In Vitro Tensile Fatigue of Human Flexor Digitorum Profundus and Superficialis Tendons

by

Nicholas Charles Smith

A dissertation submitted to the Graduate Faculty of
Auburn University
in partial fulfillment of the
requirements for the Degree of
Doctor of Philosophy

Auburn, Alabama
August 3rd, 2019

Keywords: Fatigue Failure, Tendon, Duty Cycle, Carpal Tunnel Syndrome

Approved by

Dr. Sean Gallagher, Committee Chair, Associate Professor
Dr. Gerard Davis, Committee Member, Professor
Dr. Richard Sesek, Committee Member, Associate Professor
Dr. Mark Schall, Committee Member, Assistant Professor
Dr. Edward Davis, Committee Member, Assistant Professor
Dr. Michael Zabala, University Reader, Assistant Professor

Abstract

Distal upper extremity work-related musculoskeletal disorders (DUE WMSDs) such as carpal tunnel syndrome (CTS) and stenosing tenosynovitis (trigger finger) present a high cost on both society and industry. CTS in particular can result in a large number of days away from work (median=30 days). There is mounting evidence that DUE WMSDs (such as CTS) result from a fatigue failure process. This dissertation presents three experiments that contribute evidence regarding the fatigue failure of tendons associated with CTS and trigger finger; specifically, the flexor digitorum profundus (FDP) and flexor digitorum superficialis (FDS). The 'S-N' equation for FDP and FDS tendons was derived ($S = 35.178-1.86*\ln(N)$), relating imposed peak stress (S) to expected number of cycles until macroscopic failure (N). A Morrow power model was also derived ($y = 2.1864x^{-3.198}$), empowering future studies to estimate characteristic life without destructively testing the material. DC level was not a significant predictor of fatigue life ($p=0.563$) nor work per cycle ($p=0.44$). When comparing the FDP/FDS 'S-N' equation with a previously reported 'S-N' equation of EDL tendons, the FDP/FDS equation reported a higher OR for only 1 of 15 DUE outcome and repetition definition combinations using an epidemiological database. The FDP/FDS 'S-N' equation is more liberal than that of the EDL data, meaning more jobs were considered safe. This ultimately caused a higher accuracy for most DUE outcomes and repetition definition combinations. The probability functions for all DUE outcomes versus log CD for FDP/FDS data were more gradual functions, inferring a weaker dose-response relationship. Future research on the fatigue properties of FDP/FDS should focus on cyclic stresses less than 40% ultimate tensile stress (UTS) and also on cyclic compression, shear, and vibration forces.

Acknowledgments

First, to my wife, Tianqi "Tenchi" Gao Smith, for the constant encouragement on this adventure. To my children, Charlotte and Theodore, for the inspiration to be a better man. To my parents for laying the foundation of my pursuit of knowledge. To my siblings, Elaine and Alex, for showing me a thing or two. To my advisor, Dr. Sean Gallagher, for his expertise, kindness, and friendly basketball rivalry. To Dr. Richard Sesek, my committee member, for giving me a chance when few else would by accepting me into the graduate program. To Drs. Jerry Davis, Mark Schall, Edward Davis, and Michael Zabala for serving on my committee and providing invaluable insight on this dissertation. To the Auburn University Intramural Grant Program for providing a significant portion of the funding required for these experiments. And to the NIOSH "Deep South" IRC for footing the bill of my graduate and doctoral education.

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List of Abbreviations

ACGIH	American Conference for Government Industrial Hygienists
CD	cumulative damage
CSA	cross-sectional area
CTS	carpal tunnel syndrome
DC	duty cycle
DPC	damage per cycle
DUE	distal upper extremity
DUET	Distal Upper Extremity Tool
EDL	extensor digitorum longus
FDP	flexor digitorum profundus
FDS	flexor digitorum superficialis
FTOV	first-time office visit
HAL	Hand Activity Level
HR	hazard ratio
LiFFT	Lifting Fatigue Failure Tool
LMM	Lumber Motion Monitor
MVC	maximum voluntary contraction
OR	odds ratio
TLV	threshold limit value
UCS	ultimate compressive stress
UTS	ultimate tensile stress
VAS	visual analog scale
WMSDs	work-related musculoskeletal disorders

Chapter I: Background and Significance

Work-related Musculoskeletal Disorders (WMSDs)

WMSDs represent a range of debilitating, degenerative conditions affecting the biological tissues of workers in many occupations (Cohen et al., 1997; National Research Council and the Institute of Medicine [NRC-IOM], 2001). WMSDs are a leading cause of days away from work, contributing to between 29% and 35% of illnesses and injuries requiring days away from work (BLS, 2013). They are also a massive economical and societal burden. Estimates in the United States have ranged from $13 billion annually upwards to $215 billion, including direct and indirect costs related to these disorders (Praemer et al., 1999). These disorders are not local to the United States, though, as Leigh et al. (1997) estimated WMSDs account for 31% of the world's occupational diseases in 1994.

These disorders affect the muscles, tendons, ligaments, cartilage, spinal discs, and nervous system. Some of the better-known WMSDs include carpal tunnel syndrome (CTS), low back pain, tendinitis, and shoulder impingement. Although the mechanisms leading to these disorders are not fully understood, they are often associated with repeated actions under an external stress without adequate time for recovery (Costa & Vieira, 2009) . Other suggested risk factors include vibration, duration of exertion, duty cycle (DC), environment, obesity, gender, and age (Costa & Vieira, 2009). Though these disorders can manifest rapidly, symptoms typically begin as mild discomfort to the worker. If left without treatment or adequate rest, this discomfort may turn to pain and, ultimately, into debilitation.

Distal Upper Extremity (DUE) WMSDs Associated with Flexor Digitorum Tendons

CTS has been reported at a prevalence of 7.8% in certain working populations (Dale et al., 2014). CTS has historically required the most days away from work of any WMSD, with a median of 30 days (BLS, 2017). CTS is a compressive neuropathy, with the median nerve becoming entrapped at the level of the carpal tunnel. The compression is often attributed to the forearm tendons running

through the carpal tunnel becoming inflamed (tendonitis) or the tendon's synovial sheath becoming inflamed (tenosynovitis). This inflammation swells in the carpal tunnel and results in pressure on the median nerve against the carpal tunnel bones. Results from studies on the presence of inflammation in wrists with CTS have been mixed, however. Workers with symptoms of CTS often experience numbness in the radial side of the hand as well as reduced strength. Typical risk factors attributed to CTS include highly repetitive tasks, obesity, diabetes, age, gender, and environmental conditions.

Stenosing tenosynovitis, often called "trigger finger", is the inflammation of the synovial sheath of a tendon (Freivalds, 2012). As the sheath becomes inflamed, the tendon can no longer smoothly glide through the sheath. Ultimately, this leads to the tendon locking into place and requiring physical displacement. Reports have stated prevalence of trigger finger at 2% of the general population (Moore, 2000). Similar to CTS, attributed risk factors include: highly repetitive and forceful tasks, obesity, diabetes, age, gender, and environmental conditions.

DUE Ergonomics Risk Assessment Tools

Ergonomics risk assessment tools have been created to estimate a worker's risk of DUE WMSDs by performing a task or multiple tasks (Gallagher et al., 2018; Moore and Garg, 1995; Radwin et al., 2014). These assessments allow practitioners to systematically rank tasks in order of estimated risk. This ultimately saves company resources and reduces injuries by proactively and objectively targeting tasks presenting the highest risk for solution brainstorming and implementation. These assessments are also used in medical management cases to determine work-relatedness of an injury. The inputs for these assessment tools vary but often include force, repetition, and posture. Some tools have also included DC, duration of exertion, and shift duration (Gallagher et al., 2018; Moore and Garg, 1995; Radwin et al., 2014).

Interaction of Force and Repetition as a Risk Factor for Musculoskeletal Disorders

A systematic review by Gallagher and Heberger (2013) has revealed a distinct interaction

between force and repetition with respect to the risk of developing many WMSDs. This interaction shows a large increase in risk when both force and repetition are increased, rather than either solely increasing alone. The review also noted this interaction is not local to one type of WMSD. Results were consistent for CTS, hand-wrist tendonitis, low back disorders, lateral epicondylitis, and shoulder tendinitis.

The review by Gallagher and Heberger (2013) importantly notes this force and repetition interaction would be expected if musculoskeletal materials failed in accordance with fatigue failure theory, long known in the materials science world. Fatigue failure theory provides an estimate of the fatigue life of a material when it either: a) undergoes one cycle of a maximum force (called the ultimate stress of the material), or b) undergoes repeated cycles of sub-ultimate stress forces. This fatigue failure process is unique to the material being tested, with varying rates of damage accumulation based on elasticity, environmental conditions, and other factors. This process begins with microdamage nucleation due either to concentrated regional stress or high void density. A material's fatigue failure relationship is often characterized in a 'S-N' equation, with S representing the constant stress range and N being the number of cycles until failure. Development of 'S-N' equations allow for the prediction of failure at a certain cycle or time given a cyclic stress.

Implementing Fatigue Failure in Ergonomics Risk Assessment Tools

The only ergonomics assessment tools using fatigue failure as an underlying basis have been the Lifting Fatigue Failure Tool (LiFFT) and Distal Upper Extremity Tool (DUET) (Gallagher et al., 2017; Gallagher et al., 2018). LiFFT assesses a worker's risk of developing a lower back WMSD when performing a lifting task. It does so by obtaining inputs of object weight, horizontal distance between the spine and an object, and the number of repetitions performed per day. An algorithm then relates these inputs into an expected damage per cycle and, ultimately, the probability of an injury occurring. This algorithm quantifying risk is derived from compression fatigue tests of cadaveric

spinal motion segments and the resultant 'S- N' equation described previously (Brinckmann and Biggermann, 1988). LiFFT also has the ability to easily calculate the cumulative risk of multiple lifting tasks. One factor that LiFFT has to account for that materials testing often does not include is the healing of the lumbar tissues. This is done with a hypothesized 3% daily healing rate based on reported collagen turnover (Kjaer et al., 2005). With this basis, LiFFT accounted for 92% of the deviance of low back disorders in the Lumber Motion Monitor (LMM) database and 72-95% of the deviance in an automotive database (depending on the outcome measure). LiFFT uses only three simple input metrics requiring little training to attain expertise.

DUET similarly uses fatigue failure as a basis but aims to assess the risk of DUE WMSDs. Because these disorders have predominantly been linked to issues of the tendons of the hand and wrist, DUET utilizes an 'S-N' equation derived by Schechtman and Bader's (1997) fatigue failure experiment of the human extensor digitorum longus tendon. DUET has also been validated using the automotive database mentioned above and found 79.1-94.6% of the deviance in the database. The successes of LiFFT and DUET mark a clear path for the research needed to develop practical and accurate assessment tools. The following section will review previous studies that have contributed to this branch of knowledge, while also determining knowledge gaps that the remainder of this dissertation aims to satisfy.

Chapter II. Literature Review of Fatigue Testing Human Tissue

Summary

The most studied human tissue in which 'S-N' equations have been presented is certainly bone. Specifically, the lumbar spine has been reviewed in some detail, likely due to the prevalence of lower back pain. Hardy et al. (1958) released a preliminary report detailing multiple tests of repeated compressive loading on the lumbar spine. The goal was to associate mechanical compression on the lumbar spine to pressure on the annulus fibrosis with implications on low back pain. Though the intention to develop an 'S-N' equation was not evident, the results detail number of cycles endured at specific loads, which frame the first rough understanding of the degradation of biotissues under mechanical stress. Hardy employed cyclic loads ranging from 0.5 to 4.5kN and found compression fractures between 200 and 1,200,000 cycles. Since that precedent, Freeman et al. (1971) explored fatigue fracture in the subchondral bone in cadaver femoral heads. Similar to Hardy et al., the intention was not originally to develop an 'S-N' equation for femoral heads, at least not in the sense to be used for occupational biomechanics. Instead, Freeman et al. were examining the pathogenesis of osteophyte formation in osteoarthrosis. The authors utilized a load of five times the cadaver's body weight, which, while remaining constant, imposed a varying pressure on the femoral heads which varied in surface area. The result is an 'S-N' equation that spans roughly 15% of the expected ultimate compressive stress (UCS). This study provided supporting evidence towards the logarithmic failure behavior for bone. The first study to set a specific aim of developing an 'S-N' equation for the lumbar spine was Liu et al. (1983), testing 11 lumbar spine segments of two vertebral bodies and the intervening disc. Cyclic loads between 37% and 80% UCS were applied at a frequency of 0.5Hz. Hansson et al. (1987) soon followed with 17 lumbar motion segments, testing between 60% and 100% UCS. Brinckmann and Biggermann (1988) were then able to test 70 lumbar motion segments between 20% and 70% UCS. Brinckmann and Biggermann's work marked the first to discuss the

ability to predict number of load cycles until encountering fatigue fractures *in vivo*, though the authors did note potential errors due to intermittent loading, varying load magnitudes, and not accounting for recovery. Gallagher et al. (2005) then fatigued 36 lumbosacral motion segments at different flexion angles producing varying compression forces. As mentioned in Chapter I, Gallagher et al. (2017) then combined the data from Gallagher et al. (2005) and Brinckmann and Biggermann (1988) to develop the underlying risk algorithm for LiFFT. The above review of mechanical testing on the lumbar spine, culminating in LiFFT, demonstrates the potential for ergonomics risk assessment tools using fatigue failure as a basis when the necessary literature is available.

The fatigue failure of cadaveric ligaments has also been studied. Thornton et al. (2007) studied failure patterns of medial collateral ligaments (MCL) under cyclic stresses of 60%, 30%, and 15%. Lipps et al. (2013) similarly studied the fatigue failure of anterior cruciate ligaments (ACL). Only two stress levels were tested though: three times body weight and four times body weight. These both found logarithmic failure patterns, showing this biomaterial fatigue failure theory to not localized to any one biomaterial.

Unfortunately for the risk assessment of upper extremity tasks, which typically manifest WMSDs in tendons, such literature for tendons is scarce. A similar systematic review only revealed two studies that generate an 'S-N' equation for human tendons, which are Schechtman and Bader (1997) and Wren (2003).

Wren et al. (2003) performed cyclic tensile tests using stresses ranging between 30 and 80 MPa on human Achilles tendons. Unfortunately, a median UTS was not initially found for their sample, so it is unclear what % UTS at which each tendon was tested. This prevents direct implementation into ergonomics risk assessment tools as task forces cannot be normalized to the tested stress. Still, a logarithmic model was fit to the cyclic data resulting in an equation similar to that obtained by Schechtman and Bader (1997).

Schechtman and Bader (1997) were able to cyclically test tendons at 10% ultimate tensile stress (UTS) increments between 10% and 90%, which include important data points at low stress levels typically infeasible in biomechanical testing due to duration limitations. The dataset is even fit to a logarithmic of the median failure values with r=0.99 and $p<0.01$, represented by the following equation:

$$S=101.25-14.83\log(N) \qquad (3).$$

This equation is currently the underlying basis for DUET, described in Chapter I. However, this equation is derived from the testing of human EDL tendons of the foot, while DUET is attempting to assess risk of the hand, wrist, and shoulder. There are two main potential problems: 1) the UTS and all sub-maximal tensile strengths may be greater or less for the tendons in the hand, wrist, and/or elbow; and 2) the rate of the 'S-N' equation's slope may be higher or lower for tendons in the hand, wrist, and/or elbow. Wang et al. (1994) data supports the theory that tendons enduring different magnitudes of stress *in vivo* may fatigue differently. To highlight this, Figure 1 compares the 'S-N' equations for the only two fatigue studies so far performed on cadaveric tendons, one from the EDL tendons mentioned above and the other from Achilles tendons (Wren et al., 2003).

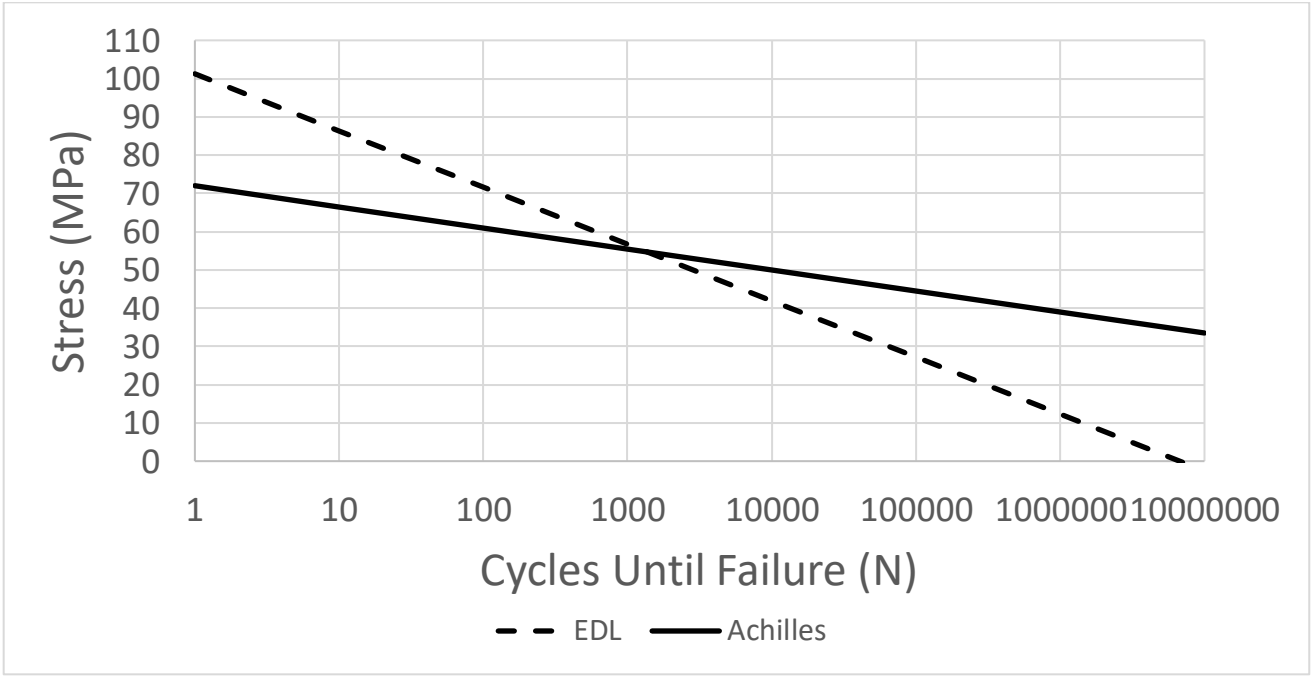


Figure 1. The 'S-N' equations for EDL (Schechtman and Bader, 1997) and Achilles tendons (Wren et al., 2003)

The former issue of potentially different UTS is remedied by DUET's use of the OMNI-RES scale, instead of specific force measurements. The latter issue of potentially different fatigue slopes, however cannot be verified unless tendons from the WMSD-prone body segments are fatigue tested in a similar manner to Schechtman and Bader's EDL specimens (Schechtman and Bader, 1997).

DC is commonly evaluated as a risk factor when assessing risk of DUE WMSDs. For example, the American Conference for Government Industrial Hygienists (ACGIH) Hand Activity Level threshold limit value (HAL TLV™) utilizes DC as a factor in determining risk (Radwin et al., 2014). However, while it makes sense that larger DCs would lead to increased injury risk, the evidence supporting this factor has been mixed. Currently, no studies have reported results on cyclic fatigue of cadaveric tissue under various DC levels. Therefore, this review will briefly discuss related findings, including results from animal tissue testing.

DC itself can be separated into two attributes: an active loading portion (e.g., maintaining a forceful grip) and inactive portion (e.g., relaxing/resting the tissues). In comparison to creep effects on tissue due to dwell, *in vitro* fatigue studies of human Achilles tendon, rabbit MCL, and wallaby tail tendon all found significantly higher hazard ratios (HR) with pure cyclic fatigue than with creep fatigue (Wren et al., 2013; Thornton et al., 2007; Wang et al., 1994). However, these studies did not test human musculoskeletal tissues, nor did they test combinations of cyclic loading and creep loading (also known as "dwell"). Resting duration, or elastic relaxation for *in vitro* specimens, during cyclic fatigue testing of biotissues has not been studied.

The results of this literature review show a great potential utility in mechanically testing biomaterials commonly afflicted with WMSD's, yet also shows a lack of such studies for tendons. This review also reveals DC to be a potential risk factor with WMSD's of the hand and wrist, with yet another lack of studies examining the such an effect on the *in vitro* fatigue of tendons.

Specific Aims

This dissertation was created to explore the knowledge gaps mentioned above and also to provide an expansion on techniques used to conduct the required testing. Three specific aims were created to achieve these ambitions:

SA #1	Determine the 'S-N' relationship for the FDP and FDS, relating cyclic peak stress (MPa) to the expected number of cycles until failure.
SA #2	Determine the effect of DC on the expected number of cycles until failure of FDP and FDS during fatigue testing.
SA #3	Evaluate the predictive ability of the FDP/FDS 'S-N' equation using an existing epidemiological database and compare these results to those of the EDL 'S-N' equation.

Table 1. Specific Aims

The following dissertation will detail the experiments undertaken to achieve these specific aims. Chapter III discusses the results of a tensile fatigue loading of cadaveric FDP and FDS tendons. Chapter IV discusses a similar study of a tensile fatigue loading of cadaveric FDP and FDS tendons at various DC levels. Chapter V presents the results from an experiment evaluating the predictive ability of the FDP and FDS 'S-N' equation using an existing epidemiological database. This validity was then compared to the previously reported validity of the EDL 'S-N' equation using the same database. Chapter VI contains the major findings from each study, elaborates on application, and suggests how to move forward with future research.

CHAPTER III: *In Vitro* Fatigue of Human Flexor Digitorum Tendons

Introduction

CTS and stenosing tenosynovitis (trigger finger) have both been linked to the overuse of the FDP and FDS tendons (Freivalds, 2011). CTS symptoms have been associated with deterioration of the FDP tendon synovial sheaths in the carpal tunnel (Millar, N.L., 2010; Fredberg, U., 2008; D'Addona, A., 2017). Trigger finger, meanwhile, has been linked to FDP tendon deterioration and kinking in the finger itself (Sampson et al., 1991). Ergonomics job evaluation tools assess the risk of developing these WMSDs as a result of work. These tools typically consider the force, repetitions, posture, and various other risk factors required to perform work.

A systematic review demonstrated a pattern between force and repetition in epidemiological studies of WMSDs (Gallagher and Heberger, 2013). This pattern suggests WMSDs may develop in a manner similar to the fatigue failure process long established in the materials science realm as a method of damage accumulation. Fatigue failure theory provides an estimate of the fatigue life of a material when it either: a) undergoes one cycle of a maximum force (called the ultimate stress of the material), or b) undergoes repeated cycles of sub-ultimate stress forces. This process begins with microdamage nucleation due either to concentrated regional stress or high void density. This microdamage accumulates until ultimate failure occurs. A material's fatigue failure relationship is often characterized by an 'S-N' equation, where S the cyclic peak stress and N is the number of cycles to failure. These 'S-N' equations allow for the prediction of failure at a certain cycle given a repeated cyclic stress.

A recent example of the use of an 'S-N' equation applied to risk assessment is LiFFT, which has shown highly significant associations between predicting risk with both repetitive and various lifting operations, due in large part to its underlying risk algorithm derived from fatigue testing of

cadaveric spines (Gallagher et al., 2017). Similarly, DUET uses an 'S-N' equation derived from human extensor digitorum longus tendons to assess risk in tasks involving the upper extremities (Gallagher et al., 2017).

DUET is an ergonomics job assessment tool targeting WMSDs of the hand and wrist (Gallagher et al., 2018). DUET incorporates the fatigue failure theory by using the 'S-N' equation derived from cadaveric EDL tendons as the underlying risk algorithm (Schechtman and Bader, 1997). Using this approach has shown a highly significant association with risk outcomes and allows for the cumulative risk assessment of multiple tasks. However, using the 'S-N' equation from EDL tendons may not be the most appropriate. Wang et al. (1994) data supports the theory that tendons enduring different magnitudes of stress *in vivo* may fatigue differently.

DUET utilizes the 'S-N' equation from EDL tendons because no fatigue failure tests of human wrist tendons have been yet been reported. Therefore, the current study's primary aim is to derive the *in vitro* fatigue properties of FDP and FDS tendons, potentially improving the accuracy of DUET to predict DUE MSD risk.

Materials and Methods

Specimens

Eleven donor cadavers (mean age=62.9 years ±9.48) provided forty-nine FDP/FDS specimens. Exclusion criteria for tendon specimens included Hepatitis A, Hepatitis B, HIV, and cases of chronic renal, metabolic, or endocrine disease, as these conditions may influence the mechanical properties of tendon (Schechtman and Bader, 1997). FDP and FDS muscles initially attach at the anterior and medial surfaces of the ulna and spans the forearm. They then quadfurcate with four tendons extending into the wrist, through the carpal tunnel, traveling through the fingers and attaching at the palmar side of each distal phalanx of the second to fifth finger. Their primary

functions are to flex the fingers and assist in flexing the hand. *In vivo*, the distal tendons of the FDP experience tensile stress during hand gripping, finger pinching, and finger pressing (as in keyboard use) (Armstrong and Chaffin, 1978; Chang et al, 2014; Kim and Johnson, 2014).

Specimen Excision

Specimens were excised from thawed, whole arm segments. Surrounding muscle and fascia were removed using rounded edge scalpels. Specimens were then immediately placed in self-sealing, air-tight plastic bags filled with 20mL of saline solution. Finally, these bags were labeled with identifiers and placed in a freezer set to -20°C.

Experimental Procedures

Mechanical testing of tendons poses three main challenges. The first is retaining the native environment of the tendons throughout testing. The fidelity of cadaveric tissue testing is constantly being reduced as tendons decompose over time without the hydration, temperature, and nutrition they have *in vivo*. Previous solutions to this issue include saline drips and control chambers, which have the added benefit of locally controlling temperature and pressure. The second issue is clamping. The fragility of the tendon structure prevents excessive compression force from being used, yet the natural liquid content and the supplied hydration during testing both reduce the friction coefficient necessary to prevent slippage. Freezing, self-tightening, and high friction clamps have all been used with varying success. Also, some tests have retained the myotendinous and osteotendinous junctions to clamp the tissue more effectively. The third challenge is converting load to tensile stress by measuring or estimating cross-sectional area (CSA). Most tendons transfer energy from a large muscle belly to a smaller attachment point, causing a thinning effect from the proximal to distal end. This thinning effect results in the weakest point of the tendon being directly at a clamp, reducing the credibility that failure resulted purely from the imposed stress and not compression from the clamp itself. Retaining the tendon entheses has helped mitigate this issue, as has utilizing tendons with large

aspect ratios. CSA has been measured with calipers, impression material, area micrometers, and estimated using length, mass, and density ratios.

Specimens were thawed at room temperature for 45 minutes before testing while submerged in the saline solution inside their individual plastic bags. To normalize stress based on each tendon's CSA, the length of the tendon was measured with electronic digital calipers (accuracy of +/- .0.2032mm) after each tendon had thawed. Then, each tendon's mass was measured with a scale. CSA was then estimated utilizing an estimated tendon density of 1120 Kg/m^3 (Ker, 1981).

Quasi-static Tensile Test

In order to fatigue test at preselected levels of % UTS, quasi-static tensile tests were conducted to estimate UTS for FDP and FDS. All tendons were tested on an ElectroPuls E3000 materials testing device (Instron, Norwood, MA, USA) with a displacement accuracy of <50 μm and a ±5 kN load cell. Eighteen specimens were randomly selected and tested to determine UTS. The distal and proximal ends of the tendons were wrapped in sandpaper and clamped. The clamps had ridged surfaces to increase surface area and resistance. Ten Nm of torque was applied to each screw on each pair of clamps, which sufficiently prevented slipping while retaining the tendon structure between the clamps. The clamp-to-clamp length was recorded after establishing a non-zero load on the tendon. Load and displacement data were recorded at 10 Hz, while UTS and strain to failure were automatically calculated. Testing was performed at room temperature with the crosshead speed set to 1% strain s^{-1}. The tendons were kept hydrated during testing with a saline drip set to 0.5 l h^{-1}.

Fatigue Test

Thirty-two specimens were tested to assess fatigue life. A sinusoidal waveform was chosen to reflect the *in vivo* loading pattern of tendon (Komi et al., 1992). Results from UTS testing revealed no significant differences between FDP and FDS ($F=0.02$, $p=0.889$), therefore these tendons were grouped for fatigue testing. Three levels of maximum peak stress were established to characterize

fatigue life: 40%, 60%, and 80% UTS (n=9, 11, and 12). Frequencies of 3Hz, 2Hz, and 1Hz were chosen for each loading level, respectively, in order to decrease testing time. Wang et al. (1994) found a common modulus for Wallaby tendons tested between 2.2Hz and 70Hz, so effects due to loading rate were not expected to be significant. 1% UTS was established as the minimum stress. Specimens were randomly assigned to a maximum peak stress group. Displacement, cycle count, and load were recorded at a sampling frequency of 10 Hz.

Data Analysis

Linear regression was used to analyze the effects of stress level. Personal characteristics including age, BMI, race, and gender were also included in the regression analysis (Wren, et al., 2003). Tukey's Honestly Significant Difference test was utilized to determine significant differences between test levels.

Weibull distribution analysis was used to characterize the probability of failure at each stress level (Weibull, 1951). This analysis has been shown to model failure with reasonable accuracy with relatively small sample sizes. Two defining parameters of the Weibull data plot are of particular interest: the slope of the line, β, provides insight regarding the mechanics of failure; and the characteristic life, α, is the cycle at which 63.2% of specimens are predicted to fail. The characteristic life is also important in utilizing the Morrow energy fatigue equation, which relates work (J) per cycle to characteristic life (Morrow, 1965). This power model is described by:

$$N_{63}=C^{1/m}W^{-1/m}; \quad (4)$$

where N_{63} is the characteristic life, W is the work per cycle, C is the fatigue ductility, and m is the fatigue exponent. This model predicts the characteristic life of a sample using a Work datapoint taken at steady state, which allows future studies to test the sample's remaining fatigue life in different ways. A one-way ANOVA was used to compare strains to failure at each stress level. Type I error rate was set at 0.05.

Results

Quasi-static Tensile Test

The flexor digitorum tendons elicited typical, non-linear stress-strain equations previously found *in vitro* for animal and human tendons (Schechtman and Bader, 1994; Wren, 2002). See Figure 2 for a resultant equation from one specimen's tensile test. This equation is often segmented into three regions: the toe-in region, which has massive gains in strain with increasing stress; the linear region, named for the steady gains in strain with increasing stress; and finally the failure region, often starting with a slight dip in stress called the yield point, rising again in stress and strain until reaching the ultimate strength, when failure occurs and increases in strain require rapidly diminishing stress.

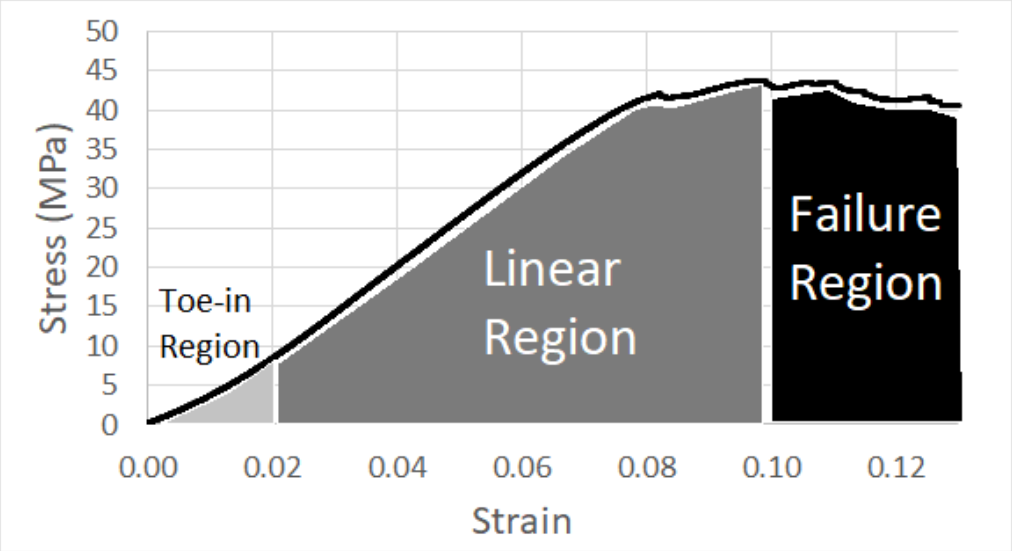


Figure 2. Example stress/strain equation from a quasi-static ultimate tensile test.

The UTS of eighteen flexor digitorum tendon specimens ranged from 23.9 MPa to 53.8 MPa with a mean value of 41.17 ± 10.01 SD MPa. The strain to failure, measured from the cross-head displacement, had a mean value of 11.08 ± 3.19%. All specimens failed in the midsubstance of the

tendon between the clamps and visual examination immediately following macroscopic failure indicated adequate hydration and effective clamping.

Fatigue Tests

Figure 3 illustrates the 'S-N' equation developed from fatigue tests. All specimens failed macroscopically between the clamps. A high degree of variability can be seen within each test level. Linear regression results demonstrated stress to be significant predictor of fatigue life ($p = 0.003$). Tukey's Honestly Significant Difference found statistical significance between the fatigue life at 40% UTS and the fatigue life at 60% UTS, as well as between 40% UTS and 80% UTS. The test did not find a statistically significant difference between the 60% UTS and 80% UTS conditions. The regression analysis indicated a need for logarithmic transformation due to the residuals originally being non-normal.

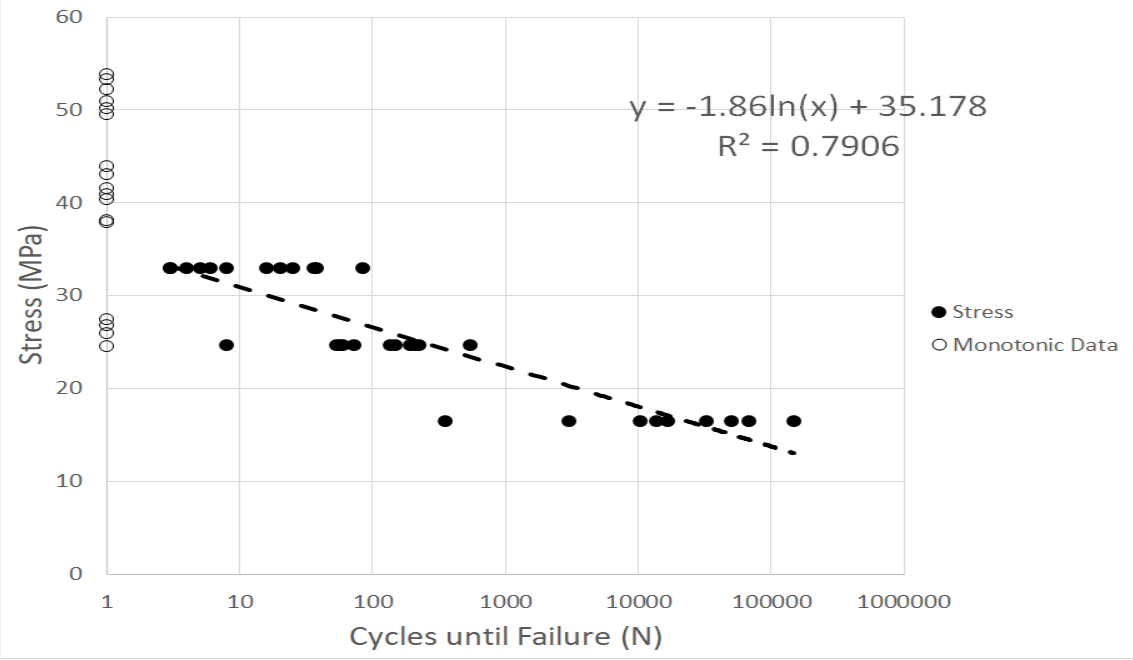


Figure 3. Fatigue life grouped by stress level fitted with a logarithmic model.

The logarithmic model resulting in the best fit was:

$$S = 35.178-1.86*\ln(N);\ R^2=0.79; \quad (1)$$

where S is the normalized stress (MPa) and N is the number of cycles to macroscopic failure. Age (p=0.17), BMI (p=0.99), race (p=0.99), and gender (p=0.93) had no effect on fatigue life.

Weibull analysis was performed at each stress level to quantify the statistical distribution of fatigue life (Table 2). It is evident that specimens loaded with high percentages of UTS are predicted to only withstand tens or hundreds of cycles before macroscopic failure; while specimens loaded at low percentages of UTS are predicted to last tens of thousands of cycles. The beta parameter for 40% UTS (0.6) is lower than that of 60% UTS (0.98) and 80% UTS (0.95).

Table 2. Weibull analysis parameters for each stress group.

Test Protocol	**Alpha (or Characteristic Life)**	**Beta (or Shape) Parameter**
40% UTS	35665.64	0.60083
60% UTS	170.68	0.983996
80% UTS	20.73	0.953787

To develop the Morrow model from this data, work (J) per cycle was calculated using rectangular integration of the hysteresis loops. These stress to strain hysteresis loops increased in area throughout the fatigue life, becoming less steep and less linear (Figure 4). The Morrow model was found by using a power line of best fit with average characteristic life plotted against average work per cycle for each stress level (Figure 5). This Morrow power model of best fit was:

$$N_{63}=2.1864*W^{-3.198},\ (R^2=0.9208); \quad (2)$$

The fatigue ductility (C= 1.277) and the fatigue exponent (m= 0.3127) were solved for using Formula

4. This model allows future studies to estimate the characteristic life of a sample once steady state work is determined, typically very early in the fatigue life. This allows future studies to test the remaining life in various ways and compare to the expected fatigue life under cyclic fatigue.

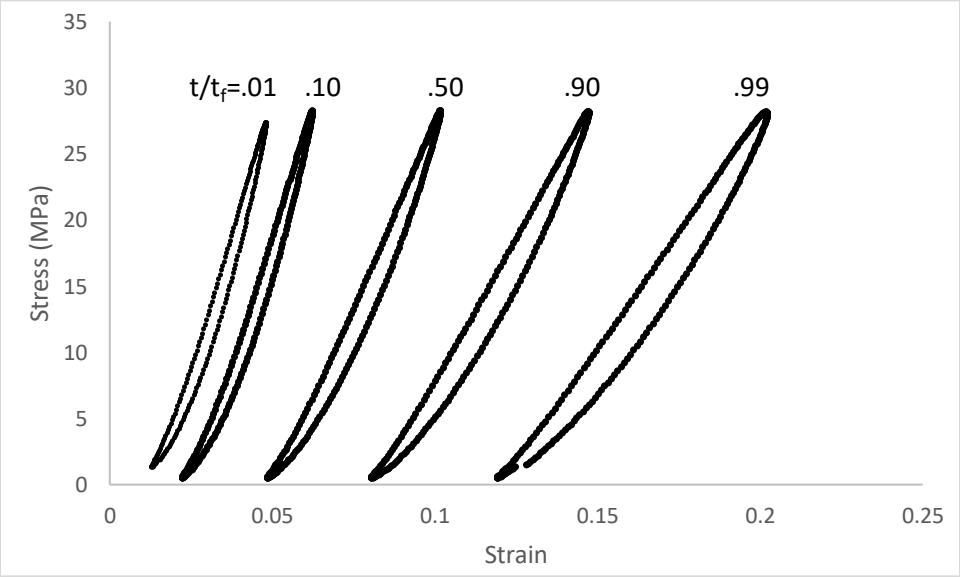


Figure 4. Typical results for hysteresis loops during 60% UTS peak stress cyclic testing. Cycle counts shown represent 1%, 10%, 50%, 90%, and 99% of fatigue life.

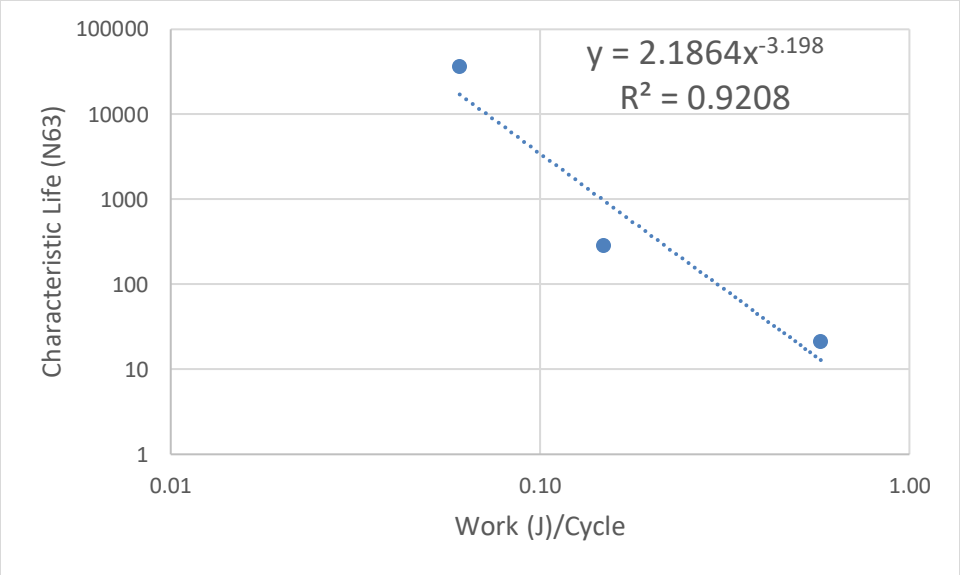


Figure 5. Log-log plot of characteristic fatigue life versus work per cycle

ANOVA results indicated stress level to be a significant factor on strain to failure ($p=0.003$). Tukey's Honestly Significant Regression then showed the 40% UTS level strain to failure was significantly higher than 60% UTS and 80% UTS, which were not significantly different from each other (Figure 6).

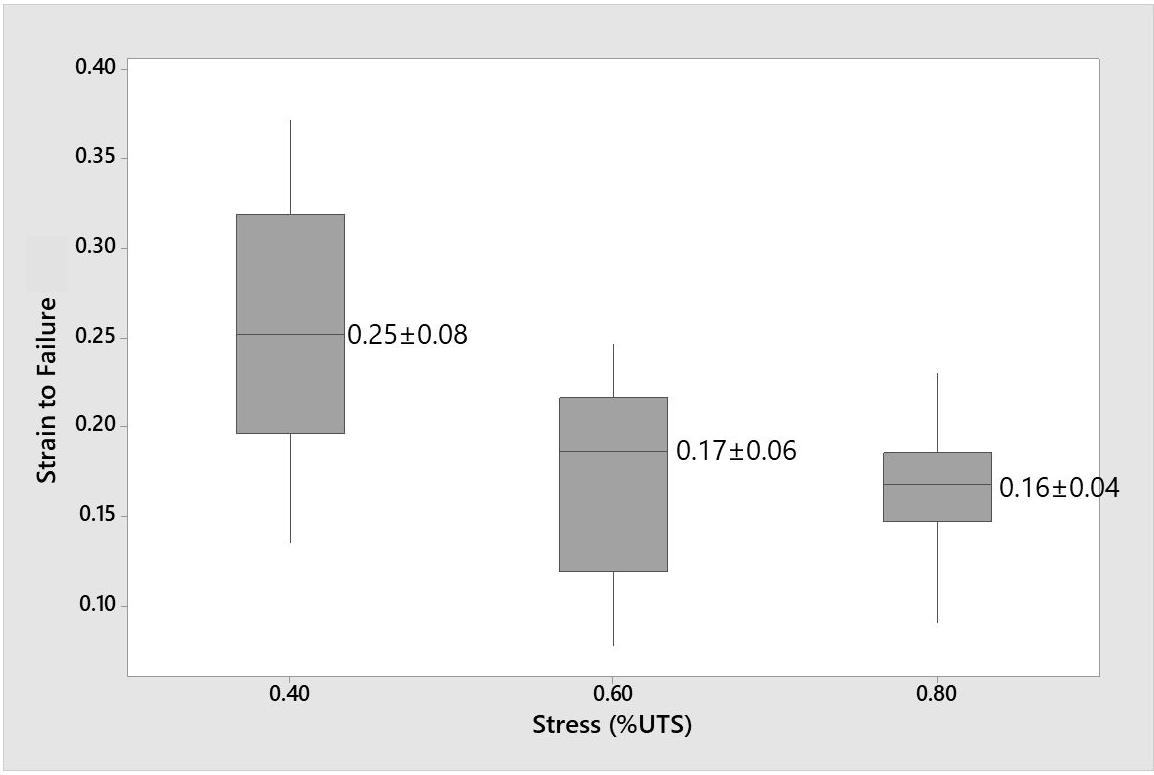


Figure 6. Boxplot of the strains to failure for each stress level. 40% UTS was significantly different from 60% UTS and 80% UTS.

Table 3. Full results from the monotonic quasi-static tensile tests.

Specimen ID	Tendon Type	Age	BMI	Sex	CSA (mm^2)	Ultimate Force (N)	Ultimate Stress (MPa)	Ultimate Strain (%)
2	RFDS	56	20.60	F	11.71	514.00	43.89	0.10
10	LFDS	56	20.60	F	19.44	477.62	24.57	0.09
22	LFDP	58	21.26	M	20.73	537.11	25.91	0.12
23	LFDP	58	21.26	M	10.42	419.98	40.31	0.15
39	RFDS	46	15.81	M	7.48	374.93	50.10	0.11
43	RFDP	46	15.81	M	7.58	403.80	53.24	0.14
49	LFDS	46	15.81	M	6.49	338.65	52.15	0.14
53	LFDP	46	15.81	M	5.59	276.80	49.49	0.06
81	RFDS	67	29.84	F	14.11	534.53	37.89	0.11
91	LFDP	67	29.84	F	10.37	277.44	26.76	0.07
106	LFDP	78	15.98	M	15.91	436.55	27.43	0.12
109	LFDP	78	15.98	M	8.78	377.98	43.03	0.08
131	LFDP	66	26.52	F	7.21	299.48	41.53	0.10
147	LFDP	65	17.23	F	7.46	283.91	38.04	0.07
I170385_R_FDP_2	RFDP	66	26.52	F	7.14	291.83	40.86	0.16
I170385_R_FDP_3	RFDP	66	26.52	F	7.94	426.96	53.76	0.17
I170385_R_FDP_4	RFDP	66	26.52	F	4.70	239.11	50.88	0.09

Table 4. Full results of each cyclic fatigue test.

Tendon Study #	Cycles Until Failure	Test Protocol	Stress (MPa)	Age	BMI	Sex	Specimen Type	CSA (mm^2)	Strain to Failure (%)
6	20	80%	32.94	61	31.32	M	RFDP	14.44	0.23
48	6	80%	32.94	46	15.81	M	LFDS	9.67	0.17
118	16	80%	32.94	65	17.23	F	LFDS	11.30	0.17
157	8	80%	32.94	78	15.83	M	RFDS	21.05	0.18
125	38	80%	32.94	65	17.23	F	LFDP	6.26	0.15
1	3	80%	32.94	61	31.32	M	RFDS	17.07	0.19
46	4	80%	32.94	46	15.81	M	RFDP	11.37	0.20
88	36	80%	32.94	67	29.84	F	LFDS	10.67	0.18
93	5	80%	32.94	67	29.84	F	LFDP	9.05	0.15
28	85	80%	32.94	61	15.82	F	RFDS	8.74	0.16
113	25	80%	32.94	65	17.23	F	RFDS	3.30	0.09
83	3	80%	32.94	67	29.84	F	RFDS	3.40	0.10
20	59	60%	24.70	58	21.26	M	LFDS	4.33	0.19
56	53	60%	24.70	56	14.76	M	RFDS	9.88	0.25
59	542	60%	24.70	56	14.76	M	RFDP	10.89	0.24
66	149	60%	24.70	56	14.76	M	LFDP	15.63	0.17
111	136	60%	24.70	65	17.23	F	RFDS	8.57	0.15
116	72	60%	24.70	65	17.23	F	RFDP	7.14	0.19
120	190	60%	24.70	65	17.23	F	LFDS	8.36	0.20
121	57	60%	24.70	65	17.23	F	LFDS	2.15	0.12
154	223	60%	24.70	56	20.60	F	LFDP	8.79	0.22
165	8	60%	24.70	78	15.83	M	LFDS	4.12	0.09
97	208	60%	24.70	78	15.98	M	RFDS	2.13	0.08
129	67113	40%	16.47	66	26.52	F	LFDS	13.22	0.37
35	10268	40%	16.47	61	15.82	F	LFDP	14.11	0.35
47	32590	40%	16.47	46	15.81	M	LFDS	10.67	0.28
51	147209	40%	16.47	46	15.81	M	LFDP	11.25	0.29
128	349	40%	16.47	66	26.52	F	LFDS	7.31	0.19
33	50063	40%	16.47	61	15.82	F	LFDS	8.68	0.25

99	13600	40%	16.47	78	15.98	M	RFDP	13.90	0.21
94	16556	40%	16.47	78	15.98	M	RFDS	10.22	0.20
92	3019	40%	16.47	67	29.84	F	LFDP	12.95	0.14
36	26773314*	20%	8.23	61	15.82	F	LFDP	18.47	
19	10368860*	20%	8.23	58	21.26	M	LFDS	13.70	
139	280612252*	20%	8.23	56	17.64	F	RFDP	7.49	

Discussion

The primary aim of this study was to derive the fatigue failure 'S-N' equation of cadaveric FDP and FDS tendons and compare with previous fatigue failure tests of cadaveric EDL and Achilles tendons. The first major finding was that the 'S-N' equation for FDP and FDS tendons was similarly logarithmic in nature as those reported for the EDL and Achilles tendons, but more conservative. The second major finding was the derived Morrow power model, allowing future work to predict characteristic life without fatiguing until failure. Finally, the Morrow power model was used to predict characteristic life for three samples tested at 20% but which dehydrated before failure. A new 'S-N' equation was then fit to the fatigue data including these predicted data points.

The 'S-N' equation proved to be logarithmic in nature, similar to those reported for EDL and Achilles tendon (Schechtman and Bader, 1997; Wren et al., 2003). However, when compared to Schechtman and Bader (1997), the UTS values for FDP and FDS (41.17 ± 10.01 SD MPa) were considerably lower than those of EDL (99.9 ± 12.2 MPa). Only at S < 9.17 MPa does the FDP/FDS tendon finally show a higher endurance (Figure 7). The most probable reason for this difference is the expected difference between *in vivo* stresses for these two tendons, as this has been shown to affect fatigue quality (Pike et al., 2000). Unfortunately, no studies have yet reported on the *in vivo* stresses of EDL or FDP/FDS tendons.

While the Weibull analysis beta value for 40% was lower than that for 60% and 80%, these values all fall within the range derived from Schechtman and Bader's EDL fatigue tests (0.5-1.72) (Gallagher, 2012). Similarly, strain to failure results were higher than the pooled results of EDL tendons (14.2 ± 5.6%) (Schechtman and Bader, 1997). Wren et al. (2003), however, reported strains as high as 40-50% in Achilles tendon. Cell morphology studies throughout the fatigue life may reveal why these differences occurred.

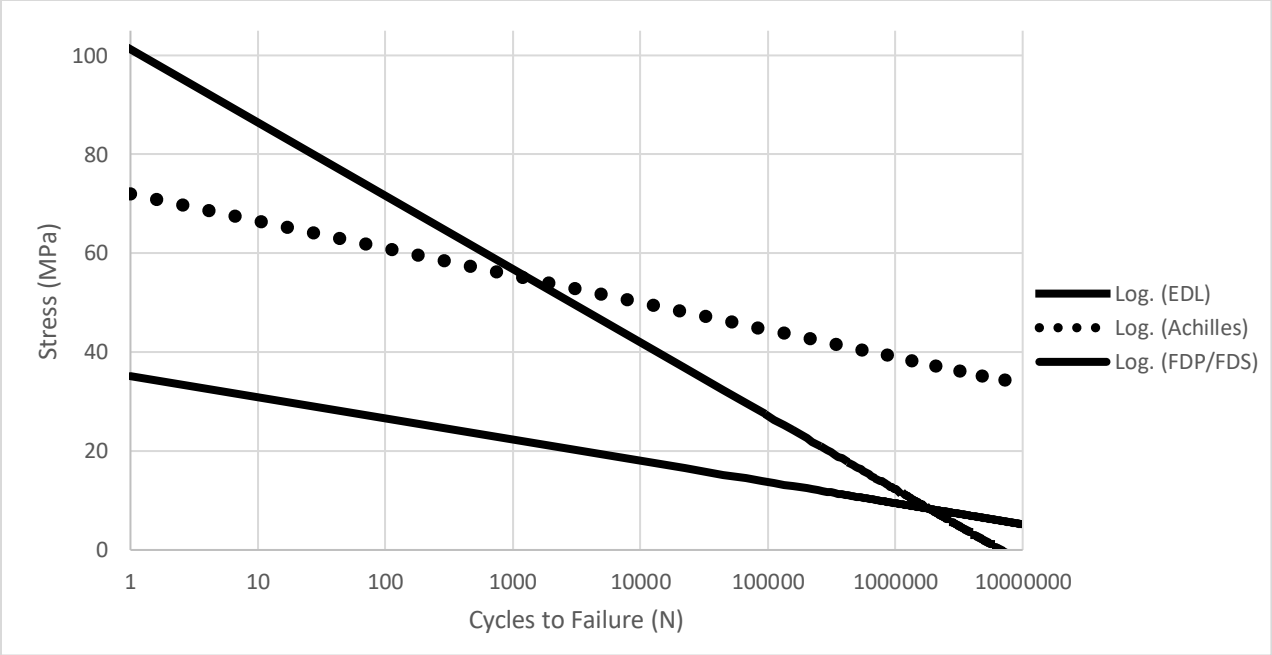


Figure 7. The 'S-N' equations for FDP/FDS, Achilles, and EDL tendon.

Three samples were tested at 20% UTS for this study, but after 24 hours at 4Hz without failure, the subjects were removed and found to be improperly hydrated with the drip system. The Morrow model derived in this study ($N_{63}=2.1864*W^{-3.198}$) was used to estimate the number of cycles until failure had dehydration not occurred. Work per cycle was found during each sample's steady state before dehydration occurred. When including these estimates, the 'S-N' equation changes to S = 33.942 - 1.585*ln(N) (Figure 8). This reduces the slope of the 'S-N' equation, predicting even more cycles until failure at stress levels less than 10 MPa.

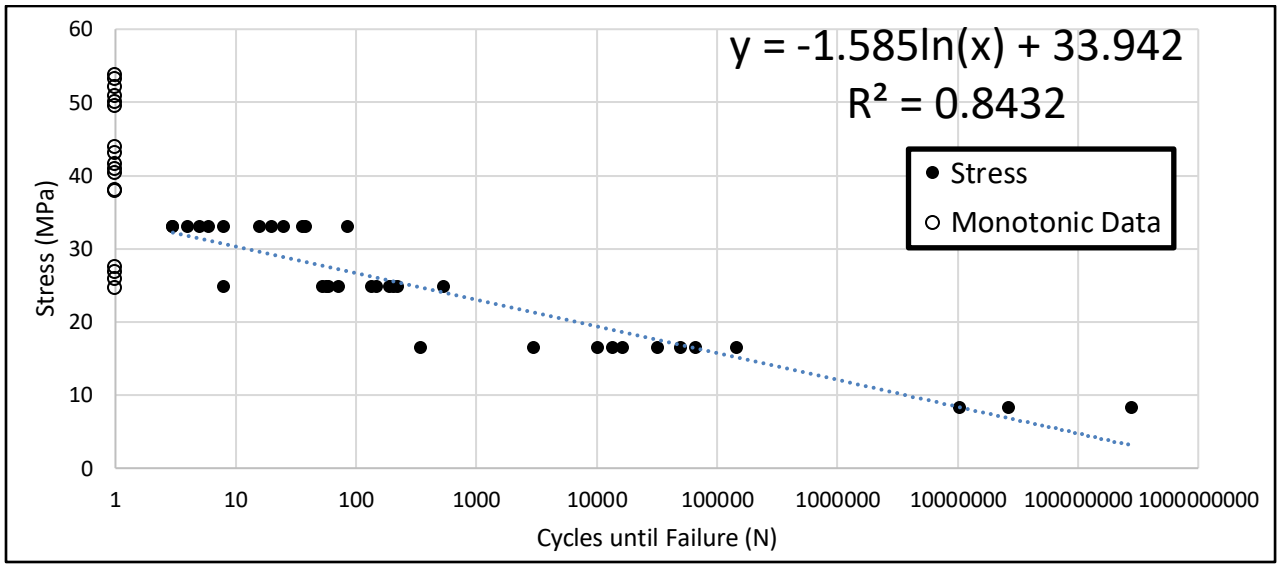


Figure 8. Revised 'S-N' equation including the censored estimates for three samples tested at 20% UTS.

It is important to note potential limitations of relating these *in vitro* results to *in vivo* WMSD development. First, specimens in this study were tested until rupture, while WMSD symptoms are likely to occur well before rupture occurs *in vivo*. This would suggest 'S-N' equations are too liberal to accurately predict risk of WMSD development. On the other hand, *in vivo* tissues have a self-healing component and possible load distribution to surrounding tissues while these *in vitro* samples simply had saline hydration. This healing component hypothesized between 1% UTS per day (Schechtman and Bader, 1997) and 2% to 3% (Kjaer, et al., 2005), would indicate an endurance limit, while these 'S-N' equations do not (Schechtman and Bader, 1997). A final limitation of the current study is the lack of tests with cyclic peak stress less than 40%. These data points could significantly alter the 'S-N' equation to be more conservative or liberal. However, even with these potential limitations, both ergonomics risk assessment tools using cadaveric 'S-N' equations for their risk algorithms, LiFFT, and the aforementioned DUET, have shown highly significant associations between predicting risk with repetitive exertions. Therefore, the results from this study should prove

useful in predicting the risk for CTS and trigger finger during work.

Conclusion

Based on the results of this study, the following conclusions are drawn:

- The 'S-N' equation for FDP/FDS tendons was derived, relating imposed peak stress to expected number of cycles until macroscopic failure ($S = 35.178-1.86*\ln(N)$). While this equation was similarly logarithmic to previously reported tendon 'S-N' equations, it was more conservative. This does provide even further evidence towards using fatigue failure equations as the underlying basis of DUE WMSD ergonomics risk assessment tools.
- A Morrow power model was derived ($y = 2.1864x^{-3.198}$), empowering future studies to estimate characteristic life without destructively testing the material. Some potential studies to utilize this are: testing variable loading patterns; comparing the effects from cyclic compression and/or shear stress; and the effect of vibration on fatigue life.

Chapter IV: The Effect of Duty Cycle (DC) on the *in vitro* Fatigue of Human Flexor Digitorum Tendons

Introduction

In ergonomics risk assessment, DC is the portion of cycle time spent stressing musculoskeletal tissues divided by the total cycle time of the task. DC is commonly evaluated as risk factor when assessing risk of DUE WMSDs. For example, the American Conference for Government Industrial Hygienists (ACGIH) Hand Activity Level threshold limit value (HAL TLV™) utilizes DC as a significant factor in determining risk (Radwin et al., 2014). However, while it makes sense that larger DCs lead to increased injury risk, the evidence supporting this factor has been mixed. One recent multi-site epidemiological study did not observe a significant HR for DC for all hand exertions. However, this study did observe a significant HR of 2.05 for DC when interacting with forceful hand exertions (Harris-Adamson, 2015). Similarly, a meta-analysis on eight existing psychophysical studies established the relationships between frequency, effort duration, DC and maximum acceptable effort (MAE) levels (Potvin et al., 2011). While frequency only revealed a weak correlation with MAE, DC provided a strong relationship ($r^2 = 0.87$). Conversely, a prospective study of wrist tendinosis revealed no significant effect from percent time with any of light pinch, heavy pinch, light power grip, or heavy power grip. Only high peak force exposure showed a significantly increased OR (Harris et al., 2001).

DC itself can be separated into two attributes: an active loading portion (e.g., maintaining a forceful grip) and inactive portion (e.g.., relaxing/resting the tissues). In comparison to creep effects on tissue due to dwell, *in vitro* fatigue studies of human Achilles tendon, rabbit MCL, and wallaby tail tendon all found significantly higher HRs with pure cyclic fatigue than with creep fatigue (Wren et al., 2013; Thornton et al., 2007; Wang et al., 1994). However, these studies did not test human musculoskeletal tissues, nor did they test combinations of cyclic loading and creep loading (also

known as “dwell”). Resting duration, or elastic relaxation for *in vitro* specimens, during cyclic fatigue testing has not been studied.

To address these gaps and to provide data regarding the effects of varying DC in the fatigue loading, the present study tested FDP and FDS tendons, tissues associated with CTS and trigger finger (Freivalds, 2011), *in vitro* using various percentages of DC. These results could provide evidence towards implementing DC or not in ergonomics risk assessment tools which use fatigue failure as their basis, such as DUET. The authors, however, hypothesize this risk to be minimal, similar to the results from previous *in vitro* studies on DC.

Materials and Methods

Specimen Excision

Seventy-one (71) specimens were excised from thawed, whole arm segments from eleven donors (mean age=62.9 ± 9.48). Hepatitis A, Hepatitis B, HIV, and cases of chronic renal, metabolic, or endocrine disease were excluded as these conditions potentially affect the mechanical properties of tendon (Schechtman and Bader, 1997). Rounded edge scalpels were used to remove surrounding muscle and fascia. Specimens were placed in self-sealing, air-tight plastic bags with 20mL of saline. These bags were identified with coded ID labels and placed in a -20°C freezer.

Experimental Procedures

Each specimen was set out to thaw at room temperature for 45 minutes while immersed in the saline solution. Each tendon’s CSA was estimated with the following formula:

$$CSA = \frac{m}{l*\rho} \qquad (5)$$

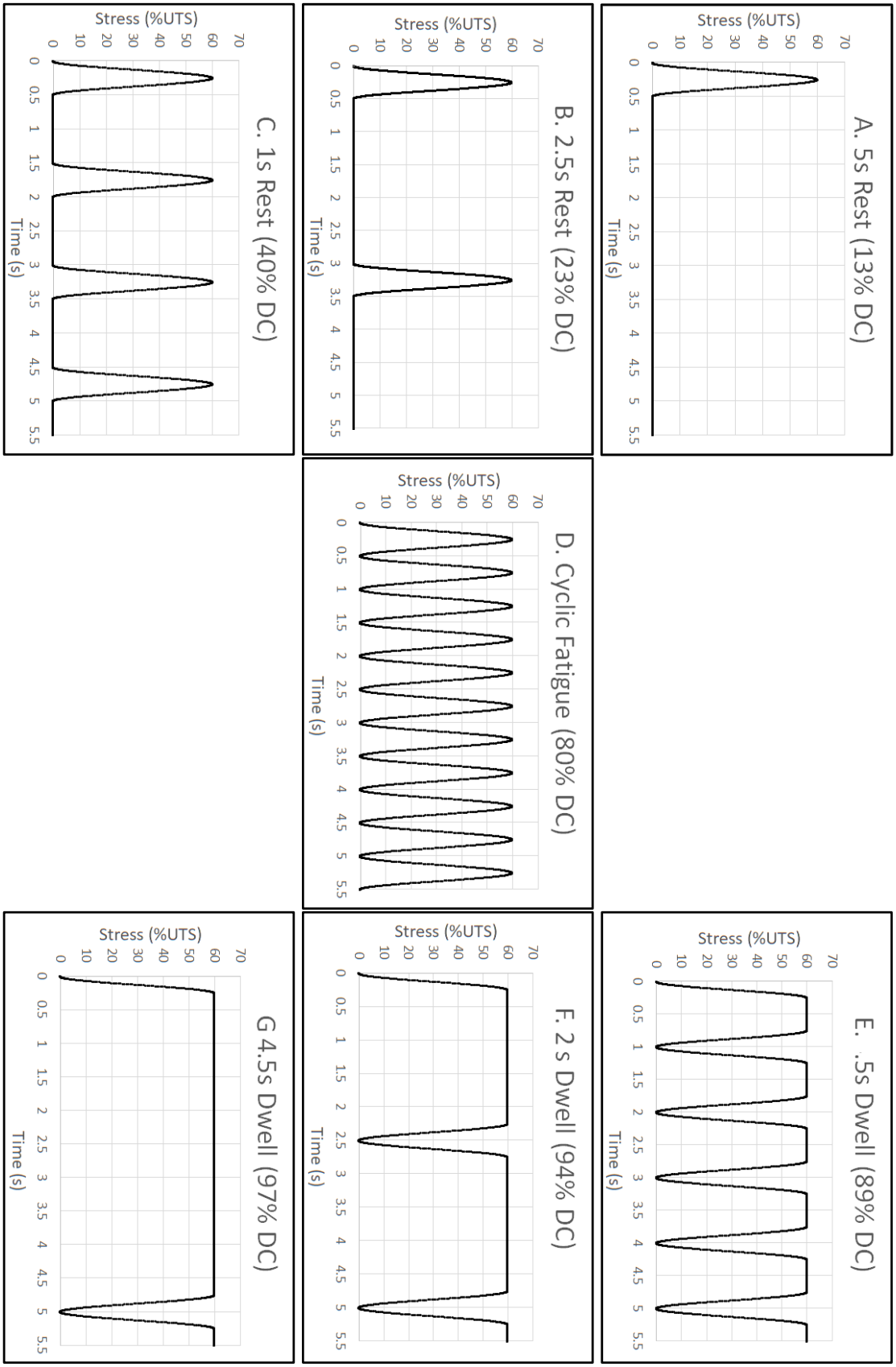
where m is the tendon mass (k(g), l is the tendon length (m), and ρ is tendon density, which was assumed to be 1120 kg/m^3 from previous research (Ker, 1981).

Each tendon's length was measured with electronic digital calipers (accuracy of ± 0.203mm). Then, tendon mass (g) was measured with a digital scale. This estimation is somewhat limited as both FDP and FDS tendons have continuously thinning CSAs from the proximal to the distal end, instead of the constant CSA assumed in this calculation. Sandpaper was wrapped around the distal and proximal ends before clamping. The clamps had ridged surfaces with large surface areas and resistance. A force of 10 Nm of torque was applied to each screw on each pair of clamps, preventing slippage without disrupting the tendon structure between the clamps. Once a non-zero load was established on the tendon, the clamp-to-clamp length was recorded.

Cyclic Fatigue Testing

An ElectroPuls E3000 materials testing device (Instron, Norwood, MA, USA; displacement accuracy <50 μm; ±5 kN load cell) was used for all tendon tests. FDP and FDS tendons were aggregated for fatigue testing, as pilot testing did not reveal a significant difference between their UTS. A sinusoidal wave loading and relaxation pattern at 2 Hz was implemented to simulate the *in vivo* loading pattern of tendon (Komi et al., 1992). Seven DC levels were chosen: 13%, 23%, 40%, 80%, 89%, 94%, and 97%. These each relate to a loading pattern of rest, cycling, and dwell time, shown in Figures 10A-G. Stress below 20% UTS was operationally defined as "rest".

A previous study found the mean UTS for FD tendons to be 41.17 MPa (Smith et al., 2019). This study also reported cyclic fatigue tests with 60% UTS peak cyclic stress having a mean fatigue life of 153.18 ± 44.37 SE cycles. The authors felt this fatigue life at 60% UTS presented enough cycles to reveal any significant effect from DC level, while also providing a feasible testing time. This peak stress was chosen because of the interaction of high force and DC reported in the epidemiological study mentioned previously (Harris-Adamson, 2015). 1% UTS was established as the minimum stress. Specimens were randomly assigned a DC loading pattern. Cycle count, displacement, and load were recorded at 10 Hz.



Figures 10A-G. Loading patterns for each DC level. Ramp and relaxation were sinusoidal at 2 Hz.

Data Analysis

The effect of DC on fatigue life was analyzed with linear regression. Personal characteristics of age, BMI, race, and gender were also included in the regression analysis, as they have historically been sources of variability (Wren et al., 2003). Significant differences between DC levels were determined by Tukey's Honestly Significant Difference. Cox regression and Kaplan-Meier survival analysis were both used to determine any effect DC had on time until failure. As each DC level has a unique cycle time, time until failure may have a different practical application than cycles until failure with respect to DC.

Weibull distribution analysis derived a probability distribution of failure for each DC. These distributions can provide reasonable accuracy predicting failure with relatively small sample sizes (Weibull, 1951). Weibull offers two defining parameters of particular interest: the slope of the line, β, gives insight towards the mechanics of failure; and the characteristic life, α, is the cycle count at which 63.2% of specimens are expected to fail.

Work (J) per cycle was calculated using rectangular integration of the hysteresis loops for each test. Work was compared between test levels in two ways: a) total work until failure; and b) distribution of work per cycle. Work due to dwell was also determined for the test levels involving dwell (DC=0.89, 0.94, and 0.97). Comparing work, rather than cycles, can better reveal any effect dwell time or rest time have on damage accumulation. This was accomplished by subtracting the rectangular integration during relaxation from the integration during ramping.

One-way ANOVA was used to test for a difference between strains to failure at each DC level. In previous fatigue failure studies, strain to failure has been found to be consistent between loading levels, proving the strongest indicator of damage accumulation (Shepherd and Screen, 2013). Type I error rate was set at 0.05.

Results

Fatigue test

All specimens failed macroscopically between the clamps. Anderson-Darling normality tests indicated a need for logarithmic transformation for cycles until failure. Linear regression results did not show DC to be significant predictor of fatigue life (F=0.01; DF=1; p=0.906). Age (F=0.41; DF=1; p=0.526), BMI (F=0.02; DF=1; p=0.902), and gender (F=0.30; DF=1; p=0.587) were also not significant predictors of fatigue life. The pooled fatigue life for all specimens was 115.03 ± 21.78 SE cycles.

Cox regression showed DC to have a significant effect on time until failure, when BMI, sex, and age were included in the model (p=0.035; Table 5). Kaplan-Meier analysis further revealed a distinct relationship between high cycle times and high survival times (Table 6). Specimens with either high rest times or high dwell times had longer survival times. DC level of 0.8, representing normal cyclic loading, had the lowest time until failure.

Table 5. Results from Cox regression.

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)
BMI	.024	.026	.910	1	.340	1.025
Sex	.158	.265	.357	1	.550	1.172
DutyCycle	.874	.413	4.464	1	.035	2.396
Age	.006	.013	.190	1	.663	1.006

Table 6. Kaplan-Meier analysis showing high survival times for high cycle time DC levels and a low survival time for pure cyclic fatigue.

	Mean[a]				Median	
			95% Confidence Interval			
DutyCycle	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error
.13	468.000	183.680	107.987	828.013	181.500	46.800
.23	360.545	149.133	68.244	652.847	69.000	80.921
.40	160.773	60.898	41.412	280.133	61.500	30.552
.80	76.591	22.186	33.106	120.076	67.000	24.772
.89	167.200	120.807	.000	403.982	42.000	19.764
.94	238.750	77.175	87.486	390.014	120.000	22.981
.97	308.750	152.394	10.058	607.442	65.000	81.317
Overall	253.957	47.153	161.538	346.377	77.000	16.733

Weibull analysis was performed at each DC level (Table 7). There is no discernable pattern for characteristic life (alpha parameter) between DC levels, which supports the linear regression model not finding DC a predictor of fatigue life. The beta parameters showed little variability between DC levels. These beta parameters are all within the range found previously for EDL specimens (0.5-1.72) (Gallagher, 2012).

Table 7. Weibull analysis parameters for each DC level.

Test Protocol	**Alpha (or Characteristic Life)**	**Beta (or Shape) Parameter**
0.13DC	96.23	0.7282
0.23DC	88.85	0.6107
0.4DC	100.14	0.8649
0.89DC	89.61	0.6097
0.94DC	103.12	0.9078
0.97DC	51.75	0.6898

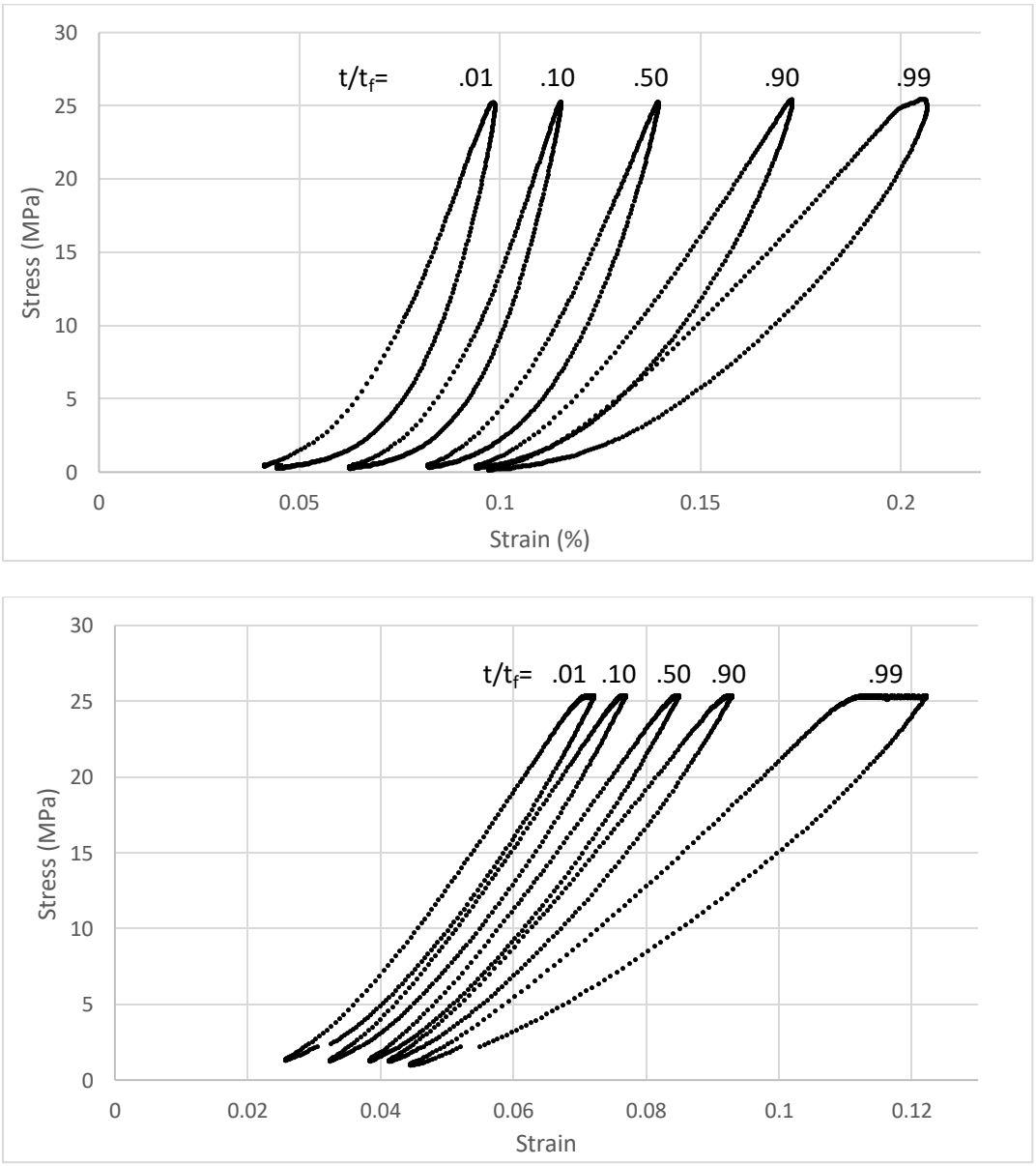


Figure 10A-B. Typical result for hysteresis loops during A) 0.4DC cyclic testing and B) 0.97DC cyclic testing. Cycles shown are at 1%, 10%, 50%, 90%, and 99% of fatigue life.

ANOVA testing revealed DC level to be a significant factor on strain to failure (p=0.012). Tukey's Honestly Significant Difference test further showed 0.4DC was significantly different from both 0.89DC and 0.97DC (Figure 11).

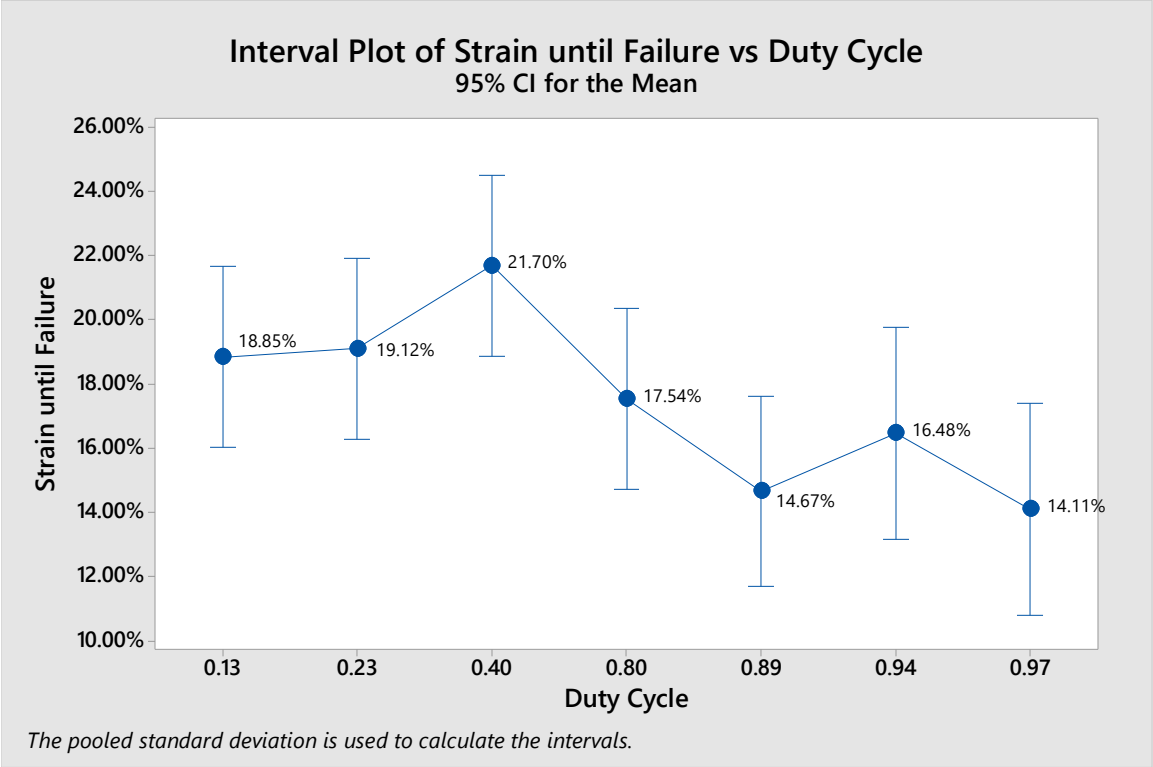


Figure 11. Interval plot results for strain until failure versus DC.

Work per cycle required logarithmic transformation based on results of the Anderson-Darling normality test. Work per cycle was not significantly different between test levels (F=.95; DF=6; p=0.46). Table 8 describes these findings. For the DC levels involving dwell time (DC=0.89, 0.94, and 0.97), significance was not found for DC having an effect on creep work per cycle (F=2.28; DF=2; p=0.125).

Table 8. Work per cycle for all DC levels as well as creep work per cycle for tests with dwell.

DC	Total work (J) per cycle	Creep work (J) per cycle
0.13	0.10 ± 0.06	
0.23	0.13 ± 0.11	-
0.40	0.11 ± 0.08	-
0.80	0.07 ± 0.05	-
0.89	0.08 ± 0.06	0.07 ± 0.04
0.94	0.07 ± 0.03	0.05 ± 0.04
0.97	0.11 ± 0.10	0.08 ± 0.07

Table 9. Full results from all cyclic tests.

Tendon study Number	Age	BMI	Sex	Race	Specimen Type	DC	Cycles Until Failure	Time Until Failure	Strain until Failure	Total Work	Total Cyclic Work
3	73	54.10	M	B	RFDS	0.13	199.00	1094.50	0.23	11.90	11.90
7	74	54.10	M	B	RFDP	0.13	5.00	27.50	0.36	1.02	1.02
15	75	54.10	M	B	LFDP	0.13	24.00	132.00	0.34	1.47	1.47
16	76	54.10	M	B	LFDP	0.13	33.00	181.50	0.36	2.31	2.31
63	56	24.00	M	W	LFDS	0.13	15.00	82.50	0.36	1.36	1.36
98	78	26.37	M	AI	RFDP	0.13	290.00	1595.00	0.31	17.39	17.39
100	78	26.37	M	AI	RFDP	0.13	33.00	181.50	0.21	1.89	1.89
112	65	29.32	F	W	RFDS	0.13	17.00	93.50	0.36	3.23	3.23
114	65	29.32	F	W	RFDP	0.13	14.00	77.00	0.28	1.60	1.60
133	56	29.12	F	W	RFDS	0.13	34.00	187.00	0.42	3.98	3.98
150	56	33.48	F	W	LFDS	0.13	272.00	1496.00	0.22	8.74	8.74
5	71	54.10	M	B	RFDP	0.23	10.00	30.00	0.30	3.42	3.42
9	72	54.10	M	B	LFDS	0.23	23.00	69.00	0.27	2.06	2.06
21	58	37.27	M	W	LFDP	0.23	60.00	180.00	0.50	6.27	6.27
44	46	26.10	M	W	RFDP	0.23	114.00	342.00	0.34	6.60	6.60
68	56	24.00	M	W	LFDP	0.23	251.00	753.00	0.25	10.84	10.84
69	71	39.35	F	B	RFDP	0.23	11.00	33.00	0.31	1.48	1.48
71	71	39.35	F	B	RFDP	0.23	8.00	24.00	0.21	0.89	0.89
89	67	54.57	F	W	LFDS	0.23	482.00	1446.00	0.41	31.05	31.05
95	78	26.37	M	AI	RFDS	0.23	343.00	1029.00	0.35	21.30	21.30
104	78	26.37	M	AI	LFDS	0.23	18.00	54.00	0.21	1.22	1.22
163	78	29.36	M	W	LFDS	0.23	2.00	6.00	0.24	0.72	0.72
11	70	54.10	M	B	LFDS	0.40	224.00	336.00	0.41	15.09	15.09
17	58	37.27	M	W	LFDS	0.40	29.00	43.50	0.32	3.66	3.66
31	61	26.52	F	W	RFDP	0.40	66.00	99.00	0.29	5.40	5.40
32	61	26.52	F	W	RFDP	0.40	32.00	48.00	0.33	3.34	3.34
55	56	24.00	M	W	RFDS	0.40	206.00	309.00	0.34	12.75	12.75
108	78	26.37	M	AI	LFDP	0.40	85.00	127.50	0.42	4.19	4.19
117	65	29.32	F	W	RFDP	0.40	19.00	28.50	0.29	2.10	2.10

126	66	41.76	F	W	RFDS	0.40	446.00	669.00	0.32	20.29	20.29
144	56	29.12	F	W	LFDP	0.40	25.00	37.50	0.27	1.92	1.92
152	56	33.48	F	W	LFDP	0.40	41.00	61.50	0.42	4.28	4.28
156	78	29.36	M	W	RFDS	0.40	6.00	9.00	0.40	2.06	2.06
20	58	37.27	M	W	LFDS	0.80	58.00	29.00	0.30	4.01	4.01
56	56	24.00	M	W	RFDS	0.80	52.00	26.00	0.42	7.33	7.33
59	56	24.00	M	W	RFDP	0.80	541.00	270.50	0.40	25.96	25.96
66	56	24.00	M	W	LFDP	0.80	148.00	74.00	0.29	7.84	7.84
97	78	26.37	M	AI	RFDS	0.80	207.00	103.50	0.25	3.93	3.93
111	65	29.32	F	W	RFDS	0.80	134.00	67.00	0.31	6.26	6.26
116	65	29.32	F	W	RFDP	0.80	71.00	35.50	0.33	4.21	4.21
120	65	29.32	F	W	LFDS	0.80	189.00	94.50	0.20	10.93	10.93
121	65	29.32	F	W	LFDS	0.80	56.00	28.00	0.35	3.03	3.03
154	56	33.48	F	W	LFDP	0.80	222.00	111.00	0.16	8.60	8.60
165	78	29.36	M	W	LFDS	0.80	7.00	3.50	0.13	1.23	1.23
8	68	54.10	M	B	RFDP	0.89	15.00	15.00	0.29	1.84	0.22
12	69	54.10	M	B	LFDS	0.89	5.00	5.00	0.08	0.46	0.10
26	61	26.52	F	W	RFDS	0.89	42.00	42.00	0.30	3.08	0.26
54	46	26.10	M	W	LFDP	0.89	175.00	175.00	0.16	1.78	-0.72
57	56	24.00	M	W	RFDS	0.89	44.00	44.00	0.22	2.43	0.19
61	56	24.00	M	W	RFDP	0.89	19.00	19.00	0.33	1.83	0.35
72	71	39.35	F	B	RFDP	0.89	3.00	3.00	0.18	0.68	0.20
134	56	29.12	F	W	RFDS	0.89	48.00	48.00	0.23	2.28	-0.16
140	56	29.12	F	W	LFDS	0.89	76.00	76.00	0.31	4.74	0.11
148	56	33.48	F	W	LFDS	0.89	1245.00	1245.00	0.31	37.33	-2.43
25	61	26.52	F	W	RFDS	0.94	56.00	140.00	0.34	4.27	0.12
38	61	26.52	F	W	LFDP	0.94	177.00	442.50	0.25	6.98	-1.28
41	46	26.10	M	W	RFDS	0.94	48.00	120.00	0.24	3.50	-0.04
62	56	24.00	M	W	LFDS	0.94	246.00	615.00	0.18	5.81	-1.19
65	56	24.00	M	W	LFDP	0.94	163.00	407.50	0.29	6.85	-1.21
67	56	24.00	M	W	LFDP	0.94	43.00	107.50	0.30	2.96	-0.02
70	71	39.35	F	B	RFDP	0.94	24.00	60.00	0.32	2.55	0.06

142	56	29.12	F	W	LFDS	0.94	7.00	17.50	0.20	0.87	1.03
40	46	26.10	M	W	RFDS	0.97	53.00	265.00	0.27	3.29	-0.36
50	46	26.10	M	W	LFDS	0.97	35.00	175.00	0.11	0.91	-0.38
64	56	24.00	M	W	LFDS	0.97	13.00	65.00	0.20	1.30	-0.05
73	71	39.35	F	B	LFDS	0.97	5.00	25.00	0.36	1.21	0.06
96	78	26.37	M	AI	RFDS	0.97	252.00	1260.00	0.19	6.37	-1.35
101	78	26.37	M	AI	RFDP	0.97	121.00	605.00	0.18	3.67	1.81
149	56	33.48	F	W	LFDS	0.97	12.00	60.00	0.29	1.78	1.26
159	78	29.36	M	W	RFDP	0.97	3.00	15.00	0.24	0.80	0.57

Discussion

This study's main goal was determining the effect DC has on the fatigue life of FD tendons. These are the first results reported on the fatigue failure of cadaveric tissue at varying DC levels. The first major finding is DC did not have a significant effect on fatigue life for specimens tested at 60% UTS. As DC levels had different cycle times, DC level did have a significant effect on survival time. Pure cyclic fatigue had a low survival time, while both rest and dwell increased this time until failure. The second major finding is DC did not have a significant effect on work per cycle, though work due to creep was higher than cyclic work for tests involving dwell. The third major finding is lower DC levels appear to have higher strains to failure, though only one DC level's strain to failure proved significantly different than another level's.

DC level not having an effect on the fatigue life is not altogether surprising. Gallagher and Huangfu (2019) produced a model from Thornton's study of rabbit MCLs that estimated the individual contributions of creep and cyclic loading at different loading levels and DC levels. This model showed creep to have a minority contribution when ligaments were loaded any greater than 20% UTS. A previously mentioned epidemiological study also supports the non-significant effect of DC (Harris et al., 2001). These results are further corroborated by the current study's survival analysis. Both Cox regression and Kaplan-Meier showed pure cyclic fatigue (DC=0.8) to have the lowest time until failure, while DC levels with either rest or dwell had higher times until failure. Therefore, it is not recommended from these results that DC be a risk factor in ergonomics risk assessment tools which utilize fatigue failure as their underlying algorithm.

The contribution of work due to creep was surprising, however. For the DC levels involving dwell, work due to creep was the majority contributor. Work due to creep seemingly caused a steep relaxation equation of each hysteresis loop, evidenced by both total work until failure and work per cycle being non-significant factors with respect to fatigue life. Often this relaxation proved steeper

than the loading equation, resulting in negative cyclic work. In terms of work per cycle, the tendons strained similarly under cyclic versus creep loading.

While the tendons across DC levels accumulated strain per cycle similarly and the fatigue life was not significantly different, lower strains to failure at higher DC levels were noticed. Dwelling appears to be causing significant damage while only mildly increasing strain. Looking at cell morphology throughout the fatigue life could grant more insight into this potential effect. Higher strain to failure at low DC levels could also be due to the longer resting periods, though strain to failure did mildly increase as resting period went down. Providing time for the collagen fibrils to fully re-crimp may allow the tendon to strain more until failure. Each DC level's average strain to failure was higher than previously reported pooled results of EDL tendons (14.2 ± 5.6%) (Schechtman and Bader, 1997). Wren et al. (2003) reported strains as high as 40-50% in Achilles tendon.

One limitation of the current study is the lack of tests at various percentages of UTS. A previous study showed a significantly larger creep effect when cyclic stress was below 50% UTS (Thornton, 2007). Results of various DCs at 60% UTS may not reflect how different DCs would influence results at other force levels. Another limitation is the lack of tissue quality assessments. All specimens were assumed to be in the same condition pre- and post- test. A final limitation is the CSA estimation assuming a uniform density of 1120 Kg/m^3.

Ultimately, this study provides further evidence regarding the relationship between fatigue failure and tendinopathies, corroborating the conclusions reported in a meta-analysis by Shepherd and Screen (2013). In application, these results suggest ergonomics risk assessment tools should not factor DC level, at least at high maximum voluntary contraction (MVC) levels.

Conclusion

Based on the results of this study, the following conclusions are drawn:

- DC level was not a significant predictor of fatigue life (p=0.563) nor work per cycle (p=0.44). Survival analysis corroborated these results by finding a significant effect of DC level on time until failure, as DC levels had different cycle times.
- Higher DC levels appeared to have lower strains-to-failure.
- Future studies should test DC levels at various percentages of UTS, particularly sub-20% UTS.

Chapter V: Concurrent Validation of Extensor Digitorum Longus Tendons and Flexor Digitorum Tendons Fatigue Failure Results Using an Epidemiological Database

Introduction

Several ergonomics risk assessment tools have been created to estimate the risk of DUE MSDs, including the Strain Index, TLV for HAL, and DUET (Gallagher et al., 2018; Moore and Garg, 1995; Radwin et al., 2014). These tools estimate risk by evaluating risk factors such as force, repetition, and posture for individual tasks. A recent prospective study found tasks requiring forceful repetitions had a much higher association with incident CTS than tasks requiring either high force or high repetition alone (Harris-Adamson et al., 2015). This finding, and other recent evidence seem to support the theory that DUE MSDs might develop from a fatigue failure process (Gallagher & Heberger, 2013; Gallagher & Schall, 2017). One recent ergonomics risk assessment tool, DUET, has incorporated fatigue failure techniques in its algorithm for risk estimation. DUET has shown highly significant associations with multiple risk outcomes for DUE MSDs using an epidemiological database (Gallagher et al., 2018; Sesek, unpublished 1999). Also, because DUET utilizes a cumulative damage model based on fatigue failure theory, it is able to assess the combined risk of multiple tasks in a workday.

Currently, the data used in DUET's weighting scheme for damage per cycle (DPC) is from the *in vitro* fatigue of cadaveric EDL tendons of the foot (Schechtman and Bader, 1997), instead of tendons associated with DUE WMSDs. Tendons which experience different *in vivo* stresses have been shown to elicit different fatigue qualities (Pike et al., 2000). A more recent study has disseminated data on the *in vitro* fatigue of the FDP and FDS tendons of the hand and wrist (Smith et al., 2019), whose deterioration has been associated with both CTS and trigger finger (Sampson et al., 1991; Millar, N.L., 2010; Fredberg, U., 2008; D'Addona, A., 2017). It would seem reasonable to expect more accurate associations with DUE health outcomes when using the fatigue failure data

derived from FDP/FDS tendons than data derived from EDL tendons. Accordingly, the primary aim for this study is to calculate the associations with DUE health outcomes with the FDP/FDS fatigue data using a previously reported epidemiological database (Sesek, 1999).

Methods

Epidemiological database

The cross-sectional database that was previously used for DUET's validation has been used in this study for direct comparison. This database has been fully described in Gallagher et al. (2018). Job analyses, historical injury data, and symptom interviews were collected with 1,022 participants across 664 unique jobs (Sesek, 1999). Each job was assessed for five DUE outcomes: injury, pain today, pain past year, pain today plus injury, and pain past year plus injury. Each outcome was binary. For injury, a "1" was given to jobs with a first-time office visit (FTOV) for DUE symptoms occurred in the past year. A "0" was given to jobs not having a FTOV in the past year. Pain for both 'Today' and 'Past Year' were given a 1 if pain was reported greater than 15 mm on a 100 mm visual analog scale (VAS). A 0 was given for pain less than or equal to 15 VAS rating. For the pain plus injury outcomes, a 1 was given if a FTOV had occurred and pain greater than 15 VAS rating was reported. A 0 was given if neither an FTOV nor pain greater than 15 VAS rating were reported. Jobs with either a FTOV or a pain rating greater than 15 VAS were not included for these two outcomes. For age, sex, BMI, and case demographics, as well as ethical considerations, refer to Gallagher et al., 2018.

Exposure Assessment

Jobs consisted of between one and four DUE tasks. Multiple participants of the same job were assessed in some cases. For repetitions, an analysis team classified both grips and deviations by randomly sampling videos of each job. Exertion levels were obtained using the SI exertion scale available in 1998 (1 to 5) (Moore & Garg, 1995). This data was then converted to OMNI-RES. This

conversion was done with the Scale Matching method; SI ratings of 1 to 5 were matched to OMNI-RES ratings of 2, 4, 6, 8, and 10.

The FDP/FDS data resulted in an 'S-N' equation of S = 35.178-1.86*ln(N), relating the cyclic stress (S) to the estimated number of cycles until failure (N) (Smith et al., 2019). Dividing 1 by this N gives the estimated damage per cycle. In order to get an estimate of S for each task, OMNI-RES ratings were multiplied by 10%. For example, OMNI-RES effort rating of 6 was converted to 60% UTS. At 60% UTS, the FDP/FDS equation estimates 1923.5 repetitions could be endured until failure. Dividing 1 by 1923.5 gives 0.00052 damage per repetition. However, the authors of DUET recognized that the internal strain of a tendon during an MVC (suggested to be 6.6%; Kubo et al. 2014) is not equivalent to the strain expected at macroscopic failure (roughly 8-10% strain; Wren et al., 2001). Therefore, for this study, OMNI-RES ratings were similarly scaled 73% before calculating damage per effort. For example, given an OMNI-RES effort rating of 6, instead of using 60% as the effort, 43.8% was used. This is further described in Table 10.

Table 10. OMNI-RES Scale was multiplied by 73% to derive % UTS of each effort. The estimated cycles to failure for a given % UTS was found using the FDP/FDS 'S-N' equation. Finding the reciprocal of estimates cycles to failure gave a damage per cycle estimate.

OMNI-RES Scale	Description	Estimated Percentage of Tendon Ultimate Stress	Estimated Cycles to Failure	Damage per Cycle Estimate
0	very easy	3.60%	79311119	0.00000001
1		7.30%	34853589	0.00000003
2	easy	14.60%	6882169	0.00000015
3		21.90%	1358949	0.00000074
4	somewhat easy	29.20%	268337	0.00000373
5		36.50%	52986	0.00001887
6	somewhat hard	43.80%	10463	0.00009558
7		51.10%	2066	0.00048404
8	hard	58.40%	408	0.00245136
9		65.70%	81	0.01241452
10	very hard	73.00%	16	0.06287123

Cumulative damage (CD) per workday was calculated with Formula 10:

$$CD = \sum DPC_i * n_i * t_i \qquad (10)$$

where DPC is damage per repetition, n is repetitions per minute, t is minutes per workday, and *i* is the number of tasks performed in the job.

Statistical Analyses

To facilitate comparison of results from Gallagher et al. (2018), the same statistics were run for FDP/FDS damage calculations. To summarize, a cut point of 0.03 CD was chosen for a 2x2 contingency table analysis to distinguish high and low risk jobs for all outcomes. This cut point was based on a suggested collagen turnover rate for tendon of 2% to 3% per workday (Kjaer et al., 2005). Above this level, CD would be expected to accrue each day until DUE MSD symptoms revealed themselves. For each outcome, chi-square statistic, odds ratio, accuracy, sensitivity, specificity, and

positive and negative predictive values were derived. Separate analyses were conducted for three definitions of repetition: grips only, deviations only, and grips plus repetitions.

Crude and adjusted odds ratios for the log of the continuous CD were found from binary linear regression for each outcome. Categorical predictors were: site (6), sex, age, and BMI. Age and BMI were dichotomized with cut points of 40 years and BMI >30. This regression also netted the Y' equation:

$$Y' = \beta_0 + \beta_1 \times \text{Log CD} \qquad (6)$$

which allows for the calculation of the probability function of a positive outcome given a log CD value. This function follows:

$$P(\text{outcome}) = \exp(Y') / (1 + \exp(`)), \qquad (7)$$

DUET currently uses this probability function for the DUE outcome Pain Past Year + Injury as the basis for its underlying probability of risk model.

Results

Analysis of a DUET CD Cut Point of 0.03

Table 11 provides the results of odds ratios (OR with 95% CI), accuracy, sensitivity, specificity, and positive and negative predictive values for each outcome given a CD cut point of 0.03 for Smith's FDP/FDS tendon data. All three repetition definitions (grips, deviations, and grips plus deviations) demonstrated significant ORs for all outcomes.

Table 11. Odds ratios (ORs) and related measures for CD>0.03 for each DUE outcome for each repetition definition.

Grips and Deviations	Injury	Pain Today + Injury	Pain Past Year + Injury	Pain Today	Pain Past Year
Chi Square	12.37	16.76	15.68	3.70	5.92
p	<0.000	<0.000	<0.000	0.05	0.02
OR	1.68	2.39	2.16	1.34	1.42
95% CI +	2.27	3.65	3.17	1.82	1.90
95% CI -	1.26	1.56	1.47	0.99	1.07
Accuracy	0.57	0.60	0.60	0.55	0.54
Prevalence	0.38	0.35	0.43	0.33	0.54
Sensitivity	0.54	0.63	0.57	0.50	0.50
Specificity	0.59	0.59	0.62	0.57	0.42
PPV	0.45	0.35	0.53	0.36	0.58
NPV	0.68	0.82	0.66	0.70	0.51
Deviations Only					
Chi Square	13.34	13.28	17.18	3.02	7.15
p	<0.000	<0.000	<0.000	0.08	0.01
OR	1.76	2.20	2.33	1.32	1.51
95% CI	2.39	3.37	3.50	1.81	2.04
95% CI -	1.30	1.44	1.56	0.97	1.11
Accuracy	0.60	0.65	0.62	0.58	0.53
Prevalence	0.38	0.23	0.43	0.33	0.54
Sensitivity	0.42	0.47	0.44	0.38	0.38
Specificity	0.71	0.71	0.75	0.68	0.30
PPV	0.47	0.37	0.56	0.37	0.60
NPV	0.67	0.79	0.64	0.69	0.51
Grips Only					
Chi Square	6.78	6.64	8.53	1.33	3.08
p	0.01	0.01	0.00	0.25	0.08
OR	1.56	1.84	1.90	1.23	1.35
95% CI	2.19	2.91	2.93	1.74	1.89
95% CI -	1.12	1.16	1.23	0.87	0.96
Accuracy	0.60	0.67	0.60	0.61	0.50
Prevalence	0.38	0.23	0.43	0.33	0.54
Sensitivity	0.29	0.33	0.32	0.26	0.26
Specificity	0.79	0.79	0.80	0.77	0.21
PPV	0.46	0.36	0.54	0.36	0.59
NPV	0.65	0.77	0.61	0.68	0.53

Comparing ORs and Related Measures to Results from EDL Validation

For the binary logistic regression of all DUE outcomes versus log CD > 0.03, the EDL 'S-N' equation reported higher ORs for fourteen of the fifteen outcome/repetition definition combinations. Table 12 shows the results of the FDP/FDS, while Table 13 shows those of EDL. The only DUE outcome and repetition definition combination with a higher OR from FDP/FDS validation is the Injury and Grips Only combination.

Table 12. ORs from FDP/FDS 'S-N' equation.

Grips and Deviations	Injury	Pain Today + Injury	Pain Past Year + Injury	Pain Today	Pain Past Year
OR	1.68* (1.26, 2.27)	2.39* (1.56, 3.65)	2.16* (1.47, 3.17)	1.34 (0.99, 1.82)	1.42* (1.07, 1.9)
Deviations Only					
OR	1.76* (1.3, 2.39)	2.20* (1.44, 3.37)	2.33* (1.56, 3.5)	1.32 (0.97, 1.81)	1.51* (1.11, 2.04)
Grips Only					
OR	1.56* (1.12, 2.19)	1.84* (1.16, 2.91)	1.90* (1.23, 2.93)	1.23 (0.87, 1.74)	1.35 (0.96, 1.89)

Table 13. ORs from EDL 'S-N' equation.

Grips and Deviations	Injury	Pain Today + Injury	Pain Past Year + Injury	Pain Today	Pain Past Year
OR	1.70* (1.23, 2.34)	2.59* (1.58, 4.25)	2.27* (1.49, 3.46)	1.57* (1.13, 2.19)	1.5* (1.11, 2.03)
Deviations Only					
OR	1.85* (1.38, 2.49)	2.77* (1.78, 4.3)	2.89* (1.88, 4.11)	1.60* (1.18, 2.17)	1.77* (1.33, 2.36)
Grips Only					
OR	1.49* (1.12, 1.99)	2.57* (1.82, 4.44)	2.00* (1.37, 2.93)	1.58* (1.17, 2.13)	1.43* (1.08, 1.9)

Table 14 similarly shows the associated measures from FDP/FDS results, and Table 15 shows those from the EDL. The FDP/FDS results have a higher accuracy in ten out of 15 outcome/repetition definition combinations.

Table 14. Accuracy and associated measures from FDP/FDS.

Grips and Deviations	Injury	Pain Today + Injury	Pain Past Year + Injury	Pain Today	Pain Past Year
Accuracy	0.57	0.60	0.60	0.55	0.54
Sensitivity	0.38	0.35	0.43	0.33	0.54
Specificity	0.54	0.63	0.57	0.50	0.50
PPV	0.59	0.59	0.62	0.57	0.42
NPV	0.45	0.35	0.53	0.36	0.58
Deviations Only					
Accuracy	0.60	0.65	0.62	0.58	0.53
Sensitivity	0.38	0.23	0.43	0.33	0.54
Specificity	0.42	0.47	0.44	0.38	0.38
PPV	0.71	0.71	0.75	0.68	0.30
NPV	0.47	0.37	0.56	0.37	0.60
Grips Only					
Accuracy	0.60	0.67	0.60	0.61	0.50
Sensitivity	0.38	0.23	0.43	0.33	0.54
Specificity	0.29	0.33	0.32	0.26	0.26
PPV	0.79	0.79	0.80	0.77	0.21
NPV	0.46	0.36	0.54	0.36	0.59

Table 15. Accuracy and associated measures from EDL.

Grips and Deviations	Injury	Pain Today + Injury	Pain Past Year + Injury	Pain Today	Pain Past Year
Accuracy	0.51	0.49	0.56	0.48	0.56
Sensitivity	0.38	0.26	0.42	0.33	0.53
Specificity	0.75	0.81	0.77	0.74	0.72
PPV	0.37	0.38	0.40	0.35	0.37
NPV	0.42	0.32	0.49	0.36	0.56
Deviations Only					
Accuracy	0.56	0.58	0.62	0.54	0.57
Sensitivity	0.38	0.26	0.42	0.42	0.53
Specificity	0.64	0.71	0.67	0.67	0.61
PPV	0.51	0.53	0.58	0.58	0.53
NPV	0.45	0.35	0.54	0.54	0.60
Grips Only					
Accuracy	0.57	0.54	0.60	0.59	0.56
Sensitivity	0.38	0.26	0.42	0.33	0.53
Specificity	0.52	0.65	0.58	0.53	0.50
PPV	0.58	0.59	0.60	0.58	0.59
NPV	0.43	0.35	0.51	0.38	0.58

Association Between log CD Metric and Reported Pain

The log of CD was a significant predictor of VAS pain rating for both today and past year. Pain Today's linear regression was significant (F-value = 6.56; p=0.011; R^2=0.84%):

Average discomfort today = 18.64 + 1.841 * Log CD (8)

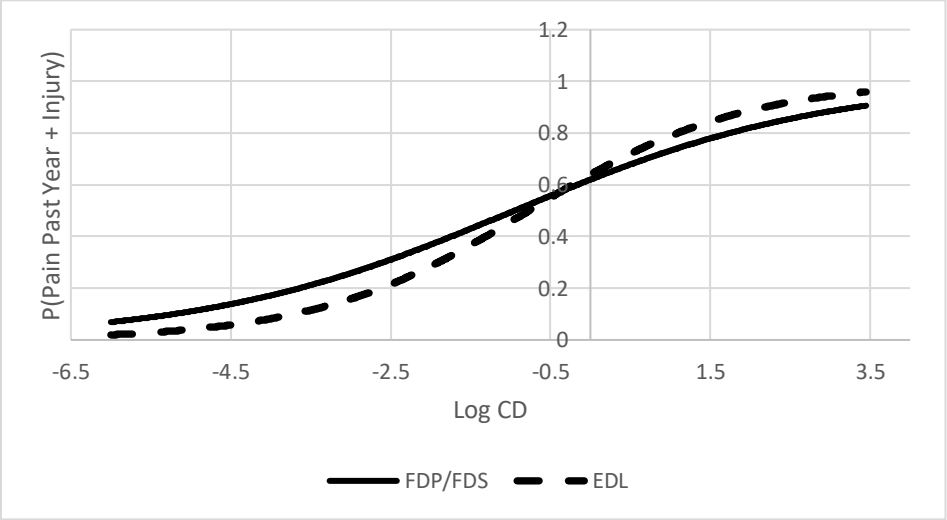
And for Pain Past Year, linear regression was again significant (F-value=16.42; p<0.000; R^2=2.09%):

Average discomfort past year = 46.47 + 4.75 * LogCD (9)

The probability functions of DUE outcomes versus the continuous log CD metric were noticeably different between 'S-N' equation results. For example, Figure 12 shows the probability functions for Pain Past Year + Injury versus the continuous log CD metric for both results. The FDP/FDS probability function is a more gradual function than that reported for EDL, with an outcome probability of 10% at a log CD value = -5.0 and a probability of 90% at a log CD = 3.2

compared to EDL's 10% probability at log CD = -3.7 and 90% probability at log CD = 2.18. This infers a weaker dose-response relationship than that reported with the EDL data.

Figure 12. Probability functions for P(Pain Past Year + Injury) versus Log CD for FDP/FDS results and EDL results.



Discussion

Analyzing the database using the FDP/FDS 'S-N' damage model proved a quality predictor for all DUE outcomes regardless of repetition definition except for the Pain Today outcome. The highest OR (2.39) was for the DUE outcome of Injury + Pain Today when repetitions were defined as grips and deviations. This provides further evidence linking fatigue failure of the tendon with tendinopathies, reinforcing the conclusions shared in the meta-analysis performed by Shepherd and Screen (2013). This meta-analysis discussed biopsies from tendons with tendinopathies showed matrix degradation similar to the degradation seen in *in vitro* fatigue failure tests. In application, the evidence indicates that fatigue failure is an accurate underlying basis for predicting WMSDs using ergonomics risk assessment tools.

Comparing the EDL damage equation with that of FDP/FDS, the EDL equation is clearly more conservative than the FDP/FDS 'S-N' equation, allowing fewer cycles until failure at each % UTS and ultimately classifying more jobs as Risky. The FDP/FDS equation showed a slightly higher accuracy for all DUE outcomes except Pain Past Year for all repetition definitions. However, the FDP/FDS equation resulted in a higher OR for only 1 of the 15 outcome/repetition definition combinations (Injury and Grips Only). One potential reason for this is the scarcity of stress levels tested for FDP/FDS, specifically at low stress levels. Schechtman and Bader (1998) tested at 10% UTS increments from 10-90%, while Smith (2019) only tested 40%, 60%, and 80%. Ultimately, using the FDP/FDS equation as the underlying basis will decrease the number of safe jobs previously considered risky (Type II error) at the cost of increasingly calling risky jobs safe (Type I error).

Conclusions

Based on the results of this study, the following conclusions are drawn:

- The FDP/FDS 'S-N' equation reported a higher OR for only 1 of 15 DUE outcome and repetition definition combinations.
- The FDP/FDS 'S-N' equation is more liberal than that of the EDL data, meaning more jobs were considered safe. This ultimately caused a higher accuracy for most DUE outcomes and repetition definition combinations.
- The probability functions for all DUE outcomes versus log CD for FDP/FDS data were more gradual functions, inferring a weaker dose-response relationship.

Chapter VI: Conclusion

The primary purpose of this dissertation was to study the *in vitro* fatigue failure of cadaveric FDP and FDS. Using *in vitro* fatigue failure models, or 'S-N' equations, to relate stress and repetitions required for occupational tasks to cause cumulative damage, and ultimately increase WMSD risk, has proved successful with LiFFT and DUET. DUET, however, uses an 'S-N' equation derived from the EDL instead of biotissue of the DUE. Therefore, this study derived the 'S-N' equation for FDP and FDS, resulting in:

$$S = 35.178\text{-}1.86*\ln(N) \quad (1)$$

This model furthers the evidence of stress or force being the dominant factor on tissue degradation, with lowering stress allowing an exponentially increasing number of cycles until failure. A serious limitation of this study, as with any *in vitro* biotissue study, is the lack of simulated recovery. While this has been estimated in various ways, the true effect this has in conjunction with cyclic stress is still not understood. A similar limitation is the lack of a temperature and hydration-controlled testing chamber to simulate the environmental conditions *in vivo*.

Alongside this model, a Morrow power model was derived:

$$y = 2.1864x^{-3.198} \quad (2)$$

With this model, future research can cyclically fatigue the tissue until steady state work is achieved, typically no more than $t/t_f = 0.1$, and then estimate the characteristic life. This leaves the remainder of the true fatigue life to be studied under a multitude of different loading conditions such as variable stresses, vibration, compression, or environmental variations.

Following this derivation, another gap in the literature targeted by this dissertation was the effect DC has on the *in vitro* fatigue failure of biotissue. DC level was not a significant predictor of fatigue life nor of work per cycle at 60% UTS cyclic stress. Interestingly, higher DC levels visually trended to have lower strains-to-failure. The immediate impact is it appears ergonomics assessment

tools utilizing fatigue failure as the underlying algorithm should use repetitions as the limiting factor rather than duty cycle. Future research should certainly test the effect of DC at various levels of UTS.

The secondary aim of this dissertation was to test the predictive ability of the derived FDP/FDS 'S-N' equation using a pre-existing automotive epidemiological database and compare these results with the validation reported previously using the EDL 'S-N' equation. The FDP/FDS 'S-N' equation reported a higher OR for only 1 of 15 DUE outcome and repetition definition combinations. The FDP/FDS 'S-N' equation was more liberal than that of the EDL data, meaning more jobs were considered safe. This ultimately caused a higher accuracy for 10 of the 15 DUE outcomes and repetition definition combinations. The probability functions for all DUE outcomes versus log CD for FDP/FDS data were more gradual functions, inferring a weaker dose-response relationship. To this end, the FDP/FDS 'S-N' equation proved a quality predictor of most DUE outcomes. However, future research is encouraged to test these tissues at stress levels below 40% UTS. This would greatly increase confidence of assessing low-force tasks with this equation.

Other suggested future projects are: studying the fatigue failure of FDP and FDS under cyclic compression, as this has also been hypothesized to be a significant source of damage *in vivo*; study the fatigue failure of FDP and FDS under variable loading, as LiFFT and DUET currently assess the cumulative risk of multiple tasks, but there is no supporting evidence on this summation of dose; and studying fatigue failure of biotissue under vibration.

Cadaveric tissue testing can provide valuable insight on the mechanical properties and degradation of tissues affected by WMSDs. Though there are limitations to using these results for direct application in assessing *in vivo* degradation, doing so has currently proved the most accurate methodology, as well as providing a vehicle for assessing the cumulative risk of multiple tasks.

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