake you up during a typical night in</td>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>the past two weeks (times/night)?</td>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3. Do you typically have pain in your hand or wrist during the daytime?</td>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4. How often do you have hand or wrist pain during the daytime (times/day)?</td>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5. How long, on average, does an episode of pain last during the daytime</td>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>(minutes)?</td>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>6. Do you have numbness (loss of sensation) in your hand?</td>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>7. Do you have weakness in your hand or wrist?</td>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>8. Do you have tingling sensations in your hand?</td>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>9. How severe is numbness (loss of sensation) or tingling at night?</td>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>10. How often did hand numbness or tingling wake you up during a typical</td>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>night during the past two weeks?</td>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>11. Do you have difficulty with the grasping and use of small objects</td>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>such as keys or pens?</td>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

### FUNCTIONAL STATUS SCALE

<table>
<thead>
<tr>
<th>QUESTION</th>
<th>SEVERITY SCALE 0= NONE; 4=SEVERE</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Writing</td>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2. Buttoning of clothes</td>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3. Holding a book while reading</td>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4. Gripping of a telephone handle</td>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5. Opening of jars</td>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>6. Household chores</td>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>7. Carrying of grocery bags</td>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>8. Bathing and Dressing</td>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

**COMMENTS:**


Appendix C: Katz Hand Diagram and Classification
<table>
<thead>
<tr>
<th>Rating</th>
<th>Description of area shaded on the hand</th>
</tr>
</thead>
</table>
| Classic (3)    | Tingling, numbness, burning or pain in at least 2 of the digits (thumb, index and long). Symptoms in palm and dorsum of hand excluded; small finger symptoms, wrist pain or radiation proximal to the wrist allowed.  
  - For index and long digits, must include shading between the distal tip and the proximal finger crease volarly, and include >1/2 of the middle phalanx &/or some of the distal phalanx. For thumb, must include shading in the distal phalanx volarly.  
  - Digit may include shading dorsally from fingernail to the distal MP mark on the hand diagram.  
  - If joint of digit (including MP) is the only area shaded and less than half of two adjacent phalanges, this may be considered arthritic complaints. |
| Probable (2)   | Same shading as for classic but allowed the shading to extend into the palm volarly unless it was confined to the ulnar aspect of the palm. |
| Possible (1)   | Tingling, numbness, burning, or pain in at least one of the digits (thumb, index and long).  
  - May include the dorsum of the hand |
| Unlikely (0)   | No shading of the primary digits or shading restricted to the dorsum of the digits only. |

\(^a\) Modifications to rules in italics
LETTER OF INFORMATION / CONSENT

Changes in Intraneural Blood Flow in the Median Nerve Following Postures
Associated with Risk of Carpal Tunnel Syndrome

Principal Investigator:
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Purpose of the Study:
The purpose of this study is to test the effect of different aspects of pinching as well as wrist posture on intraneural blood flow of the median nerve in healthy control and carpal tunnel syndrome symptomatic individuals. A secondary purpose is to determine the effect of repetitive wrist motion on intraneural blood flow.

You are invited to participate in this study about musculoskeletal disorders of the wrist and hand. Carpal tunnel syndrome is a common musculoskeletal disorder of the wrist and hand that is caused by compression of the median nerve at the wrist. Understanding how the nerve becomes damaged inside the carpal tunnel (or wrist) is important in determining the development of wrist and hand musculoskeletal disorders. The median nerve can be seen non-invasively using ultrasound.

Procedures involved in the Research:
You will be asked to complete a questionnaire about your handedness (i.e. left-handed or right-handed), general health, as well as musculoskeletal disorders of the wrist and hand. Following the questionnaire, you will complete a testing protocol no longer than 2.5 hours. You will be seated comfortably while the ultrasound technician applies ultrasound gel on the wrist of your dominant hand. Next, you will be asked to complete a series of pinching tasks in different wrist postures at different force levels while an ultrasound probe records images of the nerve in the carpal tunnel. Each posture will last no longer than 5 minutes (with rest in between each posture). After these postures, you will be asked to perform repetitive wrist motions. Ultrasound measurement of blood flow will be measured at 30° of wrist flexion and extension as well as in a neutral wrist at the end of each 3 minute block of motion.

Potential Harms, Risks or Discomforts:
Ultrasound is a safe imaging tool used to visualize tissues within your body. The wrist postures, pinching exertions, and repetitive wrist motions in this study might cause you minimal discomfort due to fatigue in some rare cases. However, we do not foresee any risks from your participation in this research. If you do feel any muscular discomfort or pain, please tell the technician. In the event that you do feel pain while performing any of the tasks, the study will be stopped immediately to ensure your safety.
Potential Benefits:

This research will not benefit you directly, except for knowing that you are helping further our understanding about the influence of wrist postures, aspects of pinching, and repetitive wrist motions on the vascular structures in the median nerve. Ultimately, we hope to prevent musculoskeletal disorders in the workplace.

Payment or Reimbursement:

You will receive $20 for your time for participating in this study. If you withdraw from this study at any time, you will still receive prorated compensation.

Confidentiality:

Your identity will be kept confidential. We will not use your name or any information that would allow you to be identified. The data obtained in this study will be used for research and teaching purposes only. Information directly pertaining to you will be stored in a locked cabinet or on a password protected computer.

Participation and Withdrawal:

Your participation in this study is voluntary. If you decide to participate, you can choose to stop at any time, even after signing the consent form, or in the middle of the study. If you decide to stop participating in this study, there will be no consequences to you. Also, all of your data will be permanently deleted.

This study has been reviewed by the Hamilton Integrated Research Ethics Board (HIREB). If you have any concerns or questions about your rights as a participant or about the way this study is conducted, contact the Office of the Chair at the HIREB at (905) 521-2199 (x 44405 or x43838).

Information about the Study Results:

You may obtain information about the study results by contacting Samantha Ehmke at (905) 525-9140 (x 20173) or Dr. Peter Keir at (905) 525-9140 (x 23543).

Questions about the Study:

If you have questions or need more information about the study itself, please contact me at:

Samantha Ehmke
ehmkeeg@mcmaster.ca

This study has been reviewed by the Hamilton Integrated Research Ethics Board (HIREB). The HIREB is responsible for ensuring that participants are informed of the risks associated with the research, and that participants are free to decide if participation is right for them. If you have any questions about your rights as a research participant, please call the Office of the Chair, HIREB, at 905.521.2100 x 42013.
CONSENT

- I have read the information presented in the information letter about a study being conducted by Samantha Ehmke and Dr. Peter Keir of McMaster University.
- I have had the opportunity to ask questions about my involvement in this study and to receive additional details I requested.
- I understand that if I agree to participate in this study, I may withdraw from the study at any time or up until approximately August, 2015.
- I have been given a copy of this form.
- I agree to participate in the study.

Signature: ____________________________ Date: __________________________

Name of Participant (Printed) ___________________________________________

1. ___ Yes. I would like to receive a summary of the study's results.
   Please send them to me at this email address ____________________________
   Or to this mailing address: ____________________________________________
   ___ No. I do not want to receive a summary of the study's results.

2. I agree to be contacted about a follow-up interview, and understand that I can always decline the request.
   ___ Yes. Please contact me at: ____________________________
   ___ No.

MNF #3, May 18, 2015

Research Ethics Board