FLEXOR TENDON MOTION WITH EXTERNAL COMPRESSION AND ISCHEMIA

EXTERNAL COMPRESSION AND PARTIAL ISCHEMIA ALTER FLEXOR TENDON AND SUBSYNOVIAL CONNECTIVE TISSUE MOTION

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THESIS ABSTRACT

Carpal tunnel syndrome (CTS) is a peripheral median neuropathy that is commonly characterized by thickening and fibrosis of the subsynovial connective tissue (SSCT) surrounding finger flexor tendons. The degenerative process affecting SSCT can be initiated with excessive relative motion between the tendon and SSCT that ruptures interconnecting collagen. We used colour Doppler ultrasound to evaluate flexor digitorum superficialis tendon motion at two movement speeds with palmar compression, forearm compression, and partial ischemia (via brachial blood pressure cuff). Partial ischemia decreased SSCT displacement (22.9 ± 3.3 mm vs. 22.0 ± 3.3 mm; $p = 0.015$) while tendon displacement did not change. There was also a trend for increased relative tendon-SSCT displacement and shear strain index (SSI – relative displacement normalized to tendon displacement), which suggested partial ischemia might increase the strain in collagen that connects tendon and SSCT. Forearm compression decreased tendon displacement (28.5 ± 4.1 mm vs. 27.0 ± 4.6 mm; $p = 0.043$) while SSCT displacement also trended to decrease (24.0 ± mm vs. 22.5 mm; $p = 0.059$). With a lack of change in relative tendon-SSCT displacement and SSI, maintaining flexion-extension range of motion may have meant that forearm compression strained the musculotendinous unit at a location where SSCT was uncompromised. Palmar compression did not significantly affect any dependent motion variables, which suggested palmar compressive forces likely do not affect tendon-SSCT shear injury risk. The fast movement speed increased relative tendon-SSCT displacement and SSI while decreasing mean velocity ratio (MVR), which suggested greater tendon-SSCT shear strain in all baseline and

compression conditions. Previously, increased relative tendon-SSCT displacement with fast movement speed was only shown in cadaveric investigations, but we confirmed this effect is transferable in an *in vivo* model. We induced ischemia proximally and found a reduction in SSCT displacement at the distal carpal tunnel. This finding suggests that the vascular network integrated within SSCT may play a role in altering tendon-SSCT excursion, independent of other external mechanical factors previously shown to increase relative motion and potential shear injury risk. Overall, this thesis showed that external mechanical compression at the palm or forearm likely do not negatively affect relative tendon-SSCT motion and that local ischemia and carpal tunnel blood flow should be considered when evaluating tendon and SSCT motion in relation to CTS development and progression.

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LIST OF ABBREVIATIONS AND SYMBOLS

ANOVA	Analysis of variance
CDI	Colour Doppler imaging
CTS	Carpal tunnel syndrome
CTP	Carpal tunnel pressure
FDP	Flexor digitorum profundus
FDS	Flexor digitorum superficialis
MRI	Magnetic resonance imaging
MVR	Maximum velocity ratio
SSCT	Subsynovial connective tissue
SSI	Shear strain index
TCL	Transverse carpal ligament
η^2	Partial eta squared

1. THESIS INTRODUCTION

Carpal tunnel syndrome (CTS) is the most commonly reported peripheral compression neuropathy; it affects the median nerve and represents 0.4% of all lost time claims reported in Ontario in 2014 (WSIB, 2014). CTS manifests in a variety of symptoms including pain, numbness, tingling, weakness (Stevens et al., 1999; Szabo et al., 1984), and impaired motor coordination (Lowe et al., 1999) of the first three and radial half of the fourth fingers. Acutely, these symptoms can be elicited from compression and ischemia of a healthy median nerve but the chronic presentation of CTS has been linked to elevated carpal tunnel pressure and cumulative tendon injury from relative displacement between tendon and its adjacent subsynovial connective tissue (SSCT). The purpose of this research was to evaluate associations between mechanical compression, acute ischemia and relative tendon-SSCT motion.

The human carpal tunnel is a small canal spanning the length of the carpal bones of the wrist through which the following ten structures traverse: median nerve, four flexor digitorum superficialis tendons (FDS), four flexor digitorum profundus tendons (FDP), and flexor pollicis longus tendon (Figure 1.1). These contents are bordered medially by the pisiform and hook of the hamate and laterally by the tubercles of the trapezium and scaphoid. On its palmar surface, the transverse carpal ligament (TCL) connects the medial and lateral boney landmarks while the carpal bones align to form a concave arch at its dorsal surface (Figure 1.1) (Schuenke et al., 2010). Previous work has subdivided the length of the flexor tendons into five zones (I – V) based on regional differences in function and morphology (Boyer et al., 2002; Guimberteau et al., 2010). The carpal

tunnel represents zone IV where the tendons and median nerve reside underneath a synovial cavity and the SSCT (Figure 1.2). This SSCT is part of the synovial system and is essential for finger flexion and extension as it attenuates tensile and shear stresses, reduces gliding friction, and allows for differential motion between carpal tunnel contents and its boundaries. Zones III (distal) and V (proximal) are distinguished by fibrous sheaths that surround the tendons and house the extension of the SSCT on either side of the carpal tunnel. Zone V extends from the musculotendinous junction to the proximal edge of the TCL while zone III extends from the distal edge of the TCL to the distal end of the fibrous sheath. Lastly, zones II and I extend from the distal end of zone III, approximately at the palmar crease, and terminate at the tendinous insertion at the intermediate (FDS) or distal (FDP) phalanges.

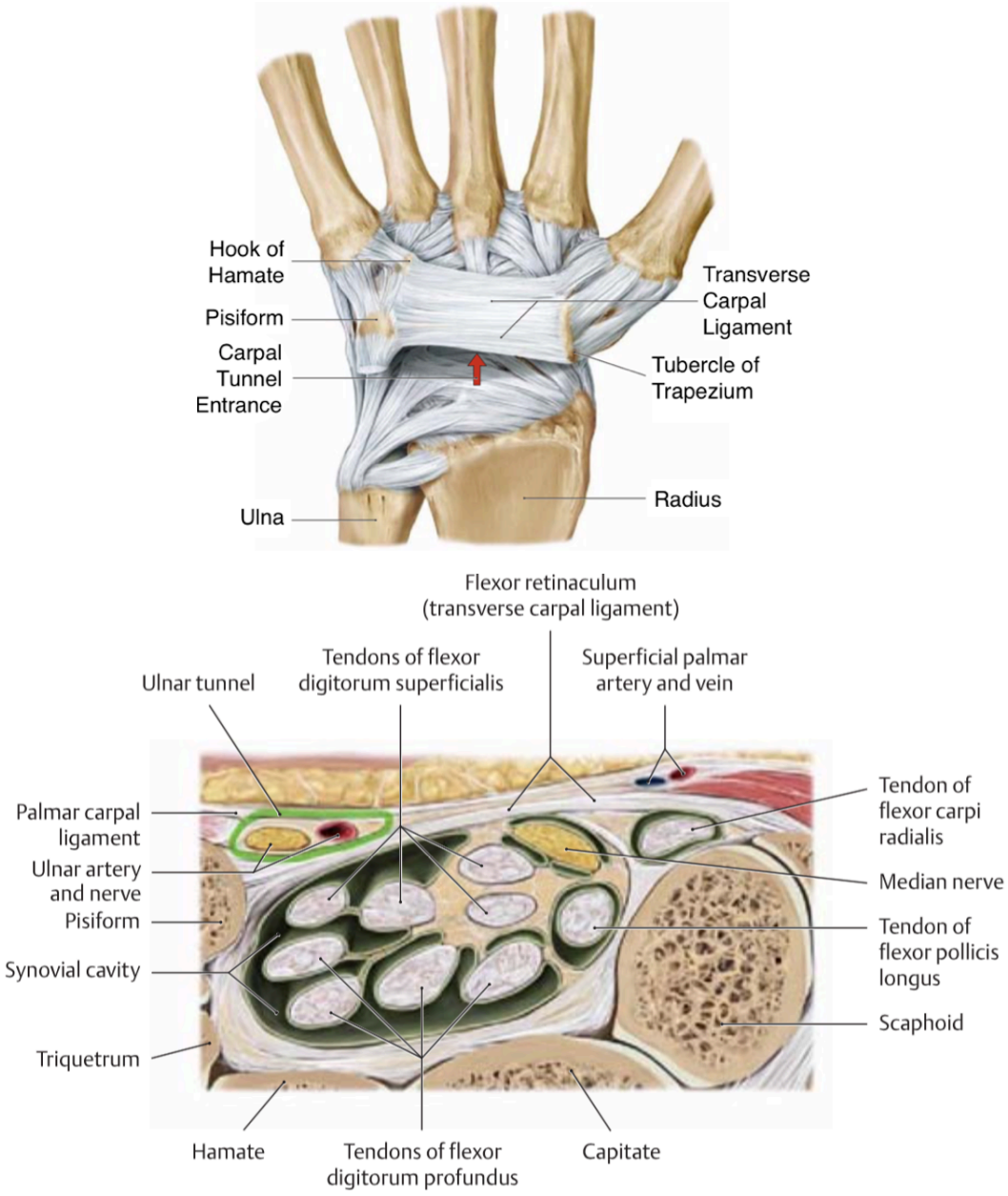

Figure 1.1. Palmar view of ligamentous and boney borders of the carpal tunnel of the right wrist (top). Distal cross-section view of the right distal carpal tunnel showing carpal tunnel contents: finger flexor tendons (flexor digitorum superficialis and profundus), flexor pollicis longus tendon, median nerve (bottom) (Adapted from Schuenke et al., 2010).

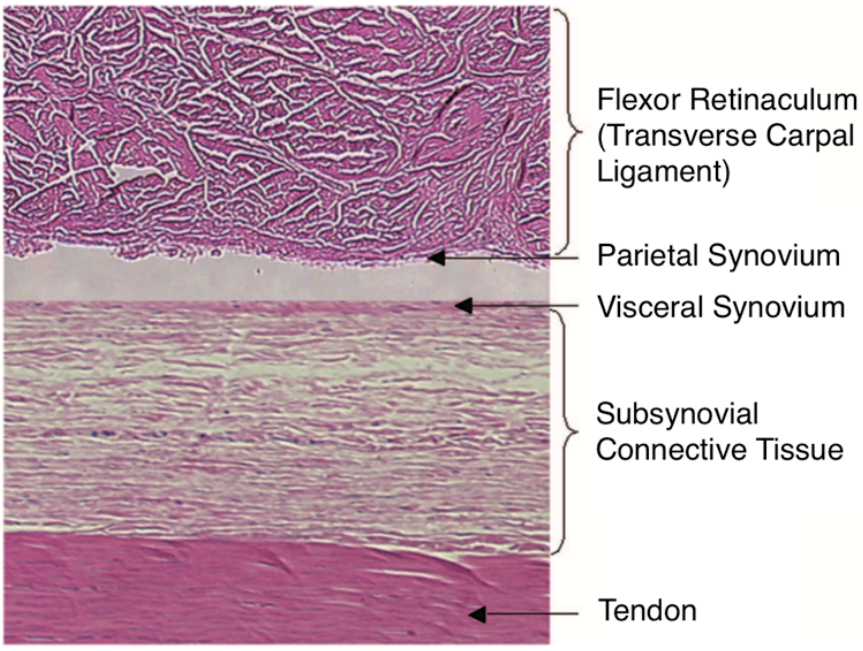

Figure 1.2. Tissue stained image showing the various layers of tissue in zone IV of flexor tendon anatomy (400x magnification). From superficial (top) to deep (bottom): transverse carpal ligament, visceral and parietal synovium, subsynovial connective tissue, and flexor tendon (Ettema et al., 2006).

The SSCT possesses structural and biochemical properties for redistributing tendon loads and facilitating gliding between collagen fibres that, in a normal state, allow smooth and near-frictionless movement through the carpal tunnel. The organization of SSCT resembles a polyhedral wireframe formed by a network of collagen bundle layers that are interconnected by thinner collagen fibrils (Ettema et al., 2006; Guimberteau et al., 2010). Blood vessels are also found permeating through the SSCT longitudinally (parallel to tendon) and transversely between collagen bundles (Figure 1.3). This network is immersed in an extracellular matrix containing macromolecules like phospholipids and proteoglycans that minimize gliding friction between collagen bundles (Riggozi et al.,

2013; Sun et al., 2008). The extracellular matrix is hydrophilic in nature; thus it can attract fluid into the area from surrounding blood vessels. With the combination of extracellular fluid and circulating macromolecules, the SSCT possesses viscoelastic properties that attenuate tensile and shear stresses during tendon excursion (Yoshii et al., 2010).

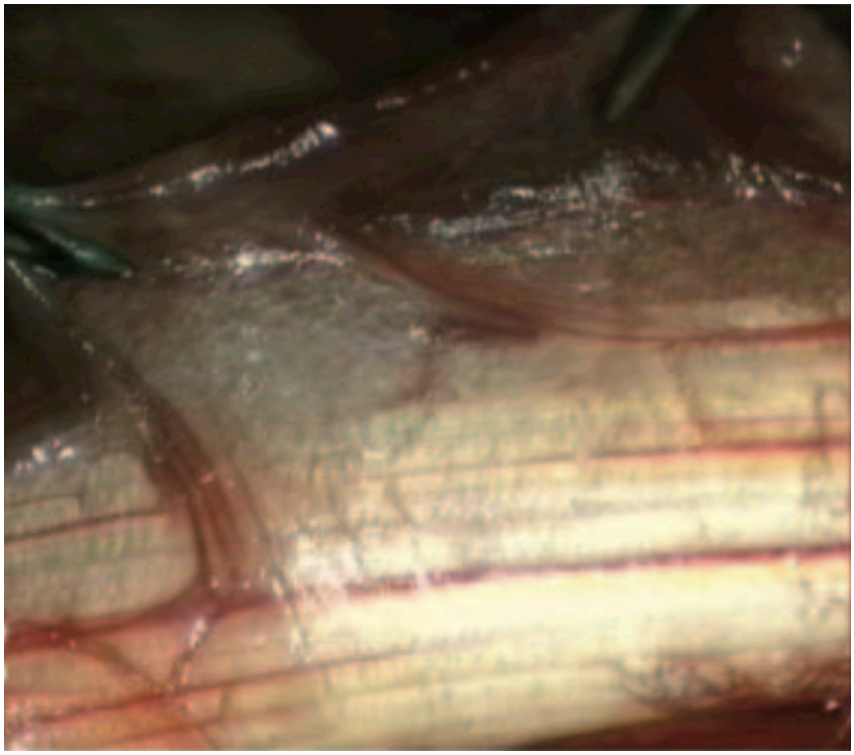

Figure 1.3. Lifting of the subsynovial connective tissue from the tendon body showing microvasculature that run longitudinally with the tendon, and transversely as seen perpendicular to the orientation of collagen fibres (Adapted from Guimberteau et al., 2010).

At the tendon-SSCT interface, a dense layer of collagenous tissue binds the SSCT to the tendon sheath allowing for contiguous gliding through the carpal tunnel during

finger flexion and extension (Ettema et al., 2006). In healthy individuals, the SSCT extends telescopically in the same direction as tendon motion such that collagen bundles nearest the tendon are recruited first and experience greater excursion than those furthest away. This telescopic movement redistributes tensile stresses across the SSCT gliding mechanism by sequentially recruiting collagen bundles through thin fibrillar connections (Figure 1.4A & B). With excessive shear stresses, however, fibrils can rupture and lead the collagenous network to lose its polyhedral structure and become disorganized (Figure 1.4C & 4D). Since the fibrillar connections nearest the tendon are recruited first, they typically experience the greatest amount of strain and are likely the first to tear in the pathomechanics of SSCT injury (Ettema et al., 2006). Osamura and colleagues (2007a) investigated the tensile and shear strength of SSCT samples from healthy cadavers and CTS pathological individuals and concluded that tendon shear strains from everyday activities may be adequate to cause failure of fibrillar connections. In another cadaver study, excursion resistance energy (area under a load-excursion curve up to peak excursion) and peak tendon force values across different tendon excursion distances (40, 60, 90, 120% of max) were measured during repeated tendon excursion cycles (Vanhees et al., 2012). Between excursion cycles, the authors found reductions in excursion resistance energy and peak tendon force at 60% and 90% of max excursion, which suggested SSCT damage can begin to occur at tendon excursions within physiological ranges of motion. As trauma is accumulated, fibroblasts begin to lay down new collagen that cause the SSCT bundles to thicken and adhere together. This fibrotic process impairs the telescopic function and increases the stiffness of the gliding mechanism, which may

increase the likelihood of sustaining further fibrillar injury if greater tendon loads are necessary to move the tendon within the fibrotic SSCT (Osamura et al., 2007a). Since new collagen is not integrated in an organized fashion, new fibrillar connections between bundles are unlikely to form and existing fibrils will experience greater stresses that will likely cause them to rupture eventually as well. This vicious cycle of SSCT injury, impaired tendon-SSCT displacement, and thickening and fibrosis will begin to occupy more space within the confined carpal tunnel boundaries and contribute to elevated carpal tunnel pressure.

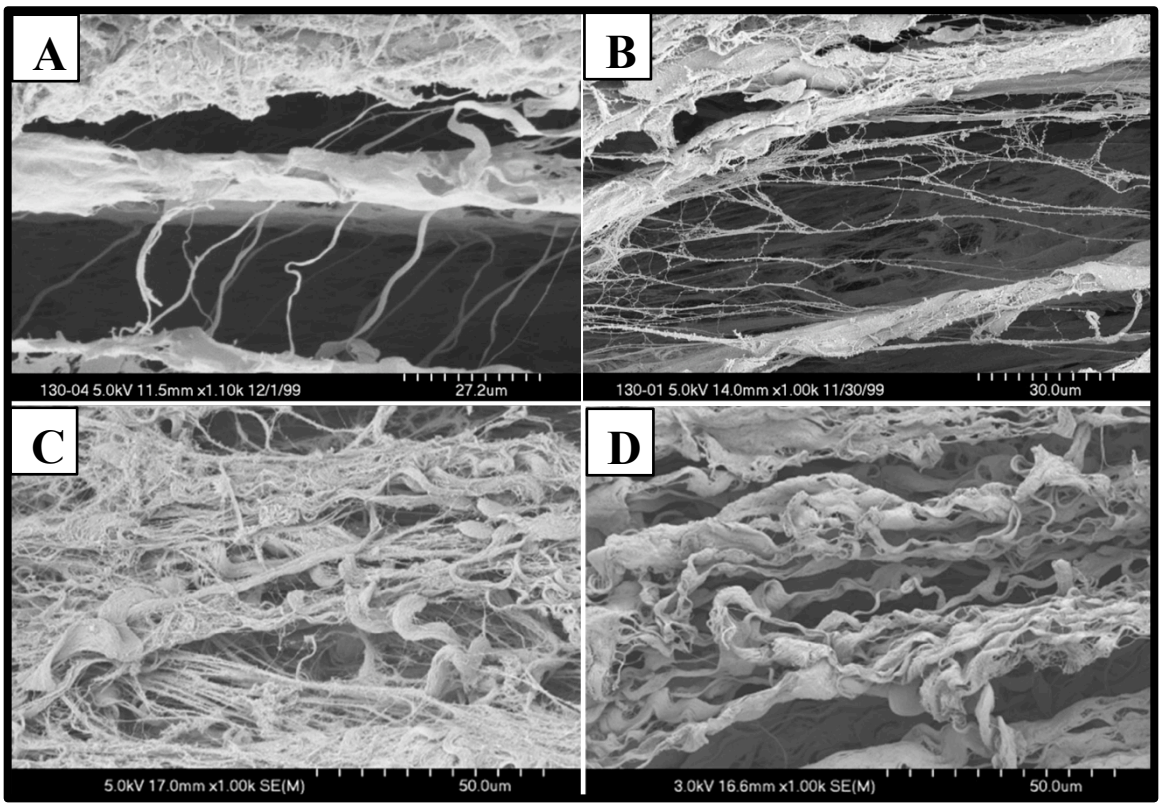

Figure 1.4. Scanning electron microscopy images of carpal tunnel subsynovial connective tissue in various states. (A) Thick horizontal collagen bundles adjoined by thinner perpendicular collagen fibrils that are loose during neutral finger and wrist postures. (B) Vertical fibrils are taut during flexor tendon excursion to transfer movement between thick bundles by sequential recruitment from deep to superficial. (C) Subsynovial connective tissue from a healthy individual where thin interconnecting collagen fibrils can be distinguished from thicker collagen bundles. (D) Subsynovial connective tissue from an individual with severe fibrosis where thin interconnecting fibrils are no longer present and only thick fibrotic collagen bundles remain in a highly disorganized fashion (Adapted from Ettema et al., 2006).

For many years, researchers and clinicians have identified elevated carpal tunnel pressure (CTP) to be closely related to CTS (Gelberman et al., 1981; Rojviroj et al., 1990). CTP is the hydrostatic pressure present within the boundaries of the carpal tunnel

canal and is directly influenced by the volume of content (fluid or solid tissue) within the carpal tunnel. Despite the proximal and distal ends of the carpal tunnel being open, the poor permeability of SSCT may play a role in maintaining elevated CTP by trapping edema that may have accumulated from tissue damage. Osamura and colleagues (2007b) demonstrated, in healthy cadaveric tissue samples, that fluid flow through SSCT only occurs at pressure gradients that exceed physiologically possible CTPs. They did this by quantifying the rate of fluid flowing through SSCT samples using a custom pressure apparatus that forced fluid across the tissue and found that the minimum pressure necessary for flow to begin was 68.9 kPa (517 mmHg). This threshold for fluid flow is expected to be even greater in SSCT samples from CTS patients who have already undergone considerable tissue fibrosis. To place this into context, previous literature has suggested CTPs of 4 kPa (30 mmHg) as a critical threshold for the impairment of axonal transport and 6.7 kPa (50 mmHg) being capable of modifying the structural integrity of the myelin sheath (Rempel et al., 1999; Keir et al., 2007). Since SSCT lacks lymphatic vessels with a large enough diameter for effective fluid drainage, hydrostatic pressure can build up and impact the median nerve to elicit CTS symptoms through several mechanisms. First, mechanical compression impedes nerve conduction, which has been established as a reliable clinical diagnostic tool for CTS (Jablecki et al., 1993). Gelberman and colleagues (1983) demonstrated in a healthy population that impaired sensory and motor function, reminiscent of CTS could be induced with an inflatable catheter inserted into the carpal tunnel. By inflating the catheter, this acutely elevated CTP and mechanically compressed on the median nerve, which led to the development of

CTS symptoms. Second, increased CTP creates peripheral resistance to blood flow, especially to the microvasculature supplying the carpal tunnel and its contents. As a result, the carpal tunnel area can become slightly ischemic, and similarly lead to the development of sensory neurological symptoms such as numbness, tingling, and pain. Szabo et al. (1984) demonstrated ischemia could elicit these neurological symptoms following one minute of blood flow occlusion from a pneumatic blood pressure cuff placed above the elbow and inflated above systolic pressure. In more chronic conditions of CTS, local ischemia can even lead to degradation and demyelination of the median nerve (Rosen et al., 1992).

Biomechanical factors affecting CTP have been studied extensively in healthy individuals in vivo and in CTS patients primarily using ex vivo models. In healthy individuals, increasing fingertip loads will elevate CTP and tasks requiring a pinch posture will have an additive effect on CTP as well (Keir et al., 1998b). Studies investigating finger and wrist postures have also shown that postures requiring finger flexion or non-neutral wrist angles (flexed or extended) can elicit CTP that are greater than values measured in neutral positions (Keir et al., 1998a; Rojviroj et al., 1990). This relationship between posture and CTP aligns with findings from Mogk & Keir (2008) who found that carpal tunnel cross-sectional area and circumference decrease with wrist postures that deviate from neutral. Szabo & Chidgey (1988) evaluated the effect of repetitive work on the response and recovery rate of CTP in healthy and CTS patients. It was found that 1 minute of repetitive wrist flexion-extension was adequate to elevate CTP in all participants; however in early- and intermediate-severity CTS participants, CTP

remained elevated for a longer duration during the 10 minute monitored recovery period compared to healthy controls. Contact stress over palmar regions closest to the carpal tunnel also elevates CTP, which may have workplace implications for tasks requiring the use of hand tools and compressive palmar forces (Cobb et al., 1995). With the increasing number of jobs requiring the use of keyboards and computer mice, research investigating the effects of forearm rests and compression have also emerged accordingly. Studies examining muscle activation and upper body kinematics associated with keyboard and mouse use (Cook et al., 2004; Nag et al., 2009) have been conducted, but little to no research has evaluated how relative tendon-SSCT displacement may also be affected by forearm compression. Together, this collection of research suggests that fingertip forces, finger and wrist postures, palmar compression, and repetition of work all have an influence on CTP, which is a risk factor and identifier of CTS. However, a drawback of many of these studies is the invasive nature of measuring CTP *in vivo*. Typically, a small surgical incision or large-gauged needle must be used for inserting a pressure-sensitive catheter directly into the carpal tunnel. This catheter remains inside the carpal tunnel for the duration of the experimental protocol, which is likely uncomfortable for the participant, especially if motion is involved or they suffer from CTS. For this reason, alternative assessments of CTS risk or progression involving non-invasive methodologies are needed.

Established SSCT injury may be a precursor to the development of CTS, thus assessment of the relative displacement between the tendon and its adjacent SSCT represents a feasible and non-invasive alternative to in vivo CTP measurement.

Specifically, the use of colour Doppler ultrasonography for evaluating the relative displacement between FDS tendon and SSCT has been introduced and validated against physically measured displacements from an *ex vivo* paradigm (Oh et al., 2007; Tat et al., 2015b). Although magnetic resonance imaging (MRI) is effective at differentiating soft tissue boundaries, like the tendon-SSCT interface, it is limited to capturing static images and has poor accessibility. Similar to MRI, ultrasonography can discriminate between tendon and SSCT but is also an appealing alternative to the drawbacks of MRI because it can capture relative tendon-SSCT displacement in static and dynamic conditions and is comparably more cost effective (Figure 1.5).

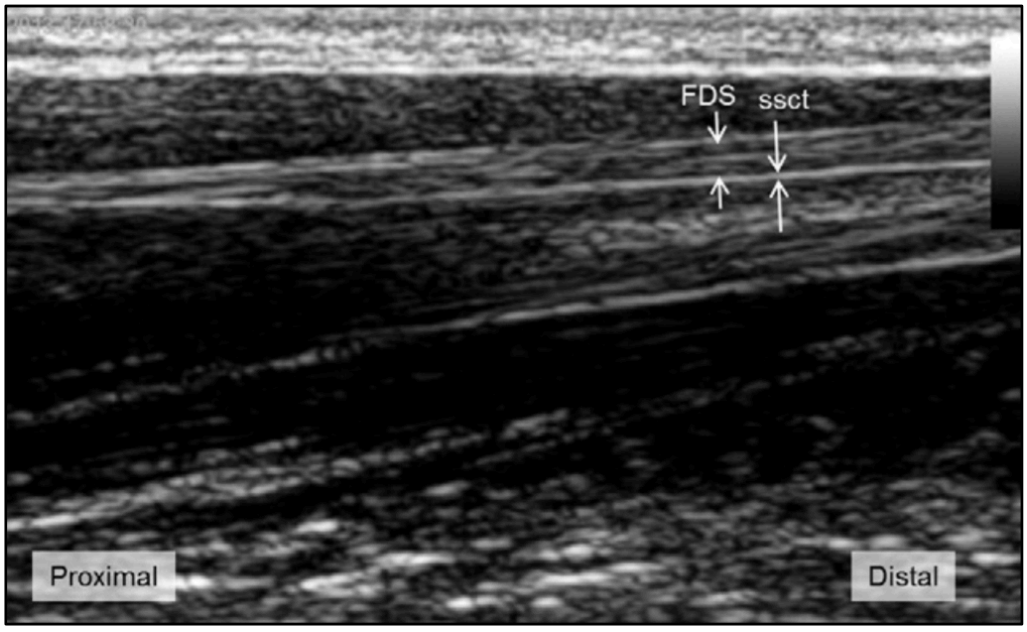

Figure 1.5. B-mode image of the flexor digitorum superficialis tendon (FDS) and adjacent subsynovial connective tissue (SSCT) (top to bottom = superficial to deep). FDS appears as a collection of fibrillar striations forming a band. SSCT appears as the thin hyperechoic layer bordering the FDS tendon on either side. (Adapted from Tat et al., 2015a).

Assessment of differential motion between the flexor tendon and SSCT allows us to comment on the potential for shear injury in the SSCT. Since the collagen fibrils are strained in the transfer of kinetic energy between thicker collagen bundles, greater relative tendon-SSCT displacement increases the likelihood of exceeding the tolerance of collagen fibres and sustaining SSCT injury. In recent years, studies have evaluated relative tendon-SSCT displacement under the influence of biomechanical factors that are also known to affect CTP. Similar to its effect on CTP, increased finger flexion increases relative tendon-SSCT displacement where full finger flexion (metacarpophalangeal and interphalangeal) elicits greater relative tendon-SSCT displacement than metacarpophalangeal flexion alone or interphalangeal flexion alone (Kociolek & Keir, 2016). Wrist flexion also increases relative displacement between the flexor tendon since increasing flexion at the phalanges and the wrist requires greater overall tendon displacement (Kociolek & Keir, 2016; Yoshii et al., 2008). However, these referenced studies that investigated wrist posture on relative tendon-SSCT displacement had opposing results in the extension direction. Kociolek & Keir (2016) attributed the conflicting results to methodological differences inherent in testing humans in vivo versus cadaveric models. In an evaluation of repetitive motion, participants performed concurrent (all fingers together) and differential (middle finger over) finger flexion and extension cycles for 30 minutes while sonographic relative tendon-SSCT displacement was continuously assessed (Tat et al., 2013). The authors demonstrated that differential finger motions generate greater relative displacement than concurrent finger motions, and that relative displacement increases over time with repetitive work.

From the research discussed, it is evident that CTP and relative tendon-SSCT displacement are both affected by biomechanical factors. The two are, in fact, related to each other in terms of the etiology of CTS as increased CTP creates greater gliding resistance between tendons sliding through the carpal tunnel. During tendon excursion from finger flexion-extension, increased gliding resistance creates greater shear between carpal tunnel contents. Subsequently, this could increase the relative tendon-SSCT displacement (shear strain) and the likelihood of sustaining SSCT shear injury. Zhao and colleagues (2011) demonstrated this relationship in a cadaveric model where gliding resistance was measured as a function of experimentally manipulated CTP. A balloon catheter was inserted into the carpal tunnel, which allowed the experimenters to control CTP (0 mmHg, 30 mmHg, 60 mmHg, 90 mmHg, 120 mmHg) during distal and proximal tendon excursion. Gliding resistance was calculated as the difference between values measured by two load transducers affixed to the same tendon on the proximal and distal side of the carpal tunnel. The authors found that 0 mmHg of CTP had significantly lower gliding resistance than any of the conditions with elevated CTP. In another study conducted by Zhao and colleagues in 2007, they corroborated the influence of biomechanical factors on risk of SSCT shear injury by displaying increased gliding resistance with flexed wrist postures and differential finger motion.

Finger movement speed has also been identified as a risk factor for increasing tendon-SSCT shear strain. Filius et al. (2012) evaluated excursion resistance energy (area under force displacement curve) and peak tendon force at two tendon excursion velocities (2 and 60 mm/s) in cadavers. They demonstrated in cadavers that high velocity

excursions resulted in greater absolute resistance energies and peak tendon forces that occurred earlier in the tendon excursion cycle. Kociolek et al. (2015) reproduced this effect of speed in cadavers but also demonstrated a multiplicative effect of wrist posture and tendon force on increasing excursion resistance energy. Other investigations examining velocity on tendon-SSCT interactions have also exhibited increased relative displacement with increased excursion velocities in cadavers (Tat et al., 2013; Yoshii et al., 2010). From these investigations, it is apparent that movement velocity has a considerable effect on tendon-SSCT shear but these findings have only been demonstrated in cadavers. Thus, testing the viscoelastic properties of SSCT in vivo by evaluating relative tendon-SSCT motion at multiple finger movement speeds is a necessary evaluation.

In CTS, the cumulative tendon-SSCT injury theory suggests that local ischemia ultimately leads to median nerve neuropathy. As such, a useful perspective may be to focus on the vascular and histological changes in the SSCT in the wake of tissue fibrosis. Oh and colleagues (2004) conducted an investigation of vascular changes in CTS pathological SSCT compared to healthy cadaveric controls. Their results gave evidence of atherosclerotic changes in pathological SSCT as demonstrated by vascular proliferation, hypertrophy, lumen obstruction, and wall thickening. The authors attributed these changes to a downregulation and redistribution of elastin away from the blood vessel, which was induced by local ischemia (Figure 1.6). Elastin plays a critical role in inhibiting proliferation and infiltration of smooth muscle into the blood vessel, a prominent characteristic of atherosclerosis (Oh et al., 2004). Other research has also

supported the notion of chronic-intermittent ischemia-induced tissue remodeling. Hypoxia has been shown to upregulate fibroblastic activity through increased transcription of platelet-derived growth factor-B (PDGF-B), vascular endothelial-derived growth, and thrombospondin-1, all of which promote atherosclerotic vessel changes and cell adhesion (Faller 1999; Song et al., 2015). Taken together, this evidence shows that chronic intermittent ischemia may play a role in local vascular histological changes characteristic of CTS and SSCT fibrosis.

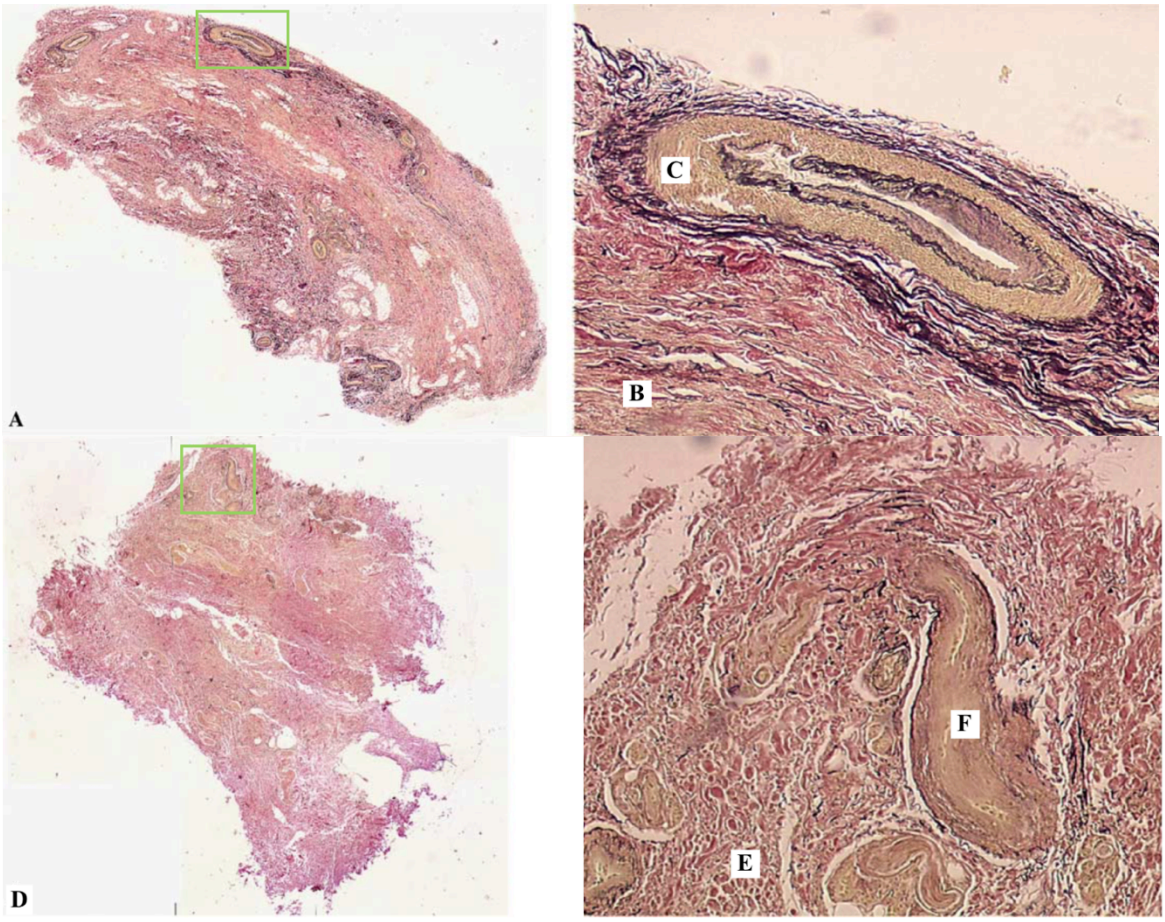

Figure 1.6. Histological differences (10x magnification) between healthy (top) and CTS pathological (bottom) subsynovial connective tissue, where the increasing colour intensity reflects greater density of that particular tissue: black = elastin, yellow = smooth muscle, red = collagen. The green boxes in images (A) and (D) represent the area that is magnified in the image to its right. Overall number of blood vessels is increased in CTS (D) compared to healthy (A). Collagen content is lower in CTS (E) compared to healthy (B) as seen by the decreased intensity of red. Quantity of elastin (black) is reduced and is not localized around blood vessel in CTS (F) compared to healthy (C) where elastin is dense around the inner and outer wall of the blood vessel. Lumen of blood vessel is visibly obstructed in CTS (F) (Adapted from Oh et al., 2004).

With acute ischemia, a powerful vasoconstrictor, endothelin-1, is upregulated in as little as 30 minutes of oxygen tension (Faller 1999; Kourembanas et al., 1991).

Although this effect is reversible upon reoxygenation, it begs the question whether relative tendon-SSCT motion can be affected by transient ischemia. We know the ability of circulating glycoproteins, such as lubricin and glycoaminoglycans, to reduce gliding friction is dependent on how much fluid is available within the extracellular matrix (Rigozzi et al., 2013; Sun et al., 2008). Additionally, the amount of fluid in the extracellular matrix may also affect the viscoelastic properties of the SSCT gliding mechanism by attenuating shear stress at high tendon velocities (Yoshii et al, 2010). Therefore under the influence of vasoconstrictors like endothelin-1, which is secreted during acute ischemia, it is possible that fluid levels in the extracellular matrix become reduced and subsequently negatively impact relative tendon-SSCT motion.

From this review of literature several key relationships have been highlighted. First, biomechanical risk factors have similar effects on CTP and relative tendon-SSCT motion during finger flexion-extension movements. Secondly, CTP and relative tendon-SSCT displacement share a connection whereby increased CTP can increase the shear strain between tendon and SSCT through increased gliding resistance. In combination with the finding that palmar pressures increased CTP from Cobb et al. (1995), this could have useful applications for investigating the effect of elevated CTP on relative tendon-SSCT motion without the need for inserting a pressure catheter directly into the carpal tunnel. Movement velocity plays a critical role in tendon-SSCT shear whereby fast tendon excursion elicits greater relative tendon-SSCT displacement. Finally, local partial ischemia can upregulate the regional transcription of vasoconstrictors to potentially alter the amount of available fluid within the extracellular matrix within the SSCT and

subsequently relative tendon-SSCT motion. A summary of how these various factors may affect relative tendon-SSCT displacement can be found in Figure 1.7.

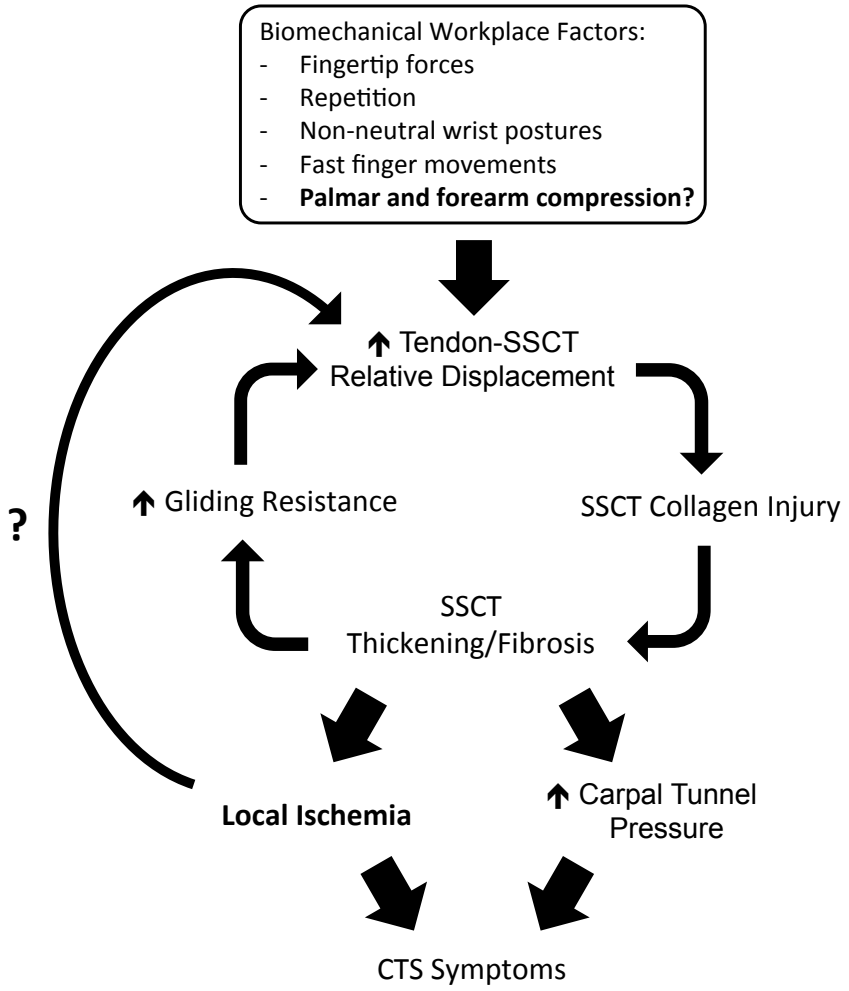

Figure 1.7. Summary of how relative tendon and subsynovial connective tissue (SSCT) motion may be influenced by biomechanical workplace factors and local ischemia. Increased relative tendon-SSCT displacement is a possible risk factor for sustaining SSCT injury. Subsequently, the collagen rebuilding and remodeling process ensues and can lead to SSCT thickening and fibrosis. With greater content taking up volume in the carpal tunnel, this has the effect of increasing carpal tunnel pressure and gliding resistance, while creating local ischemia. Ischemia and increased carpal tunnel pressure reduces blood flow supplying the median nerve and can lead to the development of carpal tunnel syndrome (CTS) symptoms acutely or median nerve degradation with chronic exposure.

1.1. Purposes and Hypotheses

The purpose of this thesis is to isolate the influence of each of these factors on flexor digitorum superficialis (FDS) relative tendon-SSCT motion of the third phalange at fast and slow movement speeds by investigating the following research questions:

1. Do palmar and forearm compression increase relative tendon-SSCT motion during repetitive finger flexion-extension at different movement speeds?
2. What is the effect of local partial ischemia on relative tendon-SSCT motion repetitive finger flexion-extension at different movement speeds?
3. Does fast movement speeds elicit greater relative tendon-SSCT motion than slow movement speeds *in vivo?*

These research questions were investigated via separate experimental sessions and we hypothesized the following:

1. Palmar and forearm compression at the fast movement speed would increase relative tendon-SSCT motion compared to movement without mechanical compression.
2. Partial ischemia at the fast movement speed would increase relative tendon-SSCT motion compared to movement without ischemia.
3. Fast movement speed would elicit greater relative tendon-SSCT motion *in vivo* compared to the slow movement speed.

2.0. RESEARCH ARTICLE

External compression and partial ischemia decreases human finger flexor tendon and subsynovial connective tissue relative motion

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Author Contributions Statement:
All authors contributed extensively to research design as well as the acquisition, analysis, and interpretation of data. Both authors also contributed heavily towards drafting and revising of the manuscript.

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compression; carpal tunnel; shear strain; tendon; subsynovial connective tissue

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2.1 Abstract

Cumulative shear strain of the subsynovial connective tissue (SSCT) of the finger flexor tendons likely plays a role in the development and progression of carpal tunnel syndrome. We used colour Doppler ultrasound imaging to examine flexor digitorum superficialis (FDS) tendon and SSCT motion during repetitive finger flexion-extension under conditions of palmar compression, forearm compression, partial ischemia (via blood pressure cuff) and different finger movement speeds. With partial ischemia, SSCT displacement decreased (22.9 ± 3.3 mm vs. 22.0 ± 3.3 mm; $p = 0.015$), while tendon displacement remained unchanged. Forearm compression reduced tendon displacement (28.5 ± 4.1 mm vs. 27.0 ± 4.6 mm; $p = 0.043$) and showed a trend for reduced SSCT displacement while palmar compression had no significant effects. We also found a main effect of movement speed across all compression conditions that showed the fast movement speed elicited greater relative tendon-SSCT displacement than the slow movement speed, in agreement with previous cadaveric studies. Demonstrating that ischemia negatively impacts tendon-SSCT displacement bridges an important gap between observations of reduced blood flow and shear injury risk. These results also indicate differential effects of compression location on tendon displacement. Taken together, these findings suggest that the location of external mechanical pressures to the forearm need to be evaluated in tendon injury risk assessments and ischemia may increase tendon-SSCT shear injury risk which could have implications for the development and progression of carpal tunnel syndrome.

2.2. Introduction

Thickening and fibrosis of the subsynovial connective tissue (SSCT) surrounding the finger flexor tendons and median nerve are commonly reported signs of carpal tunnel syndrome (CTS) (Ettema et al., 2004; Lluch, 1992). In healthy individuals, the SSCT is a vascularized network of collagen bundle layers, interconnected by thinner collagen fibrils that join the bundle layers to each other and to the adjacent tendon surface (Ettema et al., 2006; Guimberteau et al., 2010). Cumulative tendon-SSCT shear injury has been suggested as a precursor for CTS development wherein excessive differential motion between the two tissues can rupture interconnecting collagen fibrils, even at physiological ranges of motion (Vanhees et al., 2012; Yoshii et al., 2008). SSCT fibrosis ensues and adds tissue to the carpal tunnel, which compresses the median nerve compression and could lead to eventual neuropathy (Rosen et al., 1992). Various workplace risk factors such as repetitive motion (Tat et al., 2013), fast movement speeds (Filius et al., 2014; Yoshii et al., 2011), and flexed wrist postures (Kociolek & Keir, 2016) have been shown in controlled laboratory studies to increase tendon-SSCT shear strain during finger flexion-extension but the influence of mechanical compression and acute ischemia remains unknown.

External mechanical compression affects different factors related to CTS development. Cobb et al. (1995) demonstrated that compressive force applied to the palm over areas closest to the carpal tunnel had the greatest effect on increasing carpal tunnel pressure in cadavers. This could have implications for incurring tendon-SSCT shear injury because experimentally manipulated carpal tunnel pressure has been linked to

increased gliding resistance during finger flexor tendon excursion in cadavers (Zhao et al., 2011). Also using a cadaver model, Holmes et al. (2011) applied force to the carpal tunnel with various indenter sizes and found that transverse carpal ligament (TCL; superior border of carpal tunnel) stiffness increased with increasing indenter size (5-20 mm) but decreased with the largest indenter (35 mm) due to contact with carpal bones. Increased TCL stiffness restricts the motion of carpal tunnel borders and could increase mechanical compression on the flexor tendons and median nerve by increasing carpal tunnel pressure. With the universality of jobs requiring extensive keyboard and mouse use, some research examining the effect of forearm and wrist rests on workplace injury risk has emerged (e.g. Cook et al., 2004; Nag et al., 2009). These studies have primarily focused on muscle activation and kinematics of the neck, back, and upper extremity, but the effect of forearm compression on tendon-SSCT shear injury risk has gone relatively unstudied. Examining the effect of mechanical compression on relative tendon-SSCT motion could elucidate associations between occupational risk factors and potential for shear injury.

Median nerve neuropathy can ultimately be attributed to local ischemia, which causes the sensation of numbness, paresthesia, weakness, and impaired motor function commonly reported with CTS (Gelberman et al., 1983; Stevens et al., 1999; Szabo et al., 1984). In a histological investigation of individuals with CTS and healthy cadaveric controls, Oh and colleagues (2004) found evidence of atherosclerotic remodeling in the blood vessels of pathological SSCT. Chronic-intermittent ischemia has been proposed as a mechanism for upregulating fibroblastic activity, which may be responsible for long-

term vascular histological changes characteristic of CTS and SSCT fibrosis such as vascular proliferation, hypertrophy, lumen obstruction, and wall thickening (Faller 1999; Song et al., 2015). Since CTS symptoms can be elicited in healthy individuals from temporary compression of the median nerve (Gelberman et al., 1983), it begs the question whether relative tendon-SSCT motion is affected by transient ischemia as well. Acute exposure (30 minutes) to ischemia has been shown to upregulate vasoconstrictors such as endothelin-1 (Faller 1999; Kourembanas et al., 1991), which could alter the fluid concentration of the SSCT extracellular matrix and affect relative tendon-SSCT displacement. Extracellular fluid of the SSCT gives viscoelastic properties to this tissue for attenuating shear stress at higher tendon velocities. Moreover, the ability of circulating factors such as lubricin and glycoaminoglycans to reduce gliding friction is highly dependent on the extracellular matrix having adequate fluid (Rigozzi et al., 2013; Sun et al., 2008). Filius and colleagues (2014) showed that high-velocity cyclical tendon excursion lowered the threshold for SSCT shear damage compared to low-velocity excursions in cadavers. They suggested the likelihood of collagen fibrillar rupture increases at higher velocities because SSCT stiffens with the viscoelastic effects of surrounding fluid. Additional studies have similarly found decreased SSCT displacement and increased shear strain with high-velocity excursions supporting the existence of viscoelastic properties of SSCT (Tat et al., 2013; Yoshii et al., 2011). With the vascular network so closely integrated within the SSCT and ischemia having acute effects to alter the carpal tunnel fluid environment, it is possible that transient ischemia could impact

tendon-SSCT motion, independent of influence from mechanical compression at the tendon level.

The purpose of this investigation was to quantify relative motion between tendon and SSCT under conditions of external mechanical compression and ischemia. Through the use of colour Doppler ultrasound, we assessed middle finger flexor digitorum superficialis (FDS) tendon and SSCT displacement during finger flexion-extension at different movement speeds with palmar compression, forearm compression, and partial brachial artery occlusion. We hypothesized that each of the experimental conditions (palmar compression, forearm compression, partial ischemia) would increase relative motion between the tendon and SSCT.

2.3. Methods

Participants

Twenty healthy participants (10 men, 10 women) were recruited from the university population for two testing sessions (age = 23.0 ± 2.2 years, mass = 74.2 ± 15.4 cm, height = 174.4 ± 11.2 cm, forearm length = 22.7 ± 1.8 cm). Due to technical issues, one participant was excluded from the analysis. Participants were excluded from the study if they had any history of the following: hypertension, diabetes mellitus, hypothyroidism, amyloidosis, sarcoidosis, hemodialysis, gout, osteoarthritis, degenerative joint disease, wrist tendinopathy, peripheral nerve disease, acute injury to the distal upper extremity, and pain, numbness, or tingling of the hand. The study was approved by the Hamilton Integrated Research Ethics Board.

Experimental Design

A prospective comparative study design was implemented to evaluate the effects of mechanical compression, partial ischemia, and finger movement speed on relative tendon-SSCT motion in vivo. During finger flexion-extension, large relative displacements can strain and even rupture tendon-SSCT collagenous connections, which could contribute to the development and progression of CTS. Participants experienced all experimental conditions in a balanced design providing level II evidence.

Two experimental sessions involving different compression conditions were systemically randomized between participants. Sessions were separated by a minimum of 72 hours to eliminate potential carry-over effects between ischemia and external compression conditions. Palmar and forearm compression were applied in one session. In the second session, a brachial blood pressure cuff induced partial ischemia (subsystolic occlusion) to the forearm and hand. Participants were supine with their right arm rested in a shoulder-abducted, elbow extended, and forearm-supinated posture for all movement trials. Each trial consisted of 13 repetitions of full finger flexion-extension using only their middle finger (Tat et al., 2013). To isolate motion to the middle finger, Velcro straps secured the other fingers in a mid-flexed posture to a custom handgrip (Figure 2.1). We had large and small handgrips to accommodate for hand size and allow for full flexion-extension range of motion. To maintain a consistent range of motion between flexion-extension cycles, we instructed participants to contact their distal finger crease to the handgrip during flexion and their fingernail to the apparatus during extension. An audible metronome denoted the two movement speeds (0.75 and 1.25 Hz). Practice trials

were performed to familiarize participants to movement speeds. The sampling order of experimental conditions (palmar, forearm, ischemia; slow and fast for each) was systemically randomized and three trials (13 flexion-extension cycles each) were recorded in each condition.

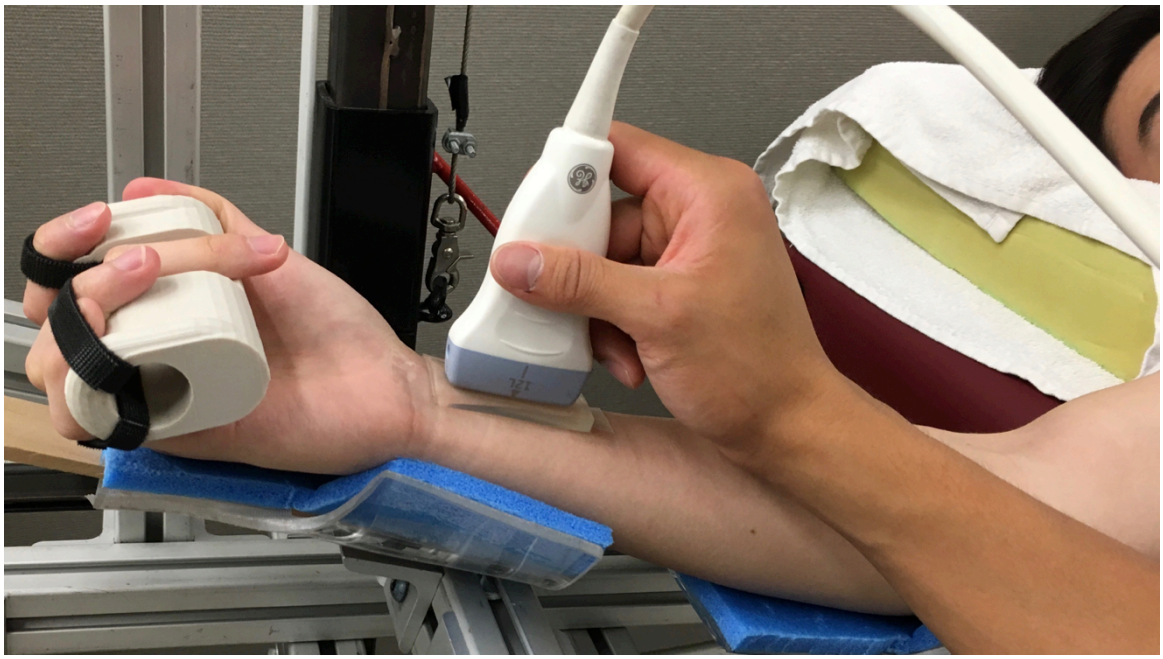

Figure 2.1. Experimental setup with participant resting in supine posture and fingers secured in custom handgrip via Velcro straps. Ultrasound transducer with gel wedge standoff was placed at the proximal wrist crease and in line with tendon motion.

Custom force applicators were 3D printed and secured a 5 kg mass via a cable that compressed the palm and forearm. The palmar force applicator had a flat, circular contact surface (2 cm diameter) that compressed the palm over the distal edge of the carpal tunnel (Figure 2.2A). The contact surface of the forearm force applicator had a width of 2 cm that compressed the forearm approximately 9 cm proximal to the distal wrist crease

(Figure 2.2B). Baseline motion trials (no force applicators) were collected prior to trials involving palmar or forearm compression. For each compressive motion trial, the centre of the force applicator was aligned with the middle FDS tendon line of action.

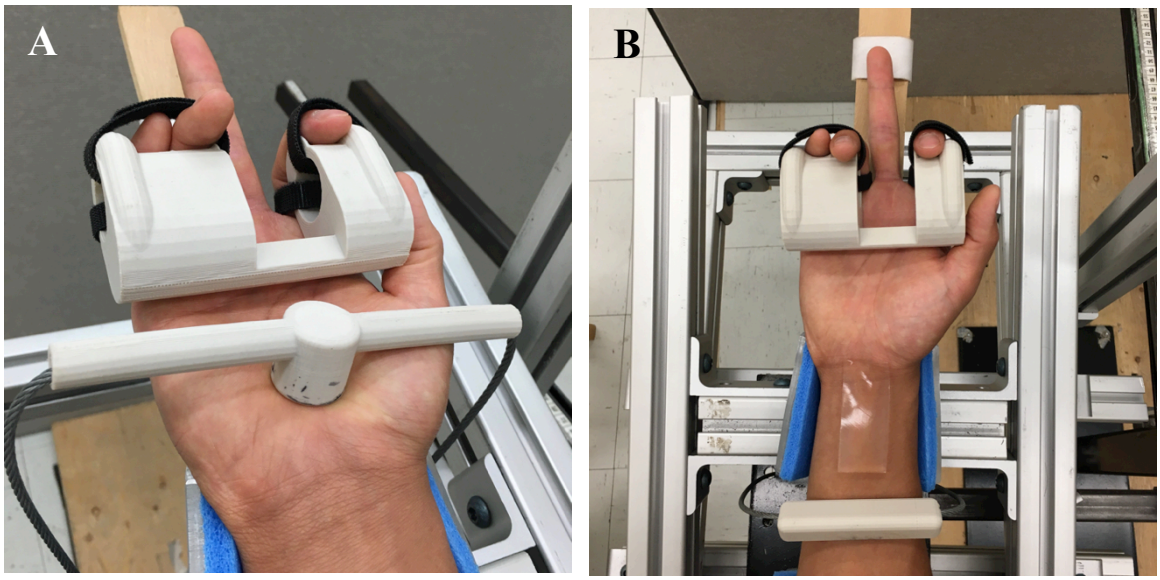

Figure 2.2. Palmar (A) and forearm (B) force applicators with 5kg weight secured to both force applicators via steel cables. Palmar force applicator contacts the palm at approximately the distal edge of the carpal tunnel. Forearm force applicator contacts the distal forearm approximately 9 cm proximal from the distal wrist crease.

At the start of the partial ischemia session, multiple resting systolic (SBP) and diastolic (DBP) blood pressure measurements (Dinamap 100 V2, GE Healthcare, Milwaukee, WI) were taken. Partial ischemia was created using a manual blood pressure cuff over the upper arm inflated to diastolic blood press plus 25% of the SBP-DBP difference. After baseline motion (without blood pressure cuff) was recorded, the cuff was secured around the distal upper arm and inflated to the designated pressure (mean =

76.0 ± 4.0 mmHg) (Figure 2.3). Participants were asked for their rating of perceived discomfort (RPD) on an analog-visual scale ranging from 0 (no discomfort at all) to 10 (intolerable discomfort). RPD was used to gauge discomfort and terminate the ischemia protocol at a score of 8, but no participants reached this threshold. Collection of ischemia motion trials began after 18-20 minutes of subsystolic occlusion and cuff pressure was released after motion trials were collected (mean occlusion time = 24.6 ± 3.8 minutes).

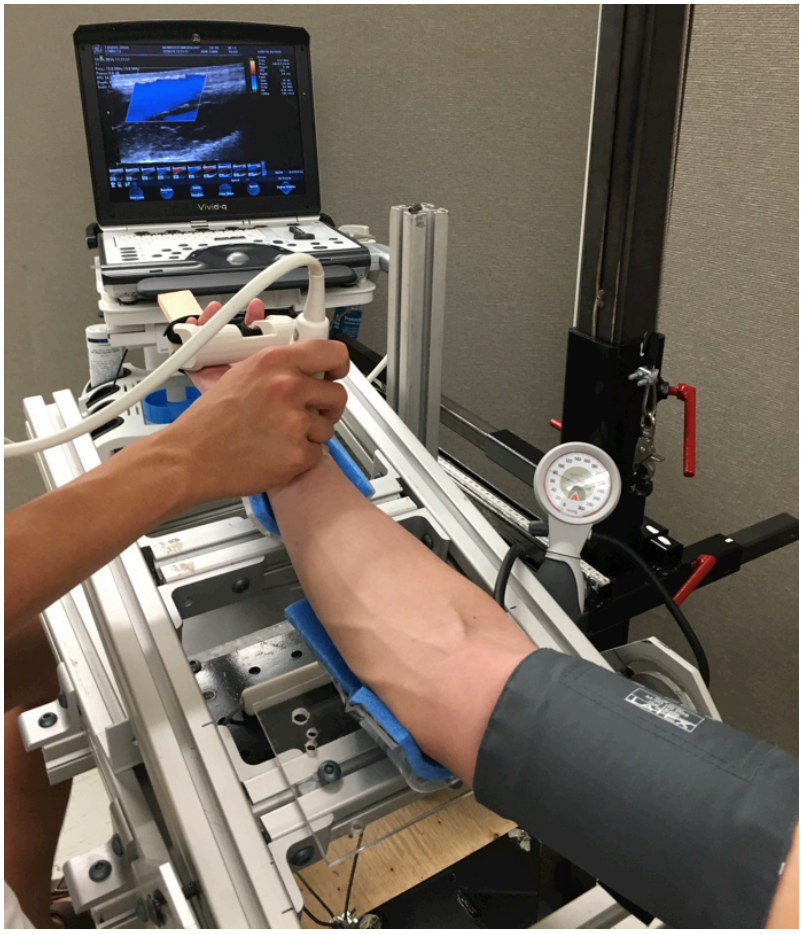

Figure 2.3. Partial ischemia condition with manual blood pressure cuff placed around distal upper arm and pressure gauge visible to monitor compression level.

All B-mode sonographic videos were captured with a linear array transducer (12L–RS) and ultrasound system (Vivid q BT10, GE Healthcare, Milwaukee, WI). The probe was positioned at the proximal wrist crease (Figure 2.1), inline with the area corresponding to zone V of the middle finger FDS tendon (Boyer et al., 2002; Kociolek et al., 2016). Tendon was visually identified by its fibrillar-striated pattern, which differs from the SSCT that appears as a thin hyperechoic band adjacent to the tendon (Figure 2.4B). Colour Doppler imaging (CDI) was used to measure tendon velocity and appears as colour maps overlaid on the B-mode image (Figure 2.4A). CDI is sensitive to the angle of insonation between the Doppler beam and moving tissue. Thus, the ultrasound probe was electronically steered to 20° and a custom aqueous gel standoff wedge (Aquaflex gel pad, Cone Instruments, Solon, OH) was used to optimize the insonation angle to approximately 60 degrees (Lui et al., 2005) (Figure 2.1). Other sonographic imaging settings included: transducer frequency = 13 MHz, tissue velocity scale = ± 17 cm/s, low-velocity reject = 1.9 cm/s, focus depth = 3.0 cm, sampling rate = 34.5 fps.

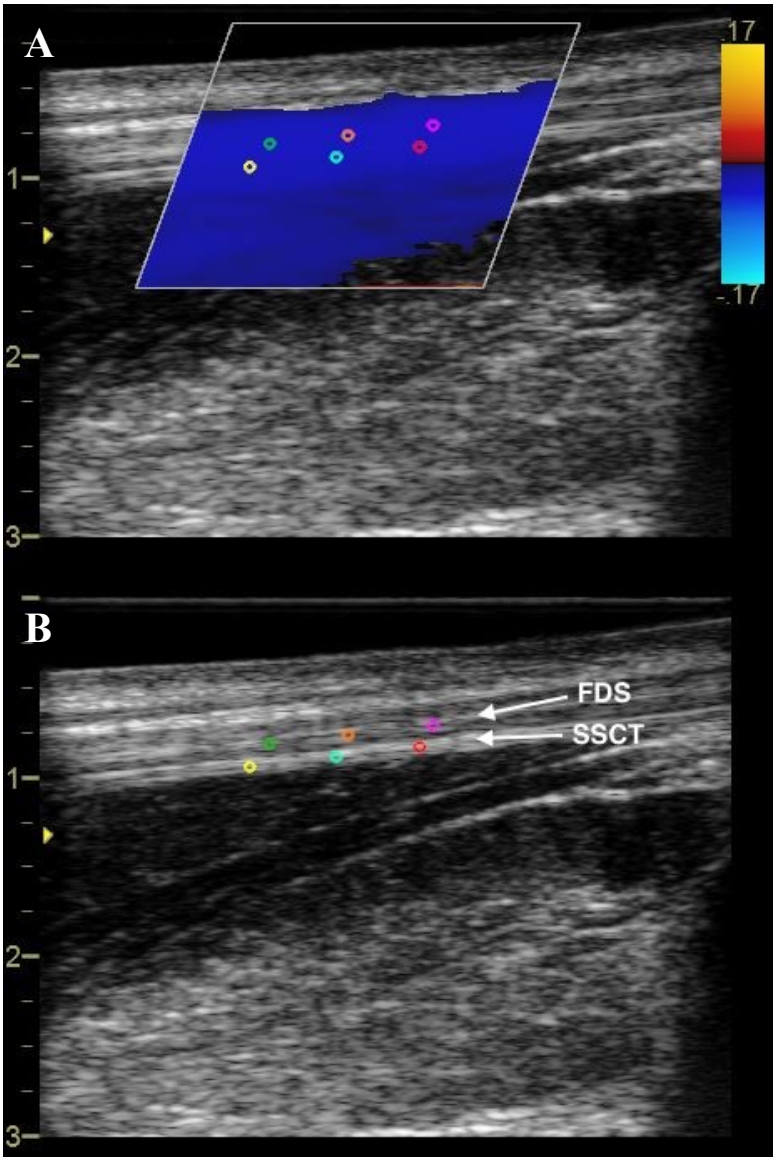

Figure 2.4. Identical B-mode images with (A) and without (B) the CDI colour map overlay. The colour scale (A) shows the detectable tissue velocity range with red-orange and blue representing extension and flexion respectively. Brighter colours represent faster tissue velocity. Regions of interest for sampling independent velocity traces are visible on both images and appear as the small multi-coloured circles. FDS tendon and SSCT tissue velocities were measured using three regions of interest for each tissue type.

Tendon and SSCT velocity were obtained offline using ultrasound dedicated analysis software (Q-Analysis, Echopac, GE Healthcare, Wauwatosa, WI). Three

stationary circular regions of interest were placed collinearly over each tissue to measure tissue velocity in multiple locations along the tissue's length (Figure 2.4). The location of each region of interest was visually inspected to maintain tracking of the appropriate tissue throughout each trial. The three velocity traces for each tissue type were averaged to create one representative tissue velocity signal, and then low-pass filtered (4 Hz, 2^{nd} order Butterworth) and corrected for angle of insonation ($\cos\theta$). Tissue displacement was calculated by integrating velocity data for each flexion-extension cycle separately. By integrating each cycle independently, integration drift error associated with calculating displacement from velocity was minimized. Two measures for describing tendon-SSCT shear strain were calculated from displacement and velocity cycle data. Shear strain index (SSI) normalized relative tendon-SSCT displacement to total tendon displacement ($(Tendon_{disp} - SSCT_{disp}) / Tendon_{disp} \bullet 100\%$). Max velocity ratio (MVR) was the quotient between peak SSCT and tendon velocities ($SSCT_{MaxVel} / Tendon_{MaxVel} \bullet 100\%$). Larger SSI and smaller MVR values represented increased tendon-SSCT shear strain. Mean and peak displacement and velocity (separated by flexion and extension) variables were also calculated for each movement cycle (Figure 2.5).

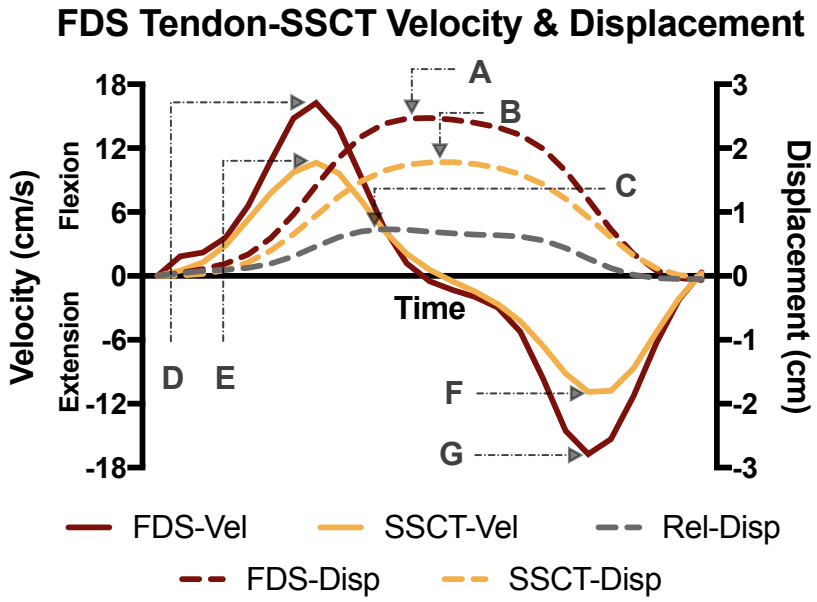

Figure 2.5. Peak FDS tendon and SSCT tissue velocity and displacement for one finger flexion-extension cycle. (A) Peak tendon displacement. (B) Peak SSCT displacement. (C) Peak relative displacement. (D) Peak flexion tendon velocity. (E) Peak flexion SSCT velocity. (F) Peak extension SSCT velocity. (G) Peak extension tendon velocity.

Statistical Analysis

For each variable, a mean value from 24 movement cycles (8 cycles x 3 trials) was calculated to represent each experimental condition (compression-speed combination). Repeated measures ANOVAs were performed to test the effects of movement speed and compression on displacement (tendon, SSCT, and tendon-SSCT relative), mean and peak velocity (tendon and SSCT in flexion and extension), SSI, and MVR. Separate analyses were conducted for the palmar and forearm compression session (3 conditions x 2 speeds) and the partial ischemia session (2 conditions x 2 speeds). Partial eta squared (η^2) effect sizes were calculated and represents the proportion of variance explained by each

independent variable. Significant main effects were followed up with Bonferonni corrected t-test comparisons. Statistical significance was set at $\alpha = .05$.

2.4. Results

2.4.1. Palmar and Forearm Compression

Displacement Variables

A main effect of compression was found for FDS displacement ($F_{2,36} = 4.3$, $\eta^2 = 0.193$, $p = 0.021$), with forearm compression eliciting significantly less tendon displacement than baseline (Figure 2.6). No significant compression effects were found for SSCT displacement, tendon-SSCT relative displacement, or SSI.

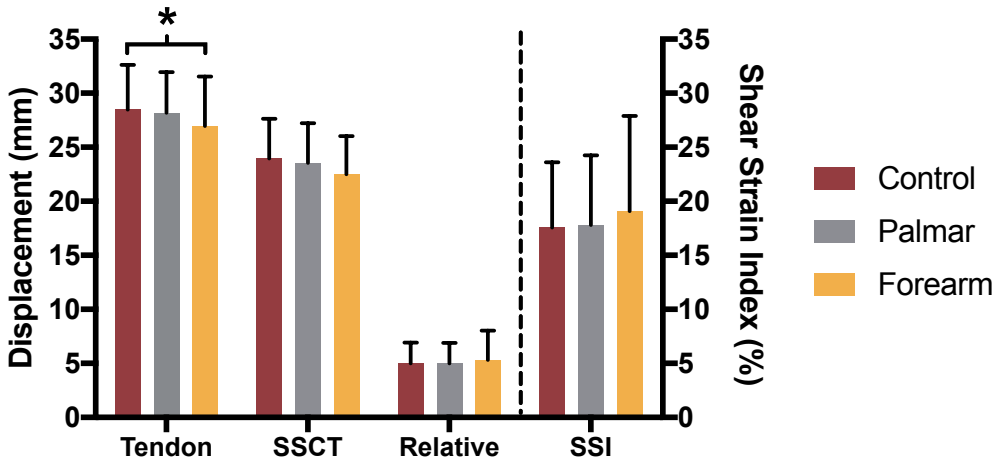

Figure 2.6. Mean FDS tendon and SSCT displacement from palmar and forearm compression session. Error bars represent one standard deviation from the mean. * Denotes significantly different from baseline ($p < 0.05$).

Movement speed significantly affected FDS displacement ($F_{1,18} = 32.0$, $\eta^2 = 0.640$, $p < 0.001$), SSCT displacement ($F_{1,18} = 142.9$, $\eta^2 = 0.888$, $p < 0.001$), relative tendon-SSCT displacement ($F_{1,18} = 35.3$, $\eta^2 = 0.662$, $p < 0.001$), and SSI ($F_{1,18} = 68.4$, $\eta^2 = 0.792$, $p < 0.001$). Compared to the slow movement speed, the fast movement speed decreased tendon and SSCT displacement, and increased relative tendon-SSCT displacement and SSI (Figure 2.7).

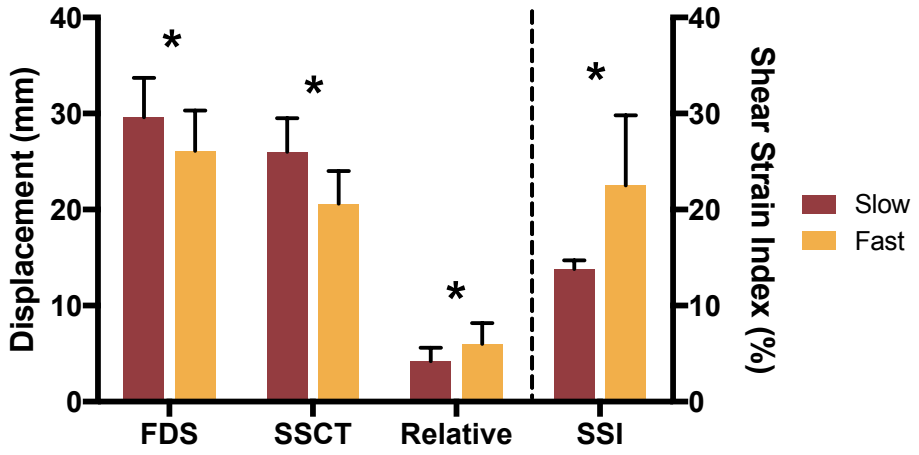

Figure 2.7. Tissue displacement and shear strain index for slow and fast movement speeds during the palmar and forearm compression session. Error bars represent one standard deviation from the mean. * Denotes significant difference between slow and fast ($p < 0.05$).

Velocity Variables

In the extension direction, there was a main effect of compression on peak FDS tendon velocity ($F_{2,36} = 5.5$, $\eta^2 = 0.234$, $p = 0.008$), peak SSCT velocity ($F_{2,36} = 4.5$, $\eta^2 = 0.199$, $p = 0.019$) and mean FDS tendon velocity ($F_{2,36} = 4.5$, $\eta^2 = 0.201$, $p = 0.018$). Post-hoc evaluation revealed peak FDS tendon velocity with forearm compression (10.9 ±

1.7 cm/s) was significantly slower than during palmar compression (11.5 ± 1.7 cm/s; $p = 0.041$) or baseline (11.6 ± 1.9 cm/s; $p = 0.019$). Similarly, mean FDS tendon velocity was significantly slower with forearm compression (5.3 ± 0.7 cm/s) than palmar compression (5.6 ± 0.8 cm/s; $p = 0.024$), but not baseline (5.5 ± 0.8 cm/s). Peak SSCT velocity showed a similar trend with forearm compression (8.4 ± 1.6 cm/s) being slower than palmar compression (9.2 ± 1.7 cm/s; $p = 0.133$) and baseline (9.2 ± 1.8 cm/s; $p = 0.082$), although not delineated by post hoc tests. No compression effects were found for any velocity variables in the flexion direction.

A main effect of speed was observed for all peak and mean velocity variables in both movement directions (Table 2.1). MVR in flexion ($F_{1,18} = 94.3$, $\eta^2 = 0.840$, $p < 0.001$) and extension ($F_{1,18} = 61.2$, $\eta^2 = 0.773$, $p < 0.001$) displayed main effects of speed where the fast movement speed resulted in lower MVR than the slow movement speed (flexion: 76.0 ± 8.0% vs. 85.9 ± 5.4%, $p < 0.001$; extension: 76.0 ± 8.5% vs. 83.6 ± 7.0%, $p < 0.001$). There were no significant interactions between movement speed and compression for any variables in the palmar and forearm compression session.

Table 2.1. Main effects and post-hoc summary for velocity variables from compression session. (FDS: flexor digitorum superficialis tendon; SSCT: subsynovial connective tissue; η^2: partial eta squared)

		Main Effect of Speed			Post-Hoc Comparison		
Velocity Variable		$F_{1,18}$	η^2	p	Fast (cm/s)	Slow (cm/s)	p
Flexion	Peak FDS	206.4	0.920	< 0.001	12.6 ± 2.2	8.3 ± 1.1	< 0.001
	Peak SSCT	90.9	0.835	< 0.001	9.5 ± 1.8	7.1 ± 1.0	< 0.001
	Mean FDS	358.7	0.952	< 0.001	7.9 ± 1.2	4.8 ± 0.7	< 0.001
	Mean SSCT	90.4	0.892	< 0.001	6.0 ± 1.1	4.2 ± .0.6	< 0.001
Extension	Peak FDS	248.3	0.932	< 0.001	13.1 ± 2.0	9.6 ± 1.4	< 0.001
	Peak SSCT	99.0	0.846	< 0.001	9.9 ± 1.8	7.9 ± 1.3	< 0.001
	Mean FDS	533.9	0.967	< 0.001	6.6 ± 0.9	4.3 ± 0.6	< 0.001
	Mean SSCT	189.3	0.913	< 0.001	5.2 ± 0.8	3.7 ± 0.5	< 0.001

2.4.2. Partial Ischemia

Displacement Variables

There was a small but significant main effect of ischemia on SSCT displacement ($F_{1,18} = 7.3$ $\eta^2 = 0.288$, $p = 0.015$) where ischemia decreased SSCT displacement and showed a trend for increased relative tendon-SSCT displacement compared to baseline (Figure 2.8). However, ischemia did not significantly affect FDS tendon displacement, relative displacement, or SSI.

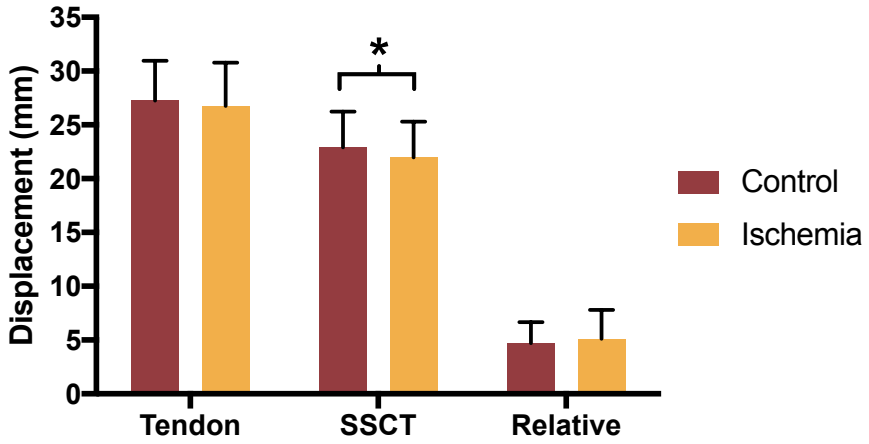

Figure 2.8. Tissue displacement from ischemia session showing a significant reduction SSCT displacement and a trend towards increased relative displacement. Error bars represent one standard deviation from the mean. *Indicates significantly different from baseline.

In the partial ischemia session, FDS tendon ($F_{1,18} = 65.4$, $\eta^2 = 0.784$, $p < 0.001$) and SSCT displacement ($F_{1,18} = 139.1$, $\eta^2 = 0.885$, $p < 0.001$) displayed significant main effects of movement speed where fast movement speed decreased FDS tendon displacement and SSCT displacement relative to the slow movement speed (Figure 2.8). Movement speed also had a significant main effect on relative tendon-SSCT displacement ($F_{1,18} = 9.2$, $\eta^2 = 0.337$, $p = 0.007$) and SSI ($F_{1,18} = 20.8$, $\eta^2 = 0.536$, $p < 0.001$). Relative tendon-SSCT displacement and SSI were greater with the fast movement speed than the slow movement speed (Figure 2.9).

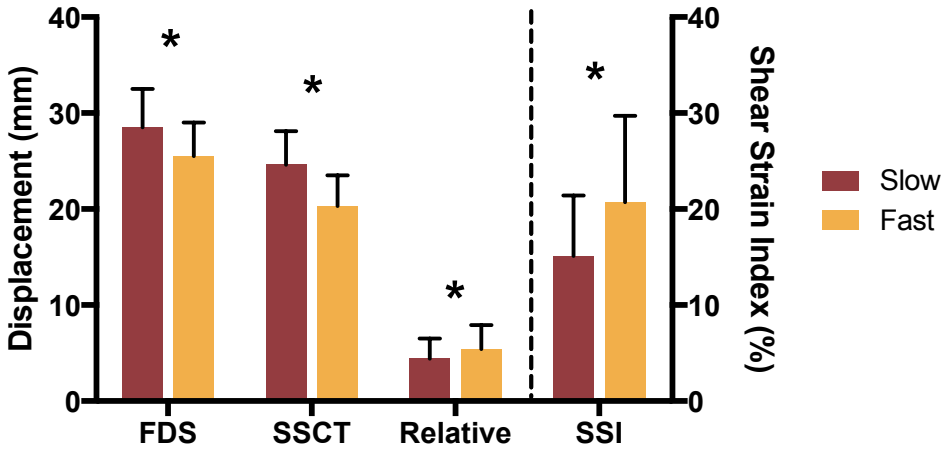

Figure 2.9. Tissue displacement and shear strain index for slow and fast movement speeds during the partial ischemia session. Error bars represent one standard deviation from the mean. * Denotes significant difference between slow and fast ($p < 0.05$).

Velocity Variables

Ischemia had a significant main effect on mean SSCT velocity in flexion ($F_{1,18} = 4.7$, $\eta^2 = 0.209$, $p = 0.043$) and extension ($F_{1,18} = 5.4$, $\eta^2 = 0.231$, $p = 0.032$). Compared to baseline, mean SSCT velocity with ischemia was slower in flexion (4.8 ± 0.8 cm/s vs. 5.0 ± 0.7 cm/s; $p = 0.043$) and extension (4.2 ± 0.8 cm/s vs. 4.4 ± 0.7 cm/s; $p = 0.032$).

Similar to the palmar and forearm compression session, peak and mean velocity variables in both directions were significantly affected by movement speed (Table 2.2). Moreover, movement speed had a significant main effect on MVR in flexion ($F_{1,18} = 36.4$, $\eta^2 = 0.668$, $p < 0.001$) and extension ($F_{1,18} = 38.1$, $\eta^2 = 0.679$, $p < 0.001$) with the fast movement speed showing lower MVR values in flexion (78.4 ± 9.7% vs. 86.2 ± 7.6%; $p < 0.001$) and extension (76.7 ± 10.0 vs. 83.2 ± 9.4%; $p < 0.001$) relative to the slow movement speed. No significant interactions between movement speed and ischemia condition were found for any variable in the ischemia session.

Table 2.2. Main effects and post-hoc summary for velocity variables from ischemia session. FDS: flexor digitorum superficialis tendon; SSCT: subsynovial connective tissue; η2: partial eta squared

		Main Effect of Speed			Post-Hoc Comparison		
Velocity Variable		$F_{1,18}$	η^2	p	Fast (cm/s)	Slow (cm/s)	p
Flexion	Peak FDS	210.8	.921	< 0.001	12.1 ± 2.1	7.8 ± 1.1	< 0.001
	Peak SSCT	148.7	.892	< 0.001	9.4 ± 1.8	6.6 ± 1.0	< 0.001
	Mean FDS	392.8	.956	< 0.001	7.4 ± 1.2	4.6 ± 0.7	< 0.001
	Mean SSCT	253.3	.934	< 0.001	5.9 ± 1.0	4.0 ± 0.6	< 0.001
Extension	Peak FDS	140.6	.886	< 0.001	12.7 ± 1.9	9.5 ± 1.5	< 0.001
	Peak SSCT	70.1	.796	< 0.001	9.7 ± 1.8	7.8 ± 1.3	< 0.001
	Mean FDS	661.6	.974	< 0.001	6.4 ± 0.8	4.1 ± 0.5	< 0.001
	Mean SSCT	188.8	.913	< 0.001	5.1 ± 0.7	3.6 ± 0.5	< 0.001

2.5. Discussion

This study evaluated the effects of palmar compression, forearm compression, partial ischemia, and movement speed on FDS tendon and SSCT motion in healthy individuals. During partial ischemia with a brachial cuff, SSCT displacement was significantly reduced while FDS displacement remained unchanged, likely increasing tendon-SSCT shear strain. Forearm compression reduced FDS tendon displacement while palmar compression did not significantly alter tendon displacement. Although neither of these mechanical compression conditions had an effect on the relative displacement of the tendon-SSCT (and likely shear strain), it demonstrates a differential effect of compression location on tendon displacement. Our study also successfully corroborated the viscoelastic properties of SSCT *in vivo* by demonstrating increased relative tendon-SSCT displacement and SSI with the fast movement speed. These

findings suggest that forearm compression, ischemia, and movement speed should be considered when evaluating tendon-SSCT motion.

We examined the influence of transient partial ischemia on tendon and SSCT motion with the intention of bridging the gap between local blood flow and tendon motion, independent of biomechanical factors shown to influence tendon-SSCT shear strain (Tat et al., 2013; Kociolek et al., 2015; Yoshii et al., 2011). With partial ischemia, we found a small but significant reduction in SSCT displacement (baseline: 22.9 ± 3.3 mm; ischemia, 22.0 ± 3.3 mm) without a significant change in FDS displacement (Figure 2.7). Flexion and extension SSCT velocity were also reduced relative to baseline suggesting ischemia could increase tendon-SSCT strain. Although not significant, relative tendon-SSCT displacement and SSI trended to increase with ischemia as well. Interestingly, these findings coincide with results from Tat et al. (2015a) who found reduced SSCT displacement in CTS symptomatic individuals compared to healthy controls, with no difference in tendon displacement between the two groups. With increased tendon-SSCT strain, collagen fibres between the tissues are more likely to rupture, which would initiate the collagen rebuilding and remodeling process (Zhao et al., 2011; Ettema et al., 2004). Repeated and cumulative exposure could lead to thickening and fibrosis of SSCT, a marked symptom of idiopathic CTS (Ettema et al., 2004). Since CTS is ultimately a pathology related to median nerve ischemia, detecting differences in relative tendon-SSCT displacement brought on by experimentally induced partial ischemia in healthy individuals may bridge an important gap in the etiological progression of the disorder.

External pressure applied to the hand has been recognized as a factor for increasing carpal tunnel pressure (Cobb et al., 1994) and transverse carpal ligament stiffness (Holmes et al., 2011). Our results indicated that 5 kg of palmar compression at the distal carpal tunnel did not affect relative tendon-SSCT displacement as evidenced by the absence of change in relative displacement and SSI. Our force applicator (20 mm diameter) was larger than the 5 mm indenter from the study by Cobb et al. (1995), which likely would have dispersed the compressive load over multiple flexor tendons rather than the middle FDS tendon alone. However, we were confident that the force applicator loaded the tendons exclusively, as Holmes et al. (2011) showed that a 20 mm indenter was small enough to not compress on the carpal bones. Moreover, our 5 kg compressive load was also greater than the 1 kg point load used in Cobb et al. (1995), which compensated for the decreased pressure experienced by each tendon due to the increased force application area. Thus, our data suggest that 5 kg of palmar compression at the distal carpal tunnel during cyclical finger flexion-extension likely does not negatively impact tendon-SSCT shear.

We found that forearm pressure significantly reduced tendon displacement and a trend for decreased SSCT displacement compared to baseline (Figure 2.5). FDS and SSCT velocities also decreased with forearm compression. Since both tissue types exhibited decreased excursion, the result of this could be interpreted as both tendon and SSCT moving less as a combined unit. If both tendon and SSCT moved less, the potential for increased relative displacement and shear strain would have similarly decreased, which likely explains the lack of change in shear strain index (SSI) and

relative displacement with forearm compression. However, since finger flexion-extension range of motion was maintained, it is possible that strain occurred elsewhere in the musculotendinous unit. Goldstein et al. (1987) demonstrated in cadaveric flexor tendons that tendon strain distal to the carpal tunnel was greater than proximal strain, and the strain difference increased with increasing tendon tensile load (20 - 80 N). The 5 kg (49 N) forearm compression used in the current study could have acted to "pin down" the tendon causing it to stretch rather than glide through the carpal tunnel to maintain full finger flexion-extension. Considering the forearm force applicator did not compress at the tendon-SSCT interface, the relative displacement would likely have not been affected. Further studies evaluating tendon shape and mechanical properties in conjunction with tendon excursion may prove to be useful in isolating this mechanism.

A consistent observation from our results was that greater relative tendon-SSCT displacement was evident with greater speed of finger motion. Across all conditions (baseline, palmar and forearm compression, ischemia), SSI and relative displacement were elevated and MVR was reduced during the faster movement trials. This finding is consistent with other studies using mechanically controlled tendon excursions in cadavers (Tat et al., 2015b; Yoshii et al., 2010; Oh et al., 2007). Admittedly, increased shear strain with greater movement speed is not a novel finding; however, our investigation was the first to reproduce these findings *in vivo*. Faster finger flexion-extension motion has been shown to produce greater tendon frictional work (Kociolek, 2015) and produce tendon forces and excursion resistance energies capable of damaging SSCT collagen fibres much earlier in the tendon excursion cycle (Filius et al., 2014). Although these measures

provide quantitative evidence, which suggests tissue damage, they are not measurable in vivo without invasive procedures. Since our data demonstrates the same trend of increased relative tendon-SSCT motion with increased movement velocity, it is possible that ultrasound-captured tendon displacement could be used as a proxy for risk of sustaining tendon-SSCT shear injury.

It is common practice in with all forms of diagnostic imaging to check for image consistency and reliability of quantitative data extracted from images (Bartlett & Frost, 2008). Our variability analysis showed standard deviation for measured velocity and displacement variables were consistently lower within-subjects than between-subjects (Table 2.2). Moreover, within-subject SD also represented smaller proportions of their respective means (8 - 11%) with smaller COV compared to between-subject COV (16 - 20%). This gives us confidence our ultrasound images were captured with considerable consistency and yielded reliable velocity and displacement data within in an individual. Although variability between-subjects was greater, this is likely the product of sampling different sized individuals that have different magnitudes of tendon excursion during finger flexion-extension.

Several limitations were present in this study. First, the sample tested consisted of young university-aged individuals, thus our findings may not be generalizable to older individuals or those with CTS. However, we demonstrated acute changes that could increase tendon-SSCT injury risk, which may have cumulative effects over longer work durations (Tat et al., 2013). Given the fixed size of the compression devices, it is unlikely compression was exactly the same for all individuals. Careful alignment of the force

applicators ensured the FDS tendon did experience a large proportion of the compressive force and broad compression over multiple tendons would be more representative of real-life conditions. Our sub-systolic compression condition was also tolerated differently between participants, which accounted for the variability in total compression time. It was a rather extreme stimulus but ensured all participants were partially ischemic prior to the start of motion measurement at the minimum compression time of 18-20 minutes. Compression at sub-diastolic levels would likely be better tolerated by individuals and perhaps be more representative of possible work conditions. Allowing venous return would result in less edema. It is possible that ischemia induces vasoconstriction in blood vessels that may serve to anchor and restrict motion of the SSCT, however, fluid-up could similarly generate viscous resistance to SSCT gliding. This future research could be beneficial in parsing out the effect of partial ischemia on SSCT displacement.

In conclusion, our investigation showed mechanical compression and partial ischemia altered FDS tendon and SSCT motion. Forearm compression reduced tendon and SSCT displacement, which reduced their relative shear strain. However, forearm compression could have pinned down the tendon causing it to stretch, rather than glide through the carpal tunnel. Partial ischemia via brachial blood pressure cuffing reduced SSCT displacement while tendon displacement did not change, suggesting increased risk for tendon-SSCT shear injury. Faster movement speeds elicited greater relative tendon-SSCT displacement *in vivo*, which was previously shown in cadaver preparations. Establishing relationships between tendon-SSCT motion with mechanical compression

and ischemia represent fundamental steps towards improving our understanding of carpal tunnel syndrome development and progression.

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3.0. THESIS DISCUSSION AND SUMMARY

Cumulative tendon and subsynovial connective tissue (SSCT) injury has been suggested as a mechanism for carpal tunnel syndrome (CTS). This thesis evaluated the acute effects of external mechanical compression and partial ischemia on the relative motion of flexor digitorum superficialis (FDS) tendon and SSCT. Palmar and forearm compression were applied to determine their effects on tendon motion. Our palmar pressure condition did not reveal any significant influences on tendon-SSCT displacement while the forearm pressure condition reduced tendon excursion when displacement and velocity variables were pooled across movement speeds. With a network of microvasculature integrated within the polyhedral structure of SSCT, we induced partial ischemia via a brachial blood pressure cuff to investigate potential associations between blood flow and tendon-SSCT motion. Subsystolic brachial compression reduced SSCT displacement while tendon displacement remained unchanged, suggesting the potential for increased tendon-SSCT shear strain. The results from this thesis provide evidence for how relative tendon-SSCT motion may be affected by mechanical compression and ischemia. Identifying how the risk of sustaining tendon-SSCT shear injury may change with different factors has useful implications for improving our understanding of the mechanisms for CTS development and its progression.

With palmar compression, the working hypothesis was that tendon-SSCT shear strain would increase with compression increasing gliding resistance. Cobb and colleagues (1995) used a 5 mm diameter indenter to apply 1 kg of compressive over several locations on the palm and distal wrist while measuring changes in carpal tunnel

pressure (CTP) with a pressure transducer catheter. They found that compression over the transverse carpal ligament (TCL) had the greatest effect on CTP with a mean pressure of 103 mmHg. In a study with cadavers, Zhao et al. (2011) demonstrated that CTP greater than 60 mmHg significantly increased gliding resistance in the carpal tunnel as measured by lightweight force transducers affixed to the middle finger FDS tendon on either side of the carpal tunnel. These studies provided data important to the rationale for palmar compression as method to increase tendon-SSCT shear strain in the current study. By elevating CTP with palmar pressure (Cobb et al., 1995), we hypothesized that gliding resistance in the carpal would increase (Zhao et al., 2011) and subsequently generate greater shear stress between the tendon and SSCT during tendon excursion. In our study, however, we used a broader force applicator (20 mm diameter) to create a pressure condition that would be more akin to something from the workplace like applying a downward force on a manual screwdriver. We attempted to match the pressure distribution from Cobb et al. (1995), but pilot testing revealed the necessary compressive weight to achieve this (15 kg) would have been too much for participants to tolerate. Thus, 5 kg (49 N) was selected, which aligns with findings from Holmes et al. (2011) that showed a 20 mm indenter was large enough to compress the transverse carpal ligament without being impacted by carpal bones. The selected force applicator size and the weight used could explain the lack of significant effects involving palmar compression were found for any tendon-SSCT displacement or velocity variables. Although this finding did not support our hypothesis, it does suggest that broad palmar compression up to 5 kg does not negatively affect tendon-SSCT motion.

With forearm compression, the initial thought we had was to apply a pressure-matched amount of compression to the tendon at a more proximal location. Unlike palmar compression, Cobb et al. (1995) demonstrated forearm compression would not influence CTP but still provide mechanical compression to the tendon. Thus, we anticipated forearm compression to elicit less relative tendon-SSCT displacement than palmar compression because CTP and gliding resistance would not have been affected by forearm pressure. Ultimately, no significant differences in displacement or velocity variables were found between palmar and forearm compression conditions. It is possible that the shape and location of the forearm force applicator may have been responsible for the lack of significant changes compared to palmar compression. In pilot testing, we tested a prototype forearm force applicator that had a rectangular contact surface with the same surface area as the circular palmar force applicator. Using the same 5 kg of compression, we found this force applicator, which had a more concentrated pressure distribution, would have been too uncomfortable to use on the distal forearm where the tissue is less stiff. In contrast to forearm, the palmar area where we compressed had greater stiffness from the TCL, carpal bones and other ligaments that would have attenuated some of the stress applied to the tendon. For this reason, we created a forearm force applicator with a broader bar-like contact surface to distribute the pressure (Figure 2.2B). Moreover, the size and placement of the ultrasound probe restricted the forearm force applicator to the distal third of the forearm but proximal to the probe. Although we attempted to target both tendon and SSCT with the forearm force applicator, its location (~9 cm proximal from the distal wrist crease) meant that the SSCT may not have been

affected. As such, this was likely the reason we did not see any significant effects on SSCT or relative tendon-SSCT displacement. Despite the broader forearm force applicator decreasing the pressure experienced by each individual tendon, it still had a significant effect on reducing FDS tendon displacement compared to baseline while finger flexion-extension range of motion was maintained. Future studies could consider imaging tendon-SSCT motion by placing the ultrasound probe more distally over the carpal tunnel, similar to the methods described by Oh et al. (2007).

The purpose of creating a partial ischemic condition was to evaluate whether ischemia in the distal forearm could affect tendon-SSCT motion without any influence from mechanical compression on the flexor tendons. Our intervention intended to induce partial ischemia of the arm and at the carpal tunnel that could initiate vasoconstriction of local vasculature (Faller 1999) and alter the fluid environment and subsequently gliding properties of the SSCT extracellular matrix (Amadio, 2013; Sun et al., 2008). By inflating a brachial blood pressure cuff to sub-systolic pressures (diastolic pressure + 0.25 (systolic pressure – diastolic pressure)), arterial flow into the forearm was reduced while venous return was occluded completely. Prior studies that used this compression protocol inflated the blood pressure cuff to absolute pressures (75 & 100 mmHg) between participants (Thijssen et al., 2009; Totosy de Zepetnek et al., 2014), however, our variable cuff pressure (76.0 ± 4.0 mmHg) was used in an attempt to normalize the pressure experienced across individuals based on their resting blood pressure. We also intended to cuff participants for 30 minutes at sub-systolic pressures prior to initiating measurement of flexor tendon motion, but pilot testing revealed that 30 minutes of partial occlusion

was intolerable. More specifically, our protocol involved repetitive finger flexion-extension that pumped more blood into the forearm and restricted flexion-extension motion for some participants. Thus, we adjusted our protocol to 18-20 minutes of compression (based on rating of perceived discomfort) prior to motion measurement such that total occlusion time, following finger flexion-extension, was approximately 25 minutes.

My thesis demonstrated that partial ischemia of the arm significantly reduced SSCT displacement while tendon displacement remained unchanged (Figure 2.7). The trend of increased relative tendon-SSCT displacement and SSI also suggested partial ischemia could increase their relative shear strain, independent of mechanical influences affecting tendon displacement. This was a critical finding because it represents a potential association between relative tendon-SSCT motion and blood flow with possible mechanical influences from associated blood vessels. This could have implications for shear injury in the development and progression of CTS from cumulative tendon trauma. Admittedly, a caveat of our study was compressing above diastolic blood pressure. Although we were confident we had induced ischemia and altered the fluid environment, lacking a direct measurement of interstitial fluid in the carpal tunnel prevented us from attributing our results to either decreased fluid levels from restricted arterial flow, or increased fluid levels from diastolic occlusion that caused a back-up. Nonetheless, we demonstrated ischemia could have an effect on relative tendon-SSCT motion and future studies could consider sub-diastolic occlusion to further evaluate the influence of fluid levels at the carpal tunnel on shear injury risk.

Other challenges that arose during this investigation were primarily related to ultrasound imaging settings. Compared to imaging settings previously used in our laboratory, several parameters had to be changed to suit the demands of our investigation. Firstly, because our fast movements (1.25 Hz) occurred at a greater frequency than previous studies (Kociolek & Keir, 2015 & 2015; Tat et al., 2013), velocity measurements were being aliased at high velocities, especially in larger participants. Thus, we had to increase velocity scale (maximum and minimum velocities detected) from ±11 cm/s to ±17 cm/s to avoid aliasing of measured tissue velocities. However, this change had an undesirable effect of increasing the low-velocity reject (minimum threshold for detecting velocity) to ±1.9 cm/s, which resulted in noisy velocity data in this velocity range where changes in movement direction occurred. This was corrected post-hoc with manual noise correction and digital filtering, but made data processing much more laborious. Another change we implemented was an increase in colour Doppler sampling frequency from 29.5 Hz to 34.5 Hz. Despite this change improving temporal resolution and meeting the minimum requirements of Nyquist theorem, we believe even greater sampling frequency would improve the quality of data, especially for quantifying tendon-SSCT motion at fast movement speeds. It is unfortunate that sampling frequency is limited by the preprogrammed settings of the ultrasound system, but our variability analysis showed within-subject variability was relatively low, which gave us confidence in the reliability of our data. Previous work from our laboratory validated the use of colour Doppler ultrasound for quantifying relative tendon-SSCT motion (Tat et al., 2013),

and in spite of the discussed drawbacks, we still believe ultrasound to be a valid measure for this purpose.

This thesis assessed finger flexor relative tendon-SSCT motion under different mechanical compressions and ischemia. It demonstrated 5 kg of compressive force applied to the palm did not appear to have an effect on tendon-SSCT motion. Within an ergonomic context, this could suggest that repetitive jobs requiring palmar pressures with finger motions, such as operating a power drill, may not affect the risk for sustaining tendon-SSCT shear injury for up to 5 kg of compression. The same compressive force applied to the forearm decreased tendon excursion while finger flexion-extension range of motion remained unchanged. Since we found no indications of changes in tendon-SSCT shear strain with forearm compression, future research could investigate where the stress from external pressure could have been distributed. Lastly, we found partial ischemia reduced SSCT displacement and trended to increase relative displacement. Although the specific mechanisms for how fluid changes in the carpal tunnel may have affected SSCT dynamics still require further investigation, our research bridged an important gap between blood flow and relative tendon-SSCT motion. Ultimately, this could improve our understanding of the role that ischemia may play in the development and progression of carpal tunnel syndrome.

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APPENDIX A: Extended Methods Section

Methods

Participants

Twenty healthy participants (10 men, 10 women) were recruited from the university population for two testing sessions (age = 23.0 ± 2.2 years, mass = 74.2 ± 15.4 cm, height = 174.4 ± 11.2 cm, forearm length = 22.7 ± 1.8 cm). Due to poor data quality, one participant was excluded from the analysis resulting in n = 19. Incoming participants were screened and excluded from the study if they had any history of the following: hypertension, diabetes mellitus, hypothyroidism, amyloidosis, sarcoidosis, hemodialysis, gout, osteoarthritis, degenerative joint disease, wrist tendinopathy, peripheral nerve disease, acute injury to the distal upper extremity, and pain, numbness, or tingling of the hand. The study was approved by the Hamilton Integrated Research Ethics Board.

Experimental Protocol

General Overview

Sonographic video clips of FDS tendon and the adjacent SSCT motion were recorded during two sessions involving different compression conditions and two movement speeds. Sessions were separated by a minimum of 72 hours to eliminate any potential carry-over. One session included compression applied to the palm and forearm using custom force applicators. In the second session, a brachial blood pressure cuff was used to induce partial ischemia to the forearm and hand. A flexion-extension protocol

was implemented to standardize the range of motion across all conditions and movement speeds (Tat et al., 2013).

Repetitive Motion Protocol

Participants were placed in a supine position with their right arm resting in a shoulder-abducted, elbow-extended, and forearm-supinated posture for both experimental sessions (Figure A1A). Each trial of the repetitive motion protocol consisted of 13 repetitions of full finger flexion-extension using only their middle finger. Tat et al. (2013) demonstrated differential finger movement elicited greater relative displacement between the FDS tendon and SSCT than concurrent finger movements. To isolate motion to the middle finger, Velcro straps secured the other fingers in a mid-flexed posture to a custom handgrip that allowed full middle finger flexion-extension range of motion (Figure A1B&C). Range of motion was standardized by instructing participants to contact their distal finger crease to the handgrip during flexion and their fingernail to the apparatus during extension. Fast (1.25 Hz) and slow (0.75 Hz) movement conditions were sampled in each condition to evoke potential viscoelastic properties of tendon-SSCT relative displacement (Yoshii et al., 2011). An audible metronome dictated the movement frequency that participants followed. Prior to data collection, practice trials were performed until participants felt comfortable with the movement speeds. In each combination of compression condition and movement speed, participants performed three trials of 13 movement cycles while sonographic videos were recorded. The session and

sampling order of condition-movement speed combinations were systematically randomized to negate any potential order effects.

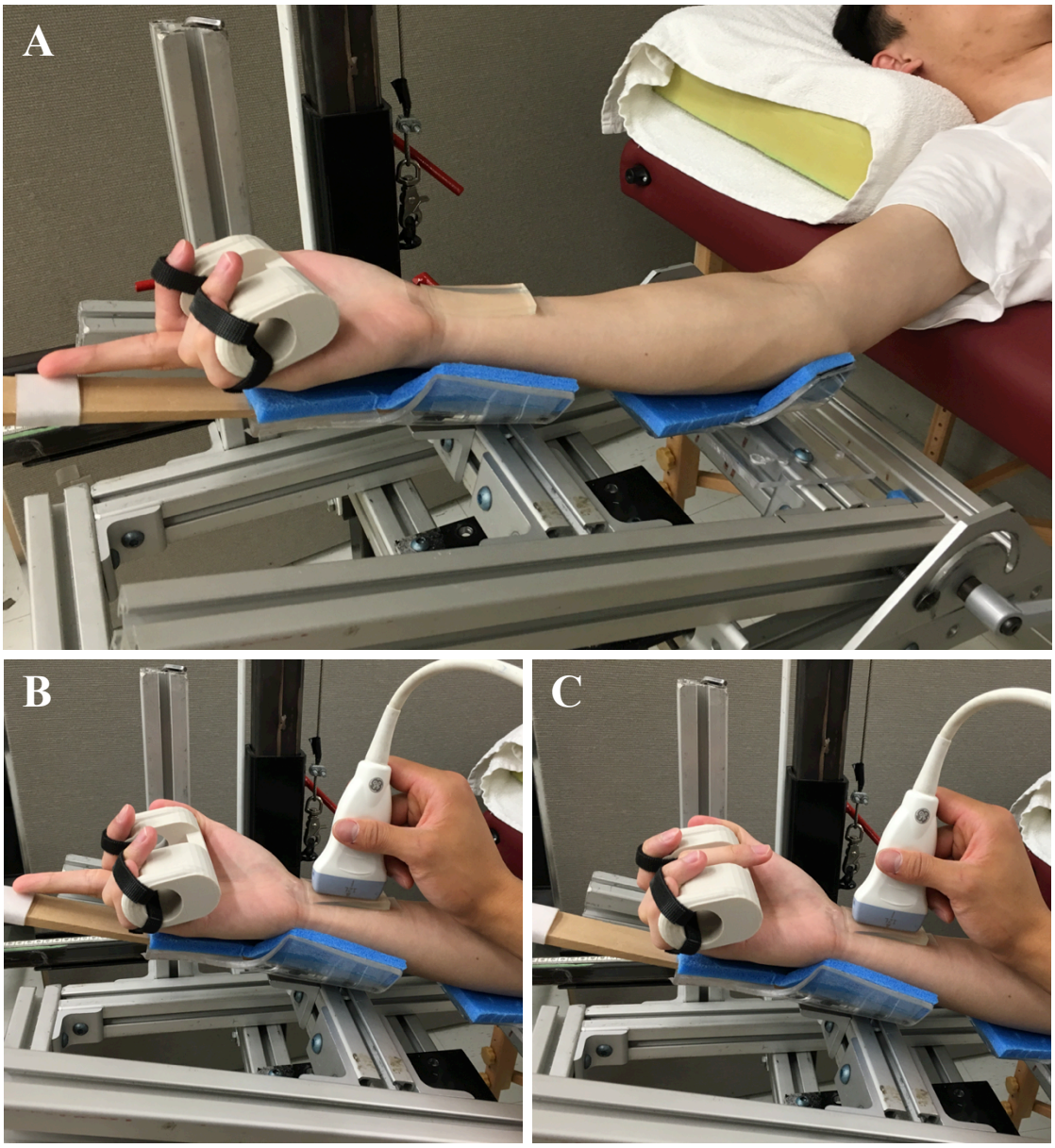

Figure A1. A) Experimental set up with participant resting in supine posture and fingers secured in custom handgrip via Velcro straps. B) Finger extended posture. C) Finger flexed posture. Ultrasound probe can be seen with its edge inline with of the ultrasound probe placed at the proximal wrist crease.

Session I - Palmar and Forearm Compression

Palmar and forearm compression trials were completed in the same session. Custom force applicators used for hanging a 5 kg mass and applying compression to the palm and forearm were 3D printed. The palmar force applicator had a flat, circular contact surface (2 cm diameter) that compressed the palm over the distal edge of the carpal tunnel (Figure A2). The contact surface of the forearm force applicator had a width of 2 cm that compressed the forearm approximately 9 cm proximal to the distal wrist crease (Figure A2). In both compression conditions, the centre of each force applicators was aligned with the line of action of the middle FDS tendon. Prior to recording each sonographic video clip, the weight and force applicator were secured and the participant began to flex and extend their finger to the designated movement speed. The order of compression-speed combinations (palmar-fast, palmar-slow, forearm-fast, forearm-slow) was systematically randomized between participants with a Williams-design to eliminate potential order effects.

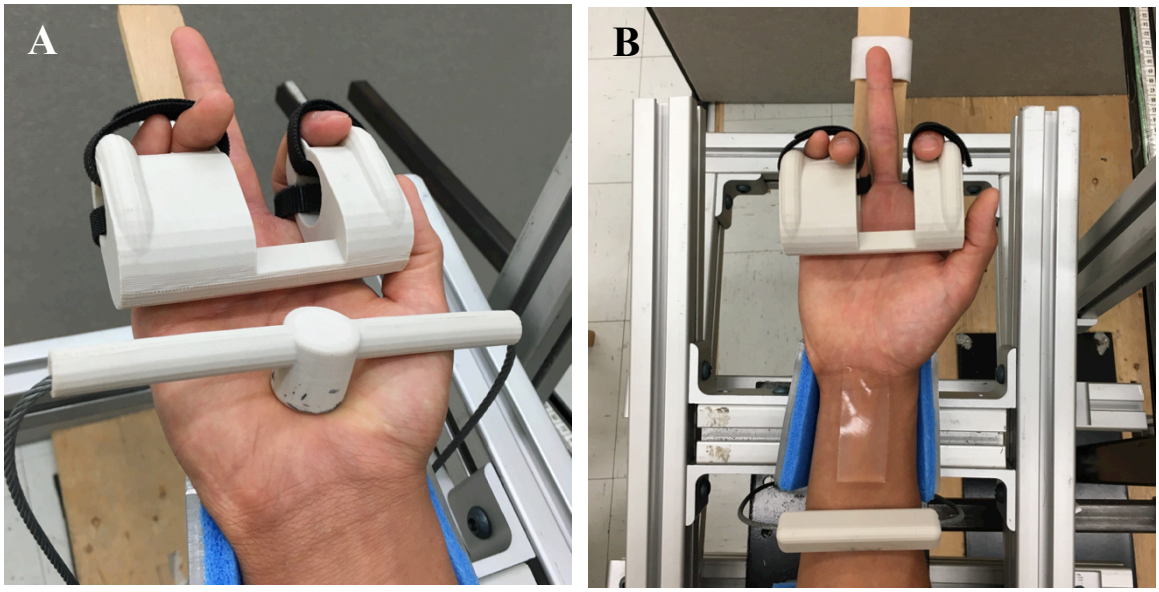

Figure A2. 3D printed palmar (A) and forearm (B) force applicators with 5kg weight secured to both force applicators via steel cables. Palmar force applicator can be seen compressing the palm at approximately the distal edge of the carpal tunnel. Forearm force applicator can be seen compressing the distal forearm approximately 9 cm proximal from the distal wrist crease.

Session II - Partial Ischemia Condition

This was conducted on a separate day from the palmar and forearm compression session. Participants were rested in a supine position for a minimum of ten minutes prior to taking a minimum of three resting blood pressure measurements (Dinamap 100 V2, GE Healthcare, Milwaukee, WI). Partial ischemia was created by using a blood pressure cuff over the upper arm inflated to diastolic blood press plus 25% of the SBP- DBP difference for approximately 30 minutes. After baseline motion was recorded, a manual blood pressure cuff was secured around the distal upper arm and inflated to the designated pressure (mean = 76.0 ± 4.0 mmHg) (Figure A3). Participants were asked every 3 minutes to rate their perceived discomfort (RPD) on an analog-visual scale ranging from

0 (no discomfort at all) to 10 (intolerable discomfort). This rating was used to initiate the collection of ischemia motion trials at 18 minutes instead of 20 minutes, if participants reached an RPD of 6. Termination criteria for the ischemia protocol was also set at an RPD of 8, but no participants reached this threshold. Following 18-20 minutes of brachial cuffing we began measuring the ischemic motions trials and the collection order (fast and slow) was randomized between participants. The cuff pressure was released after ischemic motion trials were collected resulting in an average partial occlusion time of 24.6 ± 3.8 minutes.

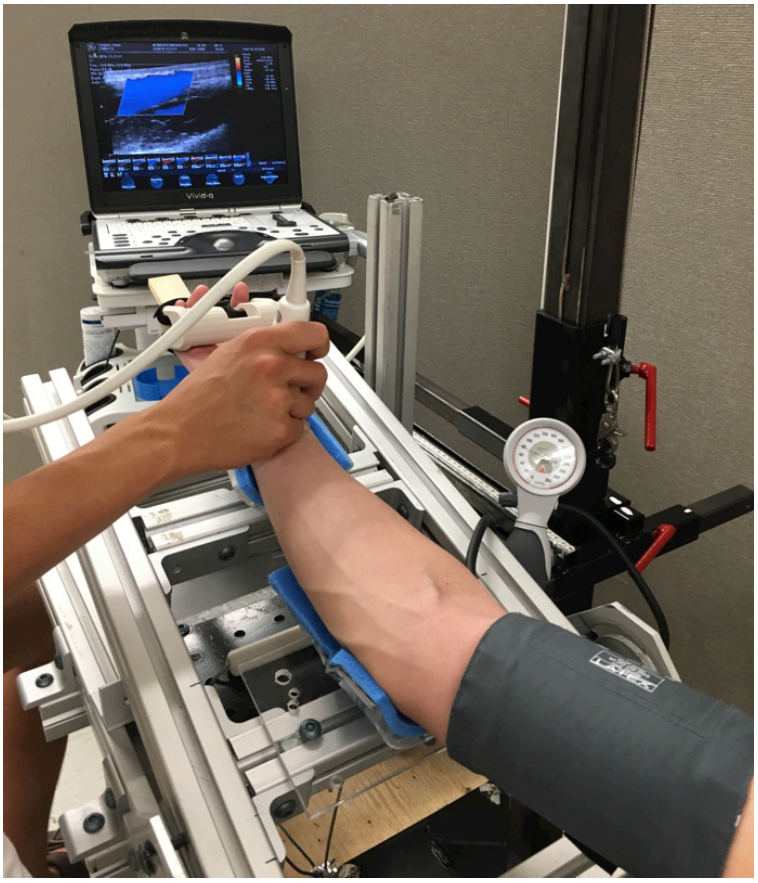

Figure A3. Partial ischemia condition with manual blood pressure cuff placed around distal upper arm and pressure gauge visible to monitor compression level.

Ultrasound Assessment

Colour Doppler Imaging

A linear array transducer (12L-RS) with a Vivid q BT10 ultrasound system (GE Healthcare, Milwaukee, WI) captured all B-mode ultrasonic video clips of tendon-SSCT excursion at the level of the wrist corresponding to zone V of the FDS tendon (Boyer et al, 2002; Kociolek & Keir, 2016). The probe was positioned at the proximal wrist crease longitudinally with the length of the middle finger FDS tendon (Figure A1B & C). To isolate the middle finger FDS, participants performed differential flexion-extension movements. Isolated flexion-extension of the middle finger distal interphalangeal joint differentiated between the tendons of FDS and FDP. Colour Doppler imaging (CDI) was used to measure tissue velocity and appeared as colour maps overlaid on the B-mode image (Figure A4). Image brightness settings were optimized to distinguish the FDS tendon from the adjacent SSCT. In a B-mode image, the FDS tendon should appear as a collection of fibrillar striations forming a band, bordered on either side by the SSCT that appears a thin hyperechoic layer (Figure A4).

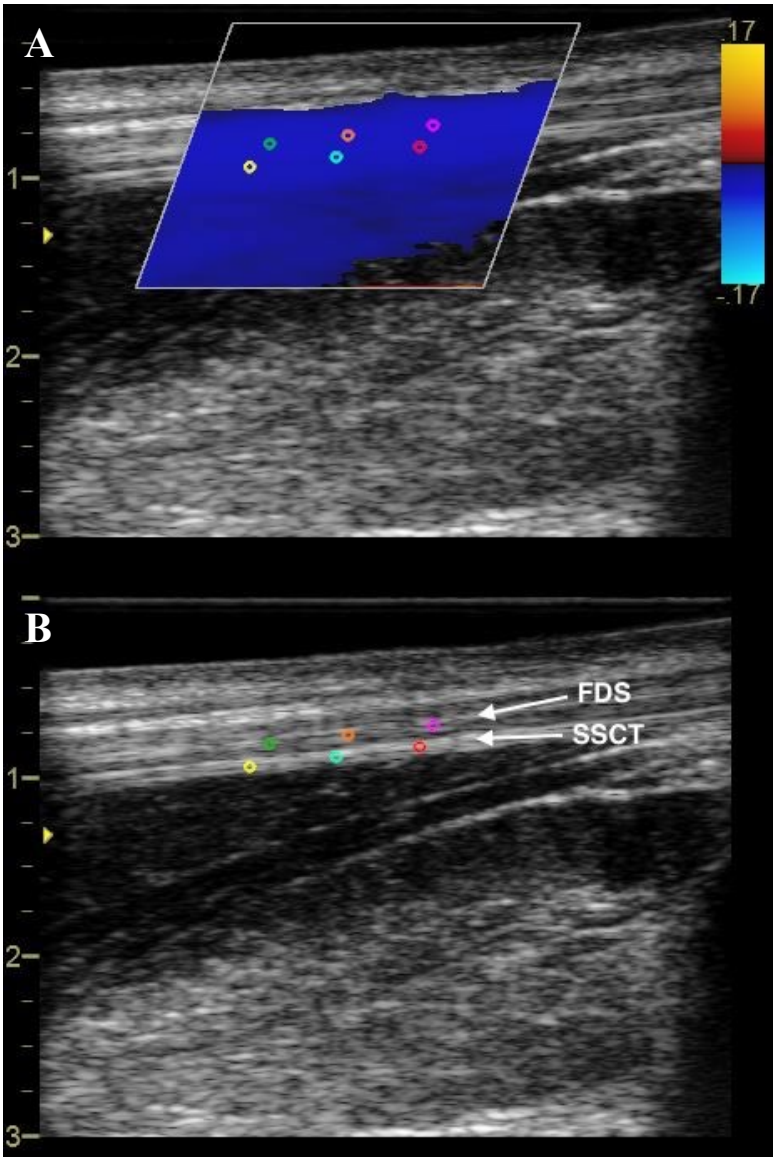

Figure A4. Identical B-mode images with (A) and without (B) the CDI colour map overlay. The colour scale (A) shows the detectable tissue velocity range with red-orange and blue representing extension and flexion respectively. Brighter colour represent faster tissue velocity. Regions of interest for sampling independent velocity traces are visible on both images and appear as the small multi-coloured circles. FDS tendon and SSCT tissue velocities were measured using three regions of interest for each tissue type.

We maximized the steering angle of the ultrasound probe to 20° and used a custom aqueous gel wedge standoff (Aquaflex gel pad, Cone Instruments, Solon, OH) to

optimize the angle of insonation to approximately 60 degrees (Figure A1). CDI is sensitive to the angle of insonation between the Doppler beam the moving tissue and common practice suggests to keep this angle below 60° to minimize velocity measurement errors (Lui et al., 2005). To ensure consistent portion of the tendon was captured between trials, the probe location was marked at the start of each session and the gel wedge was secured with tape around its perimeter. Other sonographic imaging settings included: transducer frequency = 13 MHz, tissue velocity scale = ± 17 cm/s, low-velocity reject = 1.9 cm/s, focus depth = 3.0 cm, sampling rate = 34.5 fps.

Image Processing and Data Analysis

B-mode video clips of the FDS tendon, SSCT, and overlaying colour maps were exported for analysis (Q-analysis, Echopac, GE Healthcare, Wauwatosa, WI). Velocity of the tendon and SSCT were determined using three collinear circular regions of interest placed on each tissue, parallel to tissue motion (Figure A4). An average of three velocity traces was calculated to produce one representative velocity signal for each tissue type. This was done to minimize potential error associated with measuring velocity from a single region of interest on non-homogeneous colour map. Tendon and SSCT velocity signals were low-pass filtered with a second order Butterworth filter at a 4 Hz cut-off and corrected for the angle of insonation (factor of $\cos\theta$). Displacement of each tissue type was calculated by integrating the velocity signal for each flexion-extension cycle independently to minimize the effect of integration drift (Figure A5).

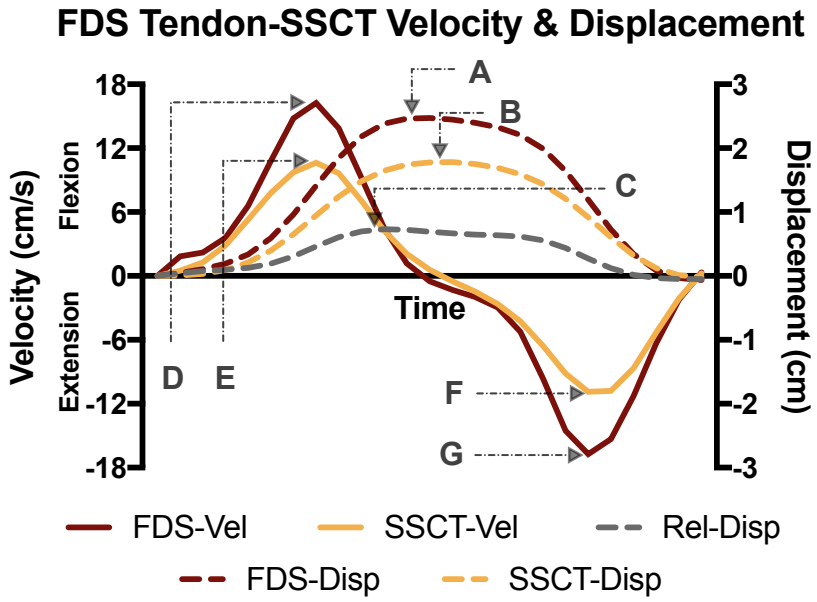

Figure A5. Peak FDS tendon and SSCT tissue velocity and displacement for one finger flexion-extension cycle. (A) Peak tendon displacement. (B) Peak SSCT displacement. (C) Peak relative displacement. (D) Peak flexion tendon velocity. (E) Peak flexion SSCT velocity. (F) Peak extension SSCT velocity. (G) Peak extension tendon velocity.

Using the displacement and velocity traces, two variables for describing relative shear strain between tendon and SSCT were calculated for each flexion-extension cycle. Relative tendon-SSCT displacement was calculated as the difference between SSCT and tendon displacement. With this value, shear strain index (SSI) was calculated to normalize the peak relative tendon-SSCT displacement to peak tendon excursion (Eqn. 1). A larger SSI value represents greater shear strain.

$$\text{Shear Strain Index (SSI)} = (\text{Tendon}_{disp} - \text{SSCT}_{disp}) / \text{Tendon}_{disp} \bullet 100\% \qquad \textbf{(Eqn. 1)}$$

A second indirect measure of tendon-SSCT shear strain was the maximum velocity ratio (MVR) between peak tendon and SSCT velocities (Eqn. 2), where a smaller MVR value represents greater shear strain.

$$\text{Maximum Velocity Ratio (MVR)} = SSCT_{MaxVel} / Tendon_{MaxVel} \bullet 100\% \quad \textbf{(Eqn. 2)}$$

In addition to these variables, mean and peak displacement and velocity values were obtained for FDS tendon and SSCT flexion-extension cycles (Figure 6). Velocity variables (mean, peak, MVR) were calculated for each movement direction as well (flexion, extension). For each variable, a mean value was calculated to represent each experimental condition (compression-speed combination) for each participant. Since each condition had three trials of 13 flexion-extension cycles each, we averaged the middle 8 cycles of each of the three trials (24 cycles total) to represent each condition.

Statistical Analysis

Repeated measures analyses of variance were performed to test the effects of movement speed and compression condition on each measured and calculated variable. The two sessions were analyzed independently using separate repeated measures ANOVAs for each variable (Table A1). The analyzed variables included: displacement (tendon, SSCT, and relative tendon-SSCT displacement), SSI, mean velocity (FDS and SSCT in flexion and extension), peak velocity (FDS and SSCT in flexion and extension), and MVR (FDS and SSCT in flexion and extension). Significant main effects were followed up with Bonferonni corrected t-test comparisons ($\alpha = .05$).

Table A1. Repeated measures ANOVAs for each dependent variable separated by session

	Independent Variables	
Session	**Conditions**	**Speeds**
Palmar & Forearm Compression	3 (Baseline, Palmar, Forearm)	2 (Fast, Slow)
Partial Ischemia	2 (Baseline, Ischemia)	2 (Fast, Slow

APPENDIX B: Extended Results

Results

Palmar and Forearm Compression

Displacement Variables

A main effect of compression was found for FDS displacement ($F_{2,36} = 4.3$, $\eta^2 = 0.193$, $p = 0.021$). Post hoc tests revealed that forearm compression elicited significantly less tendon displacement than baseline (27.0 ± 4.6 mm vs. 28.5 ± 4.1 mm; $p = 0.043$) (Figure B1). No significant compression effects were found for SSCT displacement ($F_{2,36} = 3.1$, $\eta^2 = 0.146$, $p = 0.059$), relative tendon-SSCT displacement ($F_{2,36} = 0.2$, $\eta^2 = 0.012$, $p = 0.798$), or SSI ($F_{2,36} = 0.4$, $\eta^2 = 0.020$, $p = 0.698$).

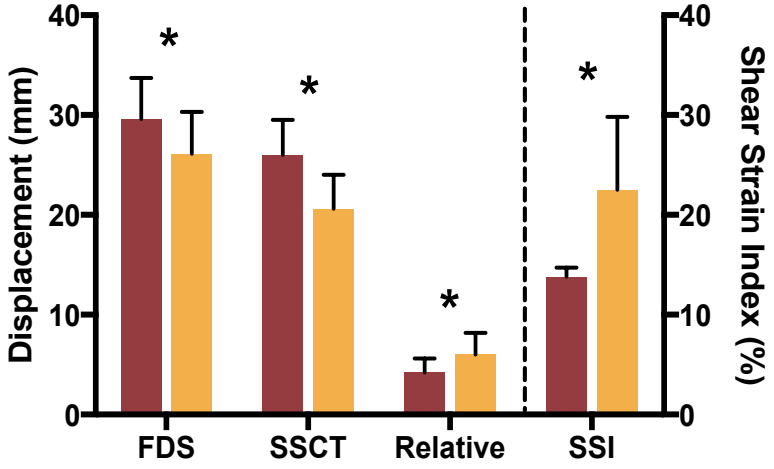

Figure B1. Mean FDS tendon and SSCT displacement from palmar and forearm compression session. Error bars represent one standard deviation from the mean.
* Denotes significantly different from baseline ($p < 0.05$).

Movement speed significantly affected FDS displacement ($F_{1,18} = 32.0$, $\eta^2 = 0.640$, $p < 0.001$), SSCT displacement ($F_{1,18} = 142.9$, $\eta^2 = 0.888$, $p < 0.001$), relative tendon-SSCT displacement ($F_{1,18} = 35.3$, $\eta^2 = 0.662$, $p < 0.001$), and SSI ($F_{1,18} = 68.4$, $\eta^2 = 0.792$, $p < 0.001$). Compared to the slow movement speed, the fast movement speed decreased tendon (29.6 ± 4.1 mm vs. 26.1 ± 4.2 mm; $p < 0.001$) and SSCT displacement (26.0 ± 3.5 mm vs. 20.6 ± 3.4 mm; $p < 0.001$), and increased relative tendon-SSCT displacement (4.2 ± 1.4 mm vs. 6.0 ± 2.2 mm; $p < 0.001$) and SSI (13.8 ± 3.8% vs. 22.5 ± 7.3%; $p < 0.001$) (Figure B2).

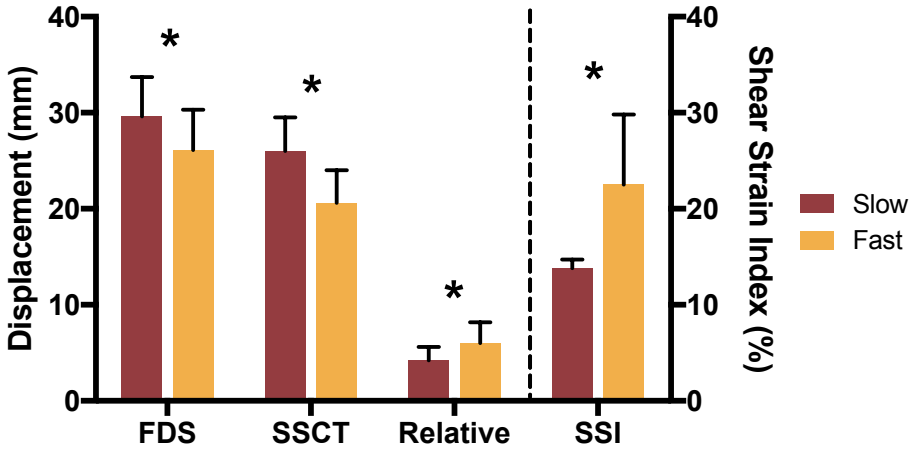

Figure B2. Tissue displacement and shear strain index for slow and fast movement speeds during the palmar and forearm compression session. Error bars represent one standard deviation from the mean. * Denotes significant difference between slow and fast ($p < 0.05$).

Velocity Variables

In the extension direction, there was a main effect of compression on peak FDS tendon velocity ($F_{2,36} = 5.5$, $\eta^2 = 0.234$, $p = 0.008$), peak SSCT velocity ($F_{2,36} = 4.5$, $\eta^2 =$

0.199, p = 0.019) and mean FDS tendon velocity ($F_{2,36}$ = 4.5, η^2 = 0.201, p = 0.018). Post-hoc evaluation revealed peak FDS tendon velocity with forearm compression (10.9 ± 1.7 cm/s) was significantly slower than during palmar compression (11.5 ± 1.7 cm/s; p = 0.041) or baseline (11.6 ± 1.9 cm/s; p = 0.019). Similarly, mean FDS tendon velocity was significantly slower with forearm compression (5.3 ± 0.7 cm/s) than palmar compression (5.6 ± 0.8 cm/s; p = 0.024), but not baseline (5.5 ± 0.8 cm/s; p = 0.113). Peak SSCT velocity showed a similar trend with forearm compression (8.4 ± 1.6 cm/s) being slower than palmar compression (9.2 ± 1.7 cm/s; p = 0.133) and baseline (9.2 ± 1.8 cm/s; p = 0.082), although not delineated by post hoc tests. No compression effects were found for any velocity variables in the flexion direction.

A main effect of speed was observed for all peak and mean velocity variables in both movement directions (Table B1). MVR in flexion ($F_{1,18}$ = 94.3, η^2 = 0.840, p < 0.001) and extension ($F_{1,18}$ = 61.2, η^2 = 0.773, p < 0.001) displayed main effects of speed where the fast movement speed resulted in lower MVR than the slow movement speed (flexion: 76.0 ± 8.0% vs. 85.9 ± 5.4%, p < 0.001; extension: 76.0 ± 8.5% vs. 83.6 ± 7.0%, p < 0.001). There were no significant interactions between movement speed and compression for any variables in the palmar and forearm compression session.

Table B1. Main effects and post-hoc summary for velocity variables from compression session (FDS: flexor digitorum superficialis tendon; SSCT: subsynovial connective tissue; η^2: partial eta squared)

		Main Effect of Speed			Post-Hoc Comparison		
Velocity Variable		$F_{1,18}$	η^2	p	Fast (cm/s)	Slow (cm/s)	p
Flexion	Peak FDS	206.4	0.920	< 0.001	12.6 ± 2.2	8.3 ± 1.1	< 0.001
	Peak SSCT	90.9	0.835	< 0.001	9.5 ± 1.8	7.1 ± 1.0	< 0.001
	Mean FDS	358.7	0.952	< 0.001	7.9 ± 1.2	4.8 ± 0.7	< 0.001
	Mean SSCT	90.4	0.892	< 0.001	6.0 ± 1.1	4.2 ± .0.6	< 0.001
Extension	Peak FDS	248.3	0.932	< 0.001	13.1 ± 2.0	9.6 ± 1.4	< 0.001
	Peak SSCT	99.0	0.846	< 0.001	9.9 ± 1.8	7.9 ± 1.3	< 0.001
	Mean FDS	533.9	0.967	< 0.001	6.6 ± 0.9	4.3 ± 0.6	< 0.001
	Mean SSCT	189.3	0.913	< 0.001	5.2 ± 0.8	3.7 ± 0.5	< 0.001

Partial Ischemia

Displacement Variables

There was a small but significant main effect of ischemia on SSCT displacement ($F_{1,18}$ = 7.3 η^2 = 0.288, p = 0.015) where ischemia decreased SSCT displacement compared to baseline (22.0 ± 3.3 mm vs. 22.9 ± 3.3 mm; p = 0.015) (Figure B3). However, ischemia did not significantly affect FDS tendon displacement ($F_{1,18}$ = 1.1, η^2 = 0.056, p = 0.317), relative tendon-SSCT displacement ($F_{1,18}$ = 2.0, η^2 = 0.097, p = 0.182), or SSI ($F_{1,18}$ = 48.0, η^2 = 0.091, p = 0.091).

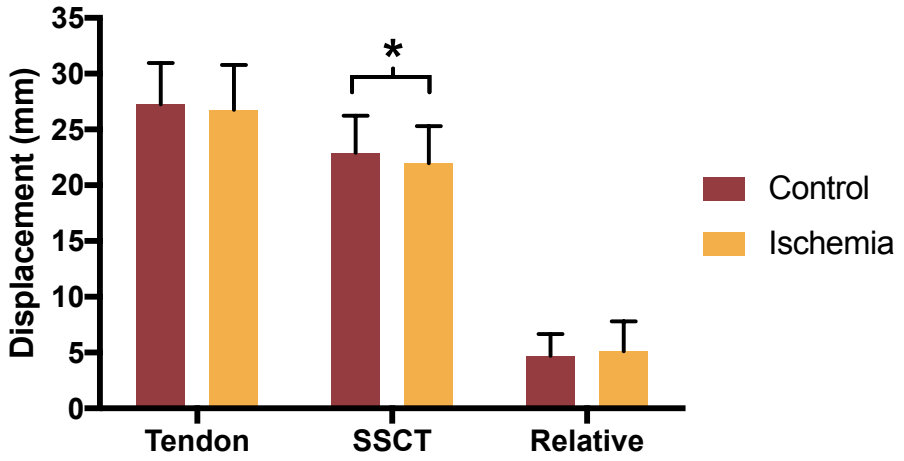

Figure B3. Tissue displacement from ischemia session showing a significant reduction SSCT displacement and a trend towards increased relative displacement. Error bars represent one standard deviation from the mean. *Indicates significantly different from baseline.

In the partial ischemia session, FDS tendon ($F_{1,18} = 65.4$, $\eta^2 = 0.784$, $p < 0.001$) and SSCT displacement ($F_{1,18} = 139.1$, $\eta^2 = 0.885$, $p < 0.001$) displayed significant main effects of speed where the fast movement speed decreased FDS tendon displacement (28.5 ± 4.0 mm vs.25.5 ± 3.5 mm; $p < 0.001$) and SSCT displacement (24.6 ± 3.5 mm vs. 20.3 ± 3.2 mm; $p < 0.001$) relative to the slow movement speed (Figure 9). Speed also had a significant main effect on relative tendon-SSCT displacement ($F_{1,18} = 9.2$, $\eta^2 = 0.337$, $p = 0.007$) and SSI ($F_{1,18} = 20.8$, $\eta^2 = 0.536$, $p < 0.001$). Relative tendon-SSCT displacement (4.4 ± 2.1 mm vs.5.4 ± 2.5 mm; $p = 0.007$) and SSI (15.1 ± 6.3% vs. 20.7 ± 9.0%; $p < 0.001$) were greater with the fast movement speed than the slow movement speed (Figure B4).

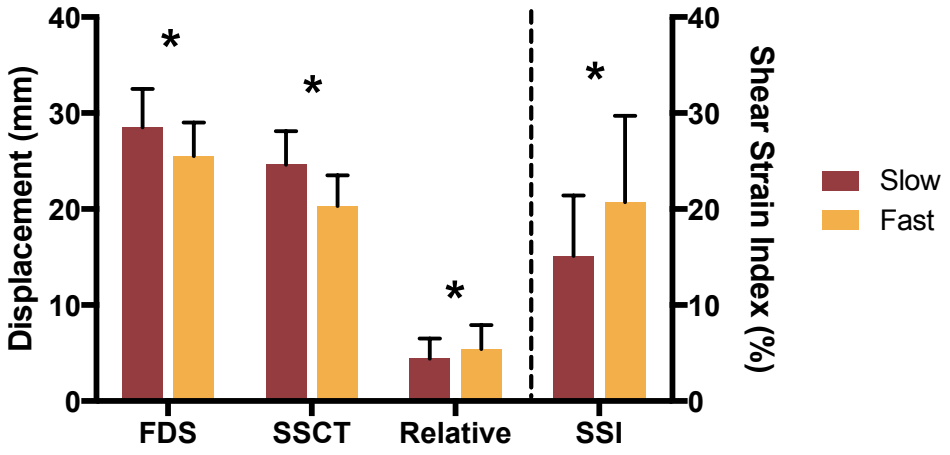

Figure B4. Tissue displacement and shear strain index for slow and fast movement speeds during the partial ischemia session. Error bars represent one standard deviation from the mean. * Denotes significant difference between slow and fast ($p < 0.05$).

Velocity Variables

Ischemia had a significant main effect on mean SSCT velocity for flexion ($F_{1,18} = 4.7$, $\eta^2 = 0.209$, $p = 0.043$) and extension ($F_{1,18} = 5.4$, $\eta^2 = 0.231$, $p = 0.032$). Compared to baseline, mean SSCT velocity with ischemia was slower in flexion (4.8 ± 0.8 cm/s vs. 5.0 ± 0.7 cm/s; $p = 0.043$) and extension (4.2 ± 0.8 cm/s vs. 4.4 ± 0.7 cm/s; $p = 0.032$).

Similar to the palmar and forearm compression session, peak and mean velocity variables in both directions were significantly affected by movement speed (Table B2). Moreover, movement speed had a significant main effect on MVR in flexion ($F_{1,18} = 36.4$, $\eta^2 = 0.668$, $p < 0.001$) and extension ($F_{1,18} = 38.1$, $\eta^2 = 0.679$, $p < 0.001$) with the fast movement speed showing lower MVR values in flexion (78.4 ± 9.7% vs. 86.2 ± 7.6%; $p < 0.001$) and extension (76.7 ± 10.0 vs. 83.2 ± 9.4%; $p < 0.001$) relative to slow movement speed. No significant interactions between movement speed and ischemia condition were found for any variable in the ischemia session.

Table B2. Main effects and post-hoc summary for velocity variables from ischemia session. (FDS: flexor digitorum superficialis tendon; SSCT: subsynovial connective tissue; η^2: partial eta squared)

		Main Effect of Speed			Post-Hoc Comparison		
Velocity Variable		$F_{1,18}$	η^2	p	Fast (cm/s)	Slow (cm/s)	p
Flexion	Peak FDS	210.8	.921	< 0.001	12.1 ± 2.1	7.8 ± 1.1	< 0.001
	Peak SSCT	148.7	.892	< 0.001	9.4 ± 1.8	6.6 ± 1.0	< 0.001
	Mean FDS	392.8	.956	< 0.001	7.4 ± 1.2	4.6 ± 0.7	< 0.001
	Mean SSCT	253.3	.934	< 0.001	5.9 ± 1.0	4.0 ± 0.6	< 0.001
Extension	Peak FDS	140.6	.886	< 0.001	12.7 ± 1.9	9.5 ± 1.5	< 0.001
	Peak SSCT	70.1	.796	< 0.001	9.7 ± 1.8	7.8 ± 1.3	< 0.001
	Mean FDS	661.6	.974	< 0.001	6.4 ± 0.8	4.1 ± 0.5	< 0.001
	Mean SSCT	188.8	.913	< 0.001	5.1 ± 0.7	3.6 ± 0.5	< 0.001

Within- and Between-Subject Variability

An assessment of measurement repeatability was performed by comparing within-subject and between-subject standard deviations (SD) and coefficients of variation (CoV) for FDS tendon and SSCT velocity and displacement (Table B3). Within-subject SD and CoV were consistently lower within-subjects than between-subjects.

Table B3. Within- and between-subject measurement variability of velocity and displacement variables. (FDS: flexor digitorum superficialis tendon; SSCT: subsynovial connective tissue; SD: standard deviation; CoV: coefficient of variation; η^2: partial eta squared)

	Within-Subject				**Between-Subject**			
	Mean SD	Min SD	Max SD	CoV (%)	Mean SD	Min SD	Max SD	CoV (%)
Peak Tendon Flexion Vel. (cm/s)	1.10	0.70	1.45	0.11	1.74	1.13	2.35	0.17
Peak SSCT Flexion Vel. (cm/s)	0.93	0.67	1.22	0.11	1.53	1.03	2.38	0.19
Peak Tendon Extension Vel. (cm/s)	1.15	0.74	1.64	0.10	1.84	1.42	2.33	0.17
Peak SSCT Extension Vel. (cm/s)	0.98	0.59	1.33	0.11	1.74	1.25	2.18	0.20
Tendon Disp. (cm)	0.23	0.17	0.29	0.08	0.43	0.35	0.63	0.16
SSCT Disp. (cm)	0.23	0.18	0.28	0.10	0.37	0.31	0.43	0.16

APPENDIX C: Ethics Amendment Approval

Hamilton Health Sciences

McMaster University
Inspiring Innovation and Discovery

St. Joseph's Healthcare Hamilton

Hamilton Integrated Research Ethics Board
AMENDMENT REQUEST

REB Project #: 11-551

Principal Investigator: Dr. Peter Keir

Project Title: Ultrasound assessment of flexor tendon excursion in the carpal tunnel

Document(s) Amended with version # and date:

- Administrative Change - Remove PI Aaron Kociolek and Co-Investigator's Dr. Joanne Hodder and Jimmy Tat
- Administrative Change - Add Calvin Tse as Primary Investigator
- Protocol - Ver: 4 Dated: 16 April, 2016
- Consent Form - Letter of Information and Consent Ver: 4 Dated: 16 April, 2016
- Advertisement - Participants Needed-Wrist Imaging Study Ver: 4 Dated: 16 April, 2016
- Screening Questions - Participant Screening Ver: 4 Dated:16 April, 2016
- Questionnaire - Ver: 4 Dated: 16 April, 2016

Research Ethics Board Review
(this box to be completed by HIREB Chair only)

[X] **Amendment approved as submitted**

[ ] **Amendment approved conditional on changes noted in "Conditions" section below**

[ ] **New enrolment suspended**

[ ] **Study suspended pending further review**

Level of Review:

[ ] Full Research Ethics Board
[X] Research Ethics Board Executive

Conditions:

The Hamilton Integrated Research Ethics Board operates in compliance with and is constituted in accordance with the requirements of: The Tri-Council Policy Statement on Ethical Conduct of Research Involving Humans; The International Conference on Harmonization of Good Clinical Practices; Part C Division 5 of the Food and Drug Regulations of Health Canada, and the provisions of the Ontario Personal Health Information Protection Act 2004 and its applicable Regulations; For studies conducted at St. Joseph's Hospital, HIREB complies with the health ethics guide of the Catholic Alliance of Canada

Continued from page 1

S. Salama

Suzette Salama PhD., Chair
Raelene Rathbone, MB BS, MD, PhD, Chair

4/27/2016
Date

All Correspondence should be addressed to the HIREB Chair(s) and forwarded to:
HIREB Coordinator
293 Wellington St. N, Suite 102, Hamilton ON L8L 8E7
Tel. 905-521-2100 Ext. 42013 Fax: 905-577-8378

APPENDIX D: Informed Consent Form

Letter of Information and Consent

Ultrasound Assessment of Tendon Excursion in the Carpal Tunnel

Local Principal Investigator: Peter Keir, PhD
Department of Kinesiology
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Phone: (905) 525-9140 (× 23543)
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Principal Investigator: Calvin Tse, BSc Kin (H)
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Hamilton, Ontario
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Sponsor: This study is funded by the Natural Sciences and Engineering Research Council of Canada (NSERC)

Introduction

You are being invited to participate in a study about musculoskeletal disorders of the wrist and hand. Common musculoskeletal disorders include tendonitis and carpal tunnel syndrome. Understanding how the tendons and nerves slide past each other inside the carpal tunnel (or wrist) is important in determining the development of wrist and hand musculoskeletal disorders. Tendons and nerves can be seen non-invasively using ultrasound.

Purpose of the Study

The purpose of this study is to observe and measure movement of the tendons that travel through the carpal tunnel using ultrasound.

Procedures Involved in the Research

At the start of the first session, you will be asked to complete a survey with questions about your handedness (i.e. left-handed or right-handed), general health, and musculoskeletal disorders of the wrist and hand. Following the questionnaire, you will complete a testing protocol ranging from 1-2 hours (depending on the randomized order of session conditions). During both sessions, you will be laying comfortably on your back while an ultrasound technician applies ultrasound gel on the wrist of your dominant hand. In one session, mechanical compression will be applied to the palm of your hand and forearm (at different times) while tendon movement is measured using ultrasound. In a second session, tendon movement will be assessed again but under the influence of acute ischemia from partial occlusion of the upper arm using a sphygmomanometer (blood pressure cuff).

During both experimental sessions, you will be asked to complete a series of finger flexion and extension movements while an ultrasound probe records images of the tendons in the carpal tunnel. Each movement will last no longer than 30 seconds (with rest in between ~~the different~~ movement bouts). The purpose of having separate sessions is to observe the effect that each experimental condition may have on tendon motion, while avoiding potential carry-over effects between interventions.

Potential Harm, Risk or Discomfort

Ultrasound is a safe imaging tool used to visualize tissues within your body. Mechanical compression applied over the hand and forearm may cause slight discomfort during finger movement bouts. In rare cases, light bruising may occur but should dissipate over the next 48-72 hours. Partial occlusion of the brachial artery from blood pressure cuff compression may lead to transient sensation of numbness and tingling or pressure in the hand and forearm for the duration of the occlusion intervention. These sensations will disappear shortly after the release of the cuff pressure without lasting effects on the function of the arm.

During finger flexion and extension movements, you will be asked to move your finger through a full range of motion over several movement bouts, which might cause minimal discomfort due to fatigue in some rare cases. If you do feel any muscular discomfort or pain, please tell the ultrasound 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 movement of tendons in the wrist under the influence of external factors. Ultimately, we hope to prevent musculoskeletal disorders in the workplace.

Payment and Reimbursement

You will receive $30.00 for your time for participating in this study. If you withdraw from this study at any time, you will still receive 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. Your individual data will be kept confidential to the fullest extent of the law. We will treat all information provided to us as subject to researcher-participant privilege.

Participation

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 partway through 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 of HIREB at (905) 521-2100 (× 42013).

Information about the Study Results

You may obtain information about the study results by contacting Calvin Tse at (905) 525-9140 (× 20175) or Peter Keir at (905) 525-9140 (× 23543).

Information about Participating in this Study

If you have questions or require more information about the study itself, please contact Calvin Tse or Peter Keir.

INFORMED CONSENT

I have read the information in this information and consent form about a study being conducted by Calvin Tse and Peter Keir at McMaster University. I have had the opportunity to ask questions about my involvement in this study, and to receive any additional details I wanted to know about the study. I understand that I may withdraw from the study at any time, if I choose to do so. I have been given a signed copy of this form. I agree to participate in this study.

_____	_____	_____
Name of Participant (Print)	Signature	Date

In my opinion, the person who has signed above is agreeing to participate in this study voluntarily, and understands the nature of the study and the consequences of participation in it.

_____	_____	_____
Name of Research Investigator Obtaining Consent (Print)	Signature	Date

APPENDIX E: Participant Screening Form

Participant Screening:

Ultrasound Assessment of Tendon Motion in the Carpal Tunnel

Hello,

I want to thank you for your interest in this study. The goal of this research is to assess motion of the flexor tendons in the wrist. Participants in this study will be asked to perform flexion and extension finger movements. While these movements are completed, ultrasound will measure tendon motion. Flexor tendon motion will be measured under mechanical compression of the palm or forearm, or slight ischemia through partial occlusion of the brachial artery. You will also be free to withdraw from the study at any time if you are uncomfortable with any aspect of the study and its methods.

I plan to begin data collection on May 1st, 2016. There are two testing sessions for this study. Mechanical compression conditions will be conducted in one session lasting 1 hour and the ischemia condition will be conducted during a different session lasting 2 hours. I am very flexible with testing times. Please let me know your availability, and I can arrange times for the two sessions.

I am looking for healthy participants. If you are still interested in participating in this study, can you please take a few minutes to fill out the questions below (so I can verify you qualify for this study)? Thanks again for your willingness to participate in this study. I look forward to hearing from you soon.

Calvin

Wrist Imaging Study Screening Questions

1) Are you between 18 and 50 years of age? ***Yes*** ***No***

2) Have you ever had any of the following health conditions or treatment protocols? [*please check all that apply*]

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

3) Are you currently on any medications? ***Yes*** ***No***

** If ***yes***, please list:

_____
_____
_____

APPENDIX F: Rating of Perceived Discomfort Scale

Rating of Perceived Discomfort

0	No discomfort at all	0%
0.5	Very light discomfort	
1	Light discomfort	
2	Fair discomfort	
3	Moderate discomfort	
4		
5	Severe discomfort	50%
6		
7	Near maximal discomfort	
8		
9		
10	Intolerable discomfort	100%

McMaster Occupational Biomechanics Laboratory