THE PENNSYLVANIA STATE UNIVERSITY
SCHREYER HONORS COLLEGE

DEPARTMENT OF MECHANICAL ENGINEERING

SHEAR WAVE ELASTOGRAPHY OF THE ANTERIOR CRUCIATE LIGAMENT

RACHEL HELLER
SPRING 2020

A thesis
submitted in partial fulfillment
of the requirements
for a baccalaureate degree
in Mechanical Engineering
with honors in Mechanical Engineering

Reviewed and approved* by the following:

Daniel Cortes
Professor of Mechanical Engineering
Thesis Supervisor

Anne Martin
Professor of Mechanical Engineering
Honors Adviser

* Electronic approvals on file.

ABSTRACT

Understanding the structural integrity of the Anterior Cruciate Ligament (ACL) could provide a quantitative method for monitoring risk of injury as well as rehabilitation after surgical reconstruction. The goal of this study is to develop and assess a protocol for evaluating the stiffness of the ACL *in vivo.* The objective is to optimize Shear Wave Elastography for screening of the ACL and to collect preliminary data of its shear modulus to determine feasibility of the method. Location of the ACL within ultrasound imaging was verified with Penn State Hershey Medical Center to be 13 millimeter inferior to the tibia plateau. B-mode imaging of a human subject was optimal using an L7-4 transducer at 5.2 MHz, tilted approximately 30 degrees against the knee bent at 120 degrees flexion. This quality was concluded to be sufficient to enable accurate selection within a Region of Interest for elastograghy measurements. Using this protocol, the shear modulus of the ACL (average ± SD) was found to be 95.68 ± 11.48 and 99.99 kPa ± 16.02 kPa for the left and right leg, respectively. The values reported were consistent with a similar study of the Ulnar Collateral Ligament.

Shear Wave Elastography was deemed feasible for quantifying the stiffness of the ACL, suggesting its future importance in preventing injury as well as understanding rehabilitation.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

ACKNOWLEDGEMENTS

First and foremost, I’d like to thank Dr. Daniel Cortes for all of the time and energy he has devoted to bringing this study together. He helped me at every stage, from teaching me the methods and equipment, to guiding my literature review, to connecting me with a team at Hershey, to gathering and interpreting data. He consistently gave me valuable feedback to help me tell the story of this project.

I would also like to thank the team at Penn State Hershey Medical Center. Without their contribution, this project could not have proceeded with the confidence necessary for data collection. I am extremely grateful to have had the chance to delve into the world of biomechanics. It has given me unique exposure to the medical field and its incredible people, technology, and insights.

Thank you to Seyedali Sadeghi and Gabi Schwartz for welcoming me into the Biomechanics and Imaging Lab and answering my numerous questions from the beginning. I wish them both the best and hope that they go onto accomplish great things.

Lastly, I’d like to thank Dr. Anne Martin. She has helped me and many other undergraduates throughout this whole process, from selection of our research, to the formulation of our literature reviews, to the final product, and I know that her insight has helped my thesis reach its full potential.

Though the data collection for this study was abruptly cut short, I sincerely hope that the findings facilitate more quantitative studies to help address the prevalence of ACL injury, which has affected many of my sports teammates and closest friends.

Chapter 1

Introduction

Pathology

A torn Anterior Cruciate Ligament (ACL) is one of the most common injuries sustained by young athletes, and arguably the most devastating. There are as many as 250,000 ACL injuries in the United States each year [1]. Injuries range from partial tears to complete tears, or ruptures. Although the torn ACL can be left untreated, most individuals opt for surgical reconstruction. Approximately 130,000 to 175,000 ACL reconstructions (ACLRs) are performed annually in the US [2,3]. Between 1994 and 2006, the rate of ACLRs per 1,000 capita increased by 37% [2]. This trend may be due to an increased incidence rate, increased preference for surgical treatment, or most likely a combination of both. Surgical treatment is both prevalent and costly. An estimated $2 billion is spent on ACL reconstruction each year [3], with a single operation costing around $9,000 to $13,000. Total preoperative and postoperative treatment will amount to a healthcare utilization cost between $13,000 and $17,000 [4]. Even non-surgical treatment may cost over $2,000 [3].

Due to the widespread and costly nature of ACL injury, extensive research has endeavored to better understand its mechanisms. Studies over the years have focused on a wide variety of external and internal risk factors, including gender, age, knee kinetics and kinematics, and athletic participation. Many results are indicative yet obscure. The strongest risk factors for

ACL injury have been proven through time and repeatability. Gender has been studied most extensively. The incidence of ACL injury is 2-8 times higher for females than for males participating in the same sport [5]. Most women tear their ACL in their late teens or early twenties, while men typically tear their ACL in their mid to late twenties [6]. In either case, ACL injury primarily affects the adolescent and young adult demographic, which may be attributed to the high sports participation rate of this age group.

Young athletes are the most susceptible to ACL rupture, and certain sports pose a higher risk than others. Athletes of soccer, football, and basketball in particular exhibit the highest ACL injury rates [7]. This trend is unsurprising, considering that these sports frequently involve the maneuvers associated with ACL rupture. ACL injury often occurs during a cutting, pivoting, or landing motion. These injuries are defined as “non-contact,” indicating that the individual performed a distinct action which produced sufficient ACL loading to cause tearing or rupture without additional force [5]. Most ACL injuries are non-contact [8], even in football, which is a high-contact sport [9].

Rehabilitation after ACL injury is a long process for both nonsurgical and surgical treatment methods. Nonsurgical recovery may involve 3-7 months of rehabilitation and prevent the individual from ever returning to high-level sports [10]. Young athletes often elect for surgical reconstruction in order to return to their original activities. ACL reconstruction involves installing a graft, typically from the patient’s patellar tendon or hamstring tendon, as a replacement ligament. This graft attaches the femur and the tibia via a bone tunnel, illustrated in Figure 1. Post-ACLR athletes are typically cleared to return to sport after a minimum 6-month recovery period [11]. Even once these individuals are able to achieve their pre-surgery fitness and performance levels, they are at risk for re-injury and future complications.

Figure 1. Reconstructed ACL with graft fixed into femoral and tibial bone tunnels [12].

There have been many studies of repeat ACL injuries after reconstruction. The total secondary ACL injury rate is about 15%, yet athletes under 25 years of age who return to their original sport have a 23% re-injury rate. These athletes are at a 30-40 times greater risk for ACL injury than other young, uninjured athletes [13]. A majority of athletes do return to sport without re-injury, but many will experience some degree of osteoarthritis in their injured knee.

Osteoarthritis (OA) is a condition involving the degeneration of articular cartilage and subchondral bone [14]. One study estimated that 79% of individuals who undergo ACL reconstruction will develop OA within 12 years post-operation [15]. Another study reported OA rates of 61% and 40% after 20 years for patellar tendon and hamstring tendon grafts, respectively [16]. Most research indicates, though, that osteoarthritis development is more likely if the ACL is treated without surgery. A six-study meta-analysis reported that a surgically reconstructed ACL has a 3.62 relative risk of OA compared with an uninjured knee, while an ACL treated non-operatively has a relative risk of 4.98 [17]. Individuals who tear their ACL are clearly prone to osteoarthritis, but ACLR may help to reduce the risk of OA development. Osteoarthritis is common after both treatments, however, and will typically develop in the patellofemoral joint. Patellofemoral OA is diagnosed with radiographic assessment, as shown in Figure 2, and is associated with anterior knee pain and decreased functionality [18]. Even individuals without radiographic evidence of arthritis in the years following ACL injury often report pain during specific actions, such as turning, twisting, and kneeling [16,19].

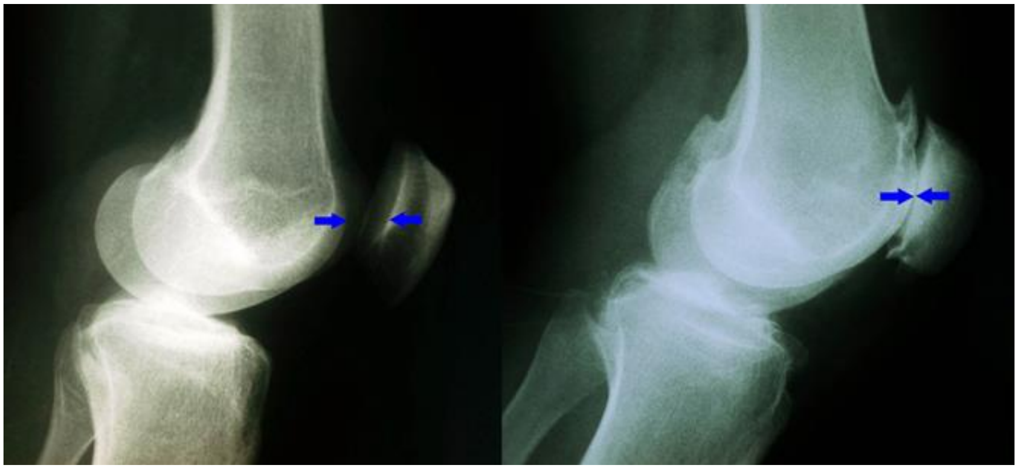

Figure 2. Radiographic comparison of a normal knee (left) and a knee with patellofemoral osteoarthritis (right) [20].

The treatment method of a torn ACL greatly influences the impact of the injury on an individual, but certain long-term effects are often inevitable. Non-operative treatment places lifelong limitations on physical activity and poses a higher risk of osteoarthritis development. This method is rarely practical for young, active individuals, and surgical reconstruction is typically selected. ACLR is very successful in enabling return to sport for young athletes devastated by a torn ACL. Yet these athletes are at high risk for re-injury, and still susceptible to osteoarthritis and painful conditions later in life. In order to avoid the restrictions of conservative ACL treatment, and the potential complications following surgical reconstruction, ACL injury should be, ideally, prevented altogether. Certain studies have validated the effectiveness of plyometric training in ACL injury prevention [21], yet incidence rates have by no means diminished. Repeat studies since the mid-1990s have indicated that the ACL injury rate has been relatively constant for soccer and basketball in particular [22,23,24]. Given the emphasis placed on athletics in U.S. society, it is unlikely that participation in recreational sports is going to diminish. ACL injury rates will remain high, and because this injury primarily affects adolescents and young adults, most of the afflicted will continue to elect for surgical reconstruction. Evidence of the complications following ACLR has already been presented. Yet statistical data can only offer so much insight into the effectiveness of a reconstructed ACL. Greater understanding of the biomechanics of the ACL is necessary to truly assess ACLR's ability to restore a torn ACL.

Functionality and Biomechanics of the ACL

Because ACL injuries are primarily non-contact, understanding the biomechanics of the knee and the ACL is crucial. The knee joint is almost always in a state of loading. Even if an external force is not acting on the knee, internal forces and moments are constantly responding to human movement. Stability is maintained by four main ligaments: the MCL, the LCL, the PCL, and the ACL. The ACL exists in the knee joint as a multitude of fascicles connected to the femur and the tibia [25]. At any point over a range of motion, different fascicles will be activated and tense. The tension in these fascicles serves to limit tibial motion with respect to the femur. When the knee is in a state of loading, caused by external force or human movement, the ACL restrains both tibial translation and rotation. The spatial relationship of these forces and motions is represented in Figure 3. In this way, the ACL stabilizes the knee throughout all of its functions and loading.

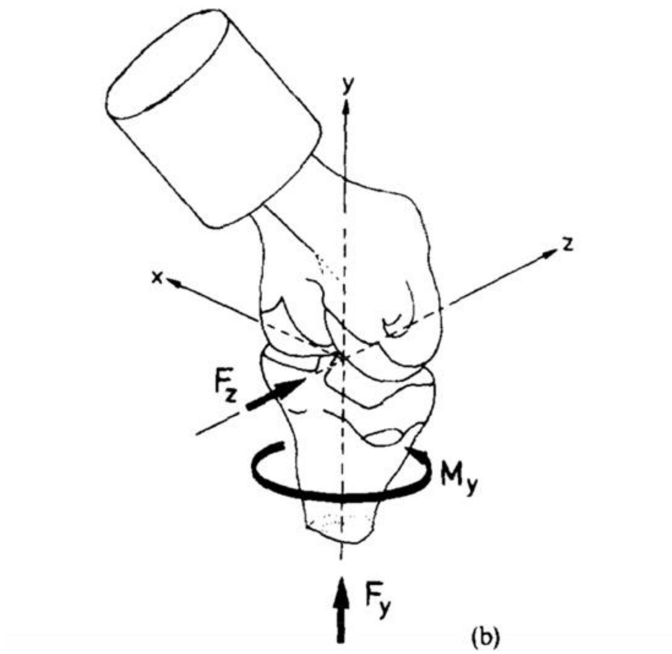

Figure 3. With applied loading, tibial translation will occur on the x-z plane. Tibial rotation will occur around the y-axis [10].

Certain actions and their resultant knee loading conditions are particularly dangerous to the ACL. Anterior tibial shear force and internal knee torque result in the highest force and strain on the ACL, based on both *in vitro* and *in vivo* studies [26,27]. The knee experiences these loads at greatest magnitude during landing, pivoting, and sidestep cutting tasks. Landing motions, especially at low angles of knee flexion, generate large quadriceps forces, which in turn produce high anterior tibial shear force [28]. Pivoting and cutting tasks have been found to produce the greatest internal knee moments [29]. These actions generate the forces proven to cause the highest force and strain on the ACL. Non-contact ACL injuries frequently occur during landing, pivoting, and cutting, because the ACL is biomechanically vulnerable during these maneuvers.

However, an athlete may execute these actions repeatedly without injury. The ACL is typically able to maintain knee stability without failure. Rupture occurs when the resultant ACL loading surpasses what the ligament can withstand. This critical state can be better understood with the properties of the ACL. Measuring ACL properties could offer insight into the ligament's response to ordinary and athletic motion.

Understanding the properties of the ACL is essential in predicting its behavior. There is limited research regarding the ACL's mechanical properties, which are nonlinear, site-dependent, and viscoelastic [30]. Because of these non-uniform qualities, it is difficult to characterize the entire ligament. One study was able to quantify the strength and strain at failure of various bundles of fascicles. Though the strength varied among the different bundles, the strain at failure was roughly the same [31]. This consistency indicates that a critical level of strain is sufficient to cause rupture of the entire ACL. Other studies have focused on ACL deformation when the entire femur-ACL-tibia complex is subjected to tensile loading. The slope of the load-elongation curve can be used to quantify the "stiffness" of the ACL. The stiffness of the ligament has been shown to decrease with age, yet young individuals have a linear stiffness of about 242 N/mm, as plotted in Figure 4.

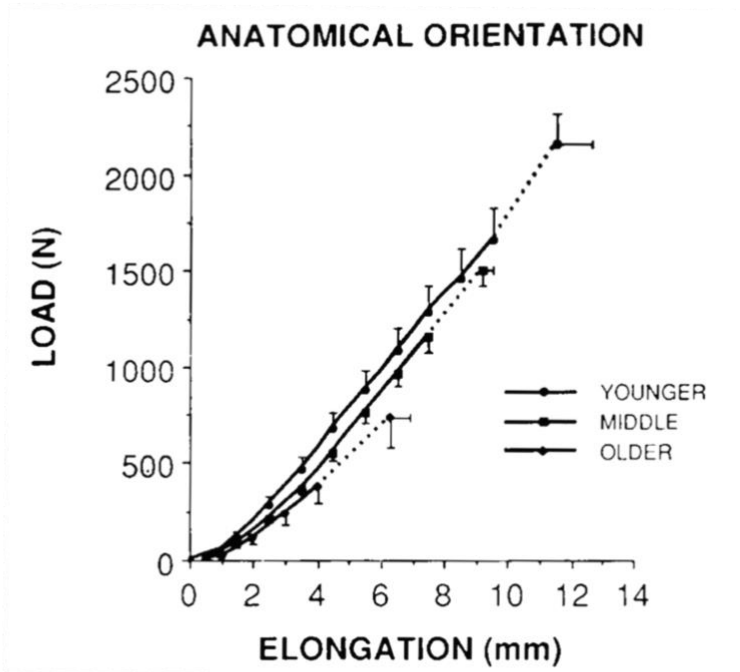

Figure 4. Stiffness data from three different age groups at 30° of knee flexion [32].

Young's modulus has also been used to describe the stiffness of the ACL. The reported modulus values are 283.1 MPa, 285.9 MPa, and 154.9 MPa for the anteromedial, anterolateral, and posterior bundles, respectively [30]. Tensile tests are involved in collection of linear stiffness as well as Young's modulus; these methods are clearly unsuitable for assessing the stiffness of a living ACL due to their invasive nature. Furthermore, an ACL is subjected to very limited tensile loading in ordinary functionality compared to shear forces and internal moments. The stiffness data generated by a load-elongation curve are not wholly representative of the ligament's response to loading *in vivo.*

The shear modulus of the ACL can also be used to characterize its stiffness. The shear modulus is defined as the ratio of shear stress to shear strain for a material under shear loading conditions. The ACL experiences shear loading when a shear force or torque is applied to the knee. Because the ACL is more likely to experience shear forces and torsion than tensile forces, especially during non-contact maneuvers, the shear modulus is particularly valuable as a gage of ligament stiffness. As mentioned previously, anterior tibial shear forces and internal knee moments pose the highest risk of ACL injury. The shear modulus defines how these loads may exert the ACL to a potentially critical state.

There is currently no existing literature on the shear modulus of the ACL. The slope of the load-elongation curve provides a general indication of the ligament's stiffness. However, actual ACL stiffness is different for every individual at any given moment. Because the ACL is comprised of living tissue, its properties can continuously change and adapt. Measuring the true stiffness of an individual ACL *in vivo* could offer insight into the ligament's response to loading after periods of activity and rest. Furthermore, stiffness measurements could be used post-reconstruction to evaluate the success of ACLR. Comparing stiffness of a patient's reconstructed knee to their uninjured knee could serve as a valuable gauge for recovery. Rehabilitation could be tailored to specifically to each patient's unique biomechanics, potentially diminishing re-injury rates for athletes who return to their sport. Clearly, measuring ACL properties such as stiffness *in vivo* would be highly valuable in ACL injury treatment. This measurement can be achieved with noninvasive, continuous Shear Wave Elastography.

Chapter 2

Methods

Shear Wave Elastography

Shear Wave Elastography (SWE) is an imaging technique with the ability to measure the viscoelastic properties of biological tissue; specifically, the shear modulus. The SWE method transmits ultrasonic bursts, which cause the displacement of a focal point within the field of view of the transducer. This displacement, often called a "push pulse," generates shear waves which propagate through the biological tissue of interest, as shown in Figure 5. Ultrasound plane wave imaging is used to track displacements in the tissue as a result of these push pulses.

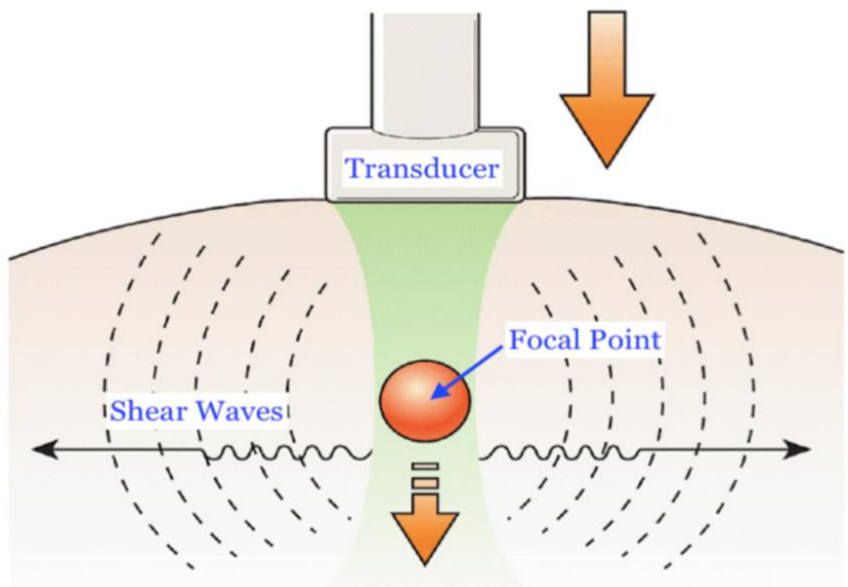

Figure 5. Schematic of shear wave propagation [32].

The speed of the shear waves through the tissue is calculated from the displacement measurements [34]. This shear wave speed is directly proportional to its shear modulus through the following simplified relation:

$$\mu = \rho c^2$$

where μ is the shear modulus, ρ is the density of the medium, and c is the shear wave speed [35]. The density of most living tissue can be approximated as that of water, about 1000 $\frac{kg}{m^3}$. Thus, the square of shear wave speed, measured in units of $\frac{m}{s}$, approximates the shear modulus in units of 1000 $\frac{N}{m^2}$ = 1 $\frac{kN}{m^2}$ or kPa. A larger shear wave speed indicates a higher shear modulus, and thus a higher stiffness in shear.

SWE has already achieved success evaluating several muscles and tendons, including the vastus lateralis and vastus medialis obliquus muscles of the leg, and the Achilles tendon [36,37]. Because SWE is entirely noninvasive, changes in the properties of living tissue can be observed *in vivo.* One study used SWE to measure the stiffness of various leg muscles before and after a running competition [38]. The data showed a diminished stiffness in the majority of muscles, and demonstrated SWE's capability of evaluating athletes over time. SWE has also measured shear wave speeds for an Achilles tendon afflicted with tendonopathy that were significantly lower than healthy tendons [39]. These results indicate that SWE has the capability to identify inadequate tendons with diminished stiffness.

Only recently has SWE been used to evaluate ligaments. One study on the Ulnar Collateral Ligament (UCL) of the elbow joint demonstrated SWE's repeatability of ligament measurements [40]. Preliminary data also compared a partially torn UCL and the healthy UCL of a collegiate baseball pitcher. The shear wave speed of the injured UCL was 79% lower than that of the uninjured UCL. This study is significant in that it both proves SWE's reliability and validates SWE as a potential method for evaluating the stiffness of ligaments. Due to its novelty, the method must be optimized for other ligaments, such as the ACL. The objective of the present study is to optimize SWE for screening of the ACL and measurement of its shear modulus through calculation of shear wave speed.

Ultrasound System

Shear Wave Elastography is achieved in this study through the use of a Verasonics Vantage 128 ultrasound system (version 3.07; Verasonics, Kirkland, Washington). The system runs through MATLAB and is used with a curved or linear array transducer. This transducer is held against the subject's skin as the system generates a real-time B-mode image, within which the user isolates a region of interest (ROI) for measurement. The user interface is shown in Figure 6. Push pulses are emitted through the transducer at a selected frequency. Propagation through the ROI is then calculated and returned to the user as a shear wave speed, in m/s.

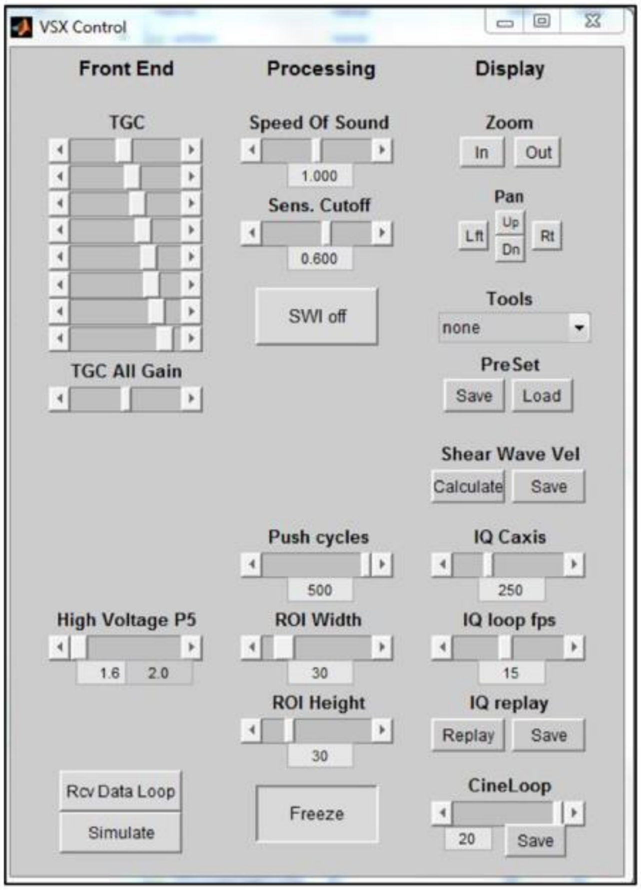

Figure 6. Verasonics control panel within MATLAB

The system enables the user to customize several settings of the process within MATLAB, such as frequency, number of angles, and angle range. Once the code is run, a control panel also allows the user to alter voltage, gain, and the ROI. Because Shear Wave Elastography has not been applied to the ACL, this customization is essential in optimizing the process for the ligament.

Different transducers can also be used with the Verasonics system for different ranges of frequency. For the present study, L6-3, L7-4, and C5-2 transducers were available.

Ultrasound Verification: Cadaveric Knee

Before measuring the ACL's shear wave speed, it is essential to ensure that the ligament is properly identified within B-mode imaging. Proper ACL identification and imaging ensures that the shear wave speed data collected through SWE is truly that of the ACL, and not nearby tissue. The first step in the development of the SWE measurement process for the ACL was to confirm the ligament's location with Penn State Hershey Medical Center.

A right, cadaveric knee was used to mark the ACL with three metal pins along the length of the ligament. An experienced orthopedic surgeon conducted the insertion (Figure 7). Using multiple incisions, for knee arthroscopy as well as for surgical tools, the surgeon placed the three pins proximally, medially, and distally from the tibial attachment. A schematic of the pins' location on the ACL can be seen in Figure 8. The proximal pin made contact with the tibia upon placement. A Siemens ultrasound system, with a 6C1 transducer, was used at a frequency of 4.00 MHz to image the ACL.

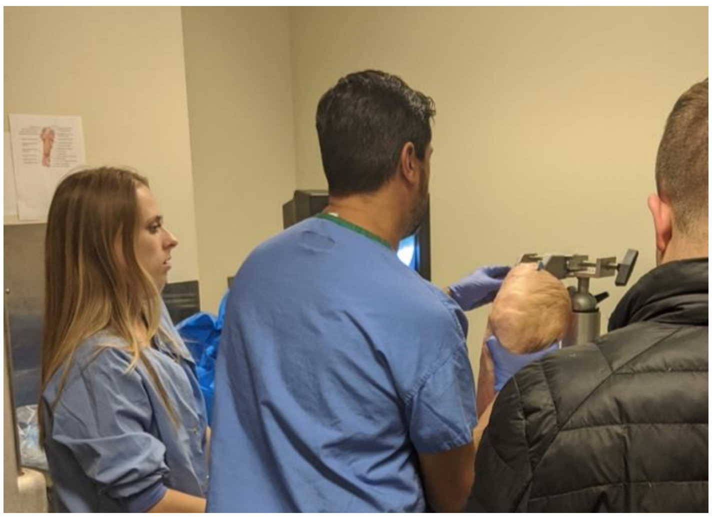

Figure 7. Image captured of the Hershey procedure.

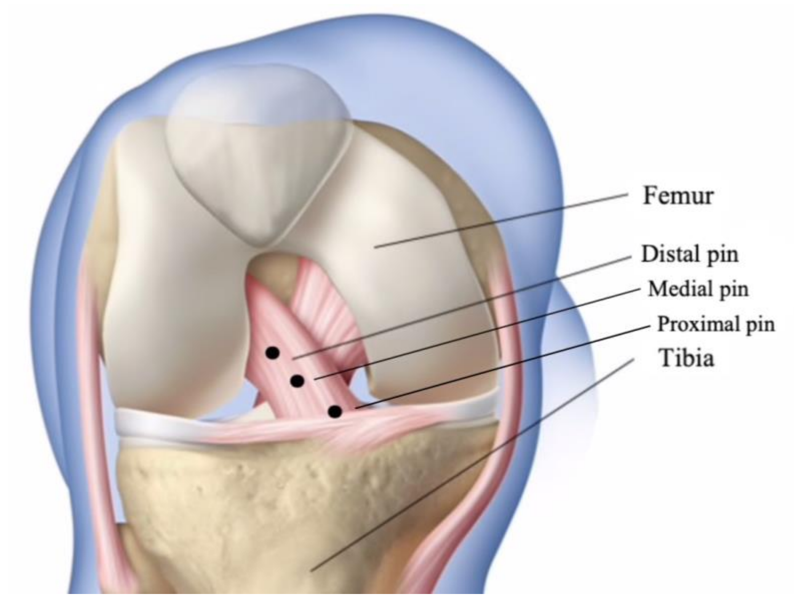

Figure 8. Indication of pins' placement along the ACL [41].

Protocol for Human Imaging

After verification of the ACL's location with ultrasound imaging at Hershey Medical Center, a protocol was developed for SWE measurement of human subjects. A combination of transducer position against the subject's skin, frequency of the ultrasound, and knee position of the subject contributes to whether the ACL is easily located within the B-mode image.

As a baseline, the first images were generated at Penn State using a C5-2 curved transducer, similar to Hershey's, but at a lower frequency. The transducer was held against the human subject's skin, slightly proximally, tilted about 30 degrees, as shown in Figure 9. This placement has been used by Chen et al. in previous works to locate the ACL [42].

Figure 9. Transducer placement against human subject's knee.

Ultrasound imaging is achieved at frequencies from 2 MHz to 15 MHz [43]. Because lower frequencies enable greater penetration, this study focused on the lower end of the range for SWE imaging. A curved 6C1 transducer was used at Hershey at a frequency of 4 MHz, yet Chen et al. reported successful ACL ultrasound using a linear L94 transducer at an unspecified frequency within a 7-9 MHz bandwidth. Initial comparisons with the Penn State Verasonics system were made between a frequency of 3.125 and 5.2 MHz, achieved with a curved and linear transducer, respectively.

Knee flexion is defined as the angle that the knee is bent from the initial 180 degrees when the leg is straightened. Chen et. al conducted ultrasonography at 90 degrees flexion. This can be accomplished with the human subject lying flat on their back, with one leg straight, and the other bent with an angle of 90 degrees between their quadriceps and calf. Though this flexion was used initially, it became evident that the ACL was easiest to locate at a higher angle. Flexion of 120 degrees was found to be the best position for the human subject to maintain as well as the best position for quick identification of the ACL.

SWE Measurement

Using the developed methods, preliminary data was collected from a few individuals to assess the feasibility of ACL evaluation via Shear Wave Elastography. Three healthy subjects, 1 male and 2 females, were used. The subjects had no history of knee injury and lead moderately active lifestyles. None of the subjects participated in athletic training or highly competitive sports.

For data collection, the subject was asked to lay flat on their back with one leg straight and the other leg bent at 120 degrees flexion. The L7-4 transducer was held against the knee of their bent leg, tilted approximately 30 degrees, as shown in Figure 10. For each leg, seven shear wave speed measurements were taken using ultrasonic frequency of 5.2 MHz.

Figure 10. Knee position of human subjects.

Chapter 3

Results

Ultrasound Verification: Cadaveric Knee

The knee arthroscopy during the cadaveric knee procedure displayed the pins' positions relative to the tibia as well as each other. The top pin, defined as the proximal pin, made contact with the tibia. The medial pin was slightly closer to the proximal pin than to the distal pin. The distal pin was placed at a noticeable slant (Figure 11).

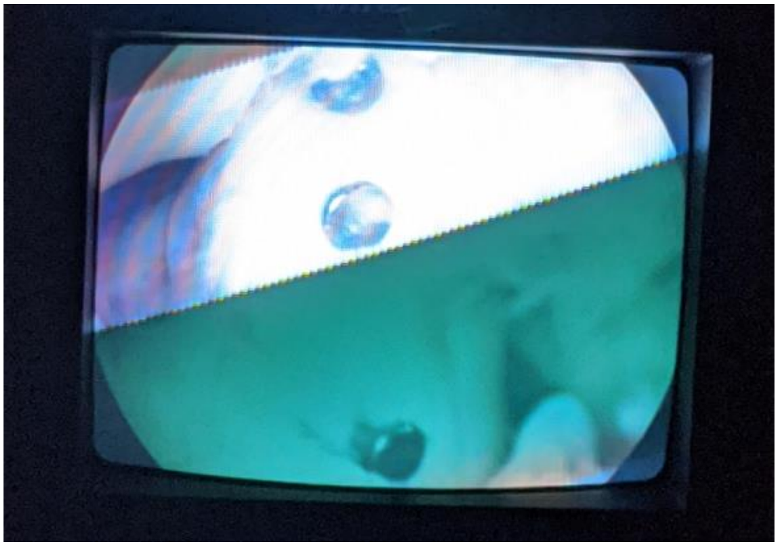

Figure 11. Live image of proximal (top), medial (middle), and distal (bottom) pins inserted into a cadaveric ACL.

Using the Siemens system, a dark band beginning approximately 20 mm inferior to the skin's surface was identified as the ACL. Though more clearly seen in video captured during the experiment, the pins were located and are indicated by Figure 12. The pins are more evident in live footage due to their echogenicity, which causes their brightness to “echo” deeper in the ligament than they were physically placed. The medial pin, in particular, yielded a clear ultrasound echo.

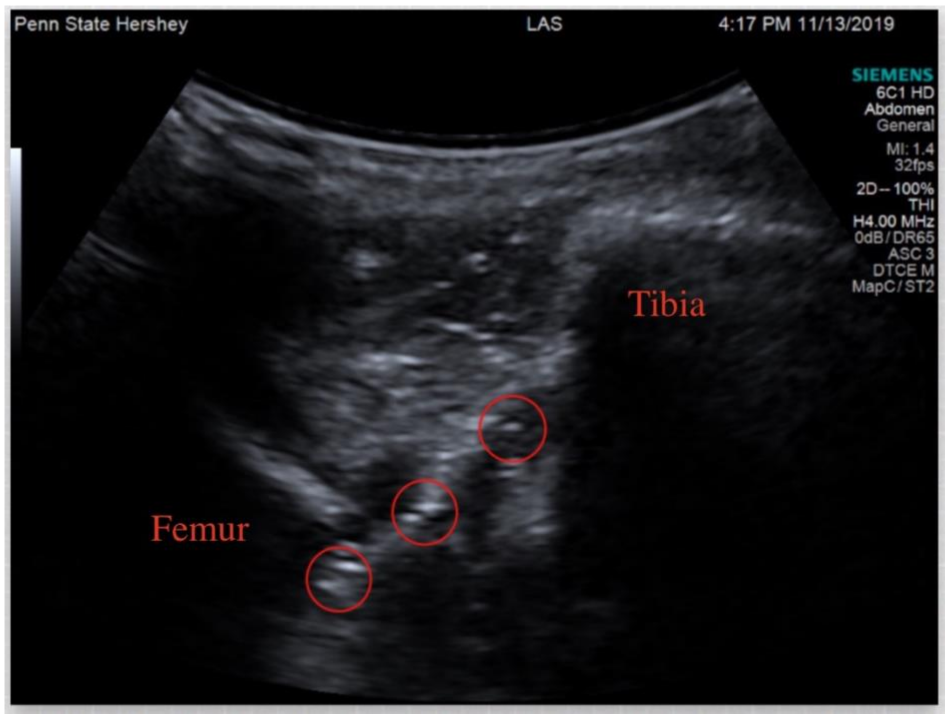

Figure 12. Ultrasound image captured of the distal, medial, and proximal pins, indicated in red.

The tibia and femur were present in the image and located correctly in relation to the ACL. Though oriented 90 degrees counterclockwise from Figure 8, the anatomical position of the ACL further confirms its presence in the image. From this, the depth of the ACL, as well as that of its tibial attachment, are landmarks for locating the ligament within ultrasound imaging.

Protocol for Human Imaging

Ultrasound imaging achieved by two different transducers, operating at different frequencies, were compared to determine the optimal combination. A curved transducer was used at 3.125 MHz and a linear transducer at 5.2 MHz. Figure 13 presents a side-by-side comparison of the resultant images.

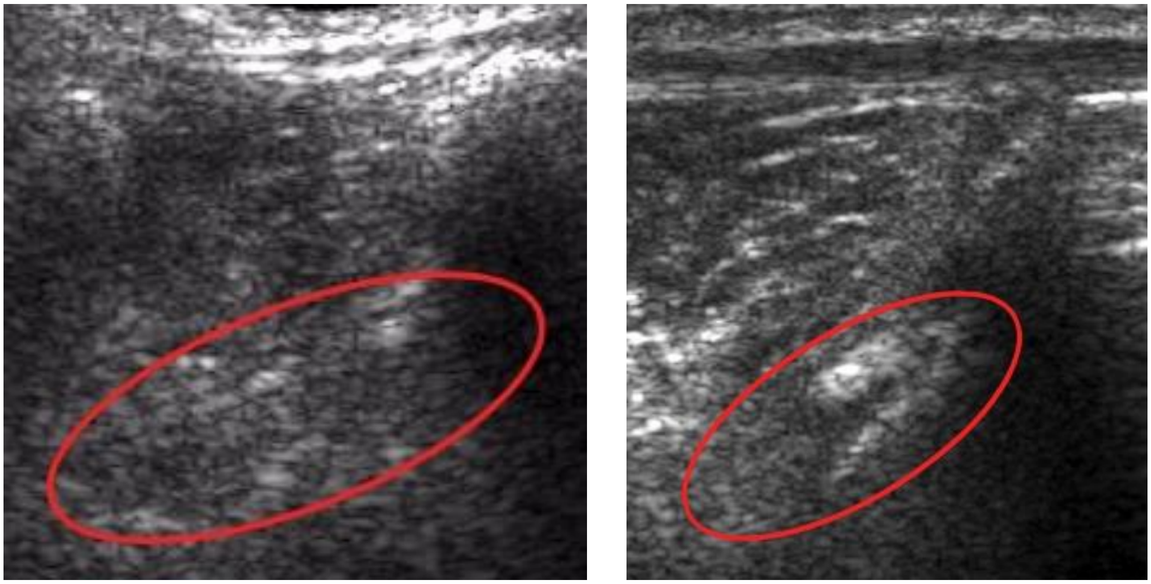

Figure 13. Comparison of ACL ultrasound achieved by SWE imaging at 3.125 MHz (left) and 5.2 MHz (right).

The linear transducer clearly achieved greater quality than the curved transducer. It was concluded that an L7-4 transducer operating at 5.2 MHz was of sufficient quality for screening the ACL for elastography measurements. The ACL was able to be located at a similar depth and tibial attachment as that discerned with the cadaveric knee. It should be noted that the cadaveric knee was screened with a curved transducer. The linear array transducer depicts the ACL at a slightly different angle from Figure 11. However, the ACL is unmistakably present as a dark band extending approximately 40 mm inferior to the surface of the skin, with a tibial attachment at 20 mm.

SWE Measurement

Elastography was conducted with a linear L7-4 transducer at 5.2 MHz. A region of interest was selected within the resultant image. A “heat map” of shear wave speed was calculated, as shown in Figure 14. The red area within the ACL at the tibial attachment was used for stiffness data.

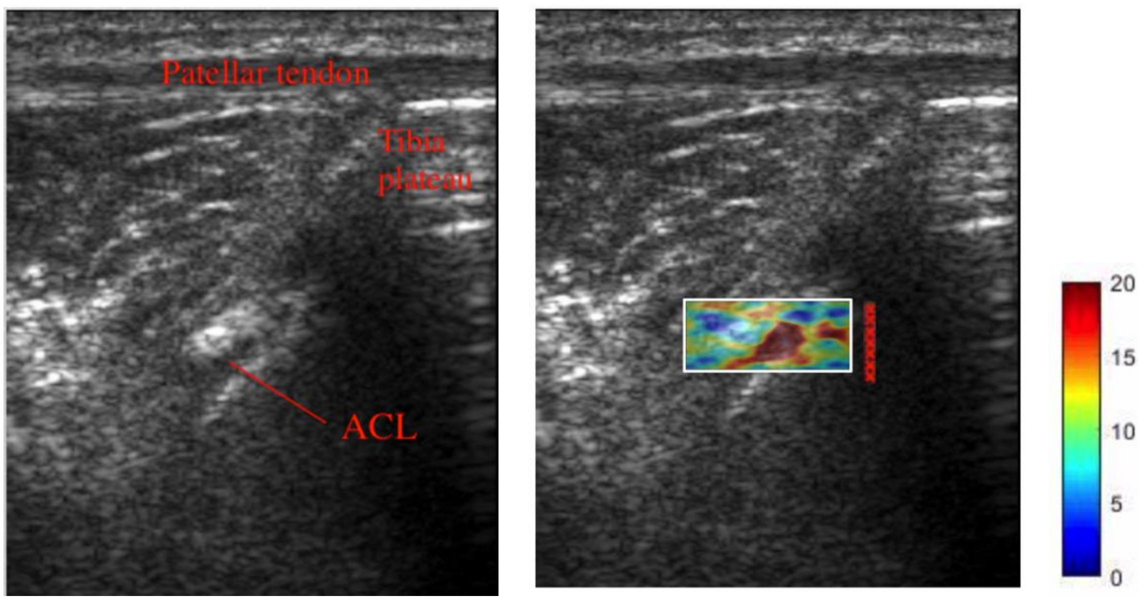

Figure 14. Real-time B-mode imaging for the ACL (left). Map of shear wave speed, indicating a region of increased stiffness at the tibial attachment of the ACL (right).

Measurements were collected from three human subjects and the averages are presented in Table 1. Seven measurements were taken from each leg, resulting in fourteen data points for each subject.

Table 1. ACL shear wave speed averages from 3 healthy subjects.

	Left leg	Right leg
Shear Wave Speed (m/s)	9.770 ± 0.5786	9.979 ± 0.7909

The shear modulus of the ACL was calculated from the subjects' shear wave speed measurements. An average of the three subjects was taken for each leg (Table 2).

Table 2. Averages of the calculated shear modulus values.

	Left leg	Right leg
Shear Modulus (kPa)	95.68 ± 11.48	99.99 ± 16.02

All three subjects produced similar ultrasound images and shear wave speed maps. The numbers were similar for both legs, and the shear wave speed and stiffness data were close for all subjects. Data for individual subjects can be found in Appendix A.

Chapter 4

Discussion

The present study verified the location of the ACL in ultrasound imaging in order to apply SWE to the ACL and collect preliminary data of the ligament's shear modulus. Methods of ultrasonically screening the ACL were adapted to a Veraonics, MATLAB-based Elastography set-up. The ACL position within the B-mode images produced by the present study was very similar to that recorded in recent sonography of the ACL. Confidence in the ACL's position was essential in collecting shear wave speed data with Shear Wave Elastography. Preliminary data in healthy individuals demonstrated a consistent shear modulus value for both knees of all subjects. These results suggest that it is feasible to apply SWE to the ACL. In the future, this method could potentially enable the clinical evaluation of rehabilitating patients of surgical ACL reconstruction, and possibly be applied to prevention of ACL injury.

With data from 33 individuals, Chen et al. concluded that the ACL is a hypoechoic band located 11 mm inferior to the tibia plateau within ultrasound imaging [42]. This study located the ACL 20 mm inferior to the skin's surface, with a tibial attachment approximately 13 mm inferior to the tibia plateau. With the Verasonics system, this was best accomplished using an L7-4 linear array transducer operating at 5.2 MHz. The shear modulus averages are feasible considering past studies involving SWE measurements of other ligaments. The Elastography study on the Ulnar Collateral Ligament (UCL) of the elbow reported shear modulus values of 109.82 ± 43.45 kPa for the right arm and 103.90 ± 35.61kPa for the left arm [40]. This study found shear modulus values of 99.998 ± 16.020 and 95.676 ± 11.479 kPA for the right and left arms, respectfully. Though the values are quite close, within 10 kPa for both right and left sides, it is perhaps surprising that the ACL has lower stiffness than the UCL. Together, the knees support nearly the entire body weight. A single knee would then support about half of an individual's weight, while each elbow joint only helps to control one arm. One explanation for the discrepancy could be the difference in elbow and knee anatomy. The knee consists of 4 main stabilizing ligaments, including the ACL, while there are only two main stabilizing ligaments in the elbow [44]. The UCL, then, may reasonably exhibit higher stiffness than the ACL, which works in tandem with three other ligaments.

The elastography values reported in this study for the ACL are lower than those reported for tendons and muscles. For the Achilles tendon, the shear modulus was found to be 291.91 ± 4.38 kPa [37]. Tendons and ligaments are anatomically different in that tendons connect muscle and bone, while ligaments connect bones. It is likely that tendons are stiffer than ligaments because they serve to transmit tensile forces from muscle to bone [45]. Various muscles in the leg were found to exhibit average shear wave speeds anywhere between 1.861 and 3.665 m/s, which equates to a range of 3.463 to 13.4322 kPa [38]. These values are significantly less than those found for the ACL. It is beyond the scope of this paper to analyze muscle stiffness.

While a repeatability study was not conducted for the subjects, the preliminary data suggests that Shear Wave Elastography is suitable for screening the ACL. The present study could have been improved through utilization of more human subjects. A repeatability study should be conducted to compare data from each subject between two data collection sessions. It should be noted, however, that Shear Wave Elastography has demonstrated excellent repeatability for other tendons and ligaments. For the Ulnar Collateral Ligament, shear modulus values were highly reliable with respect to both intra-day study as well as day-to-day. For intra-day reliability, intra-class correlation (ICC) was 0.715 (95% CI=0.587–0.828) and Cronbach's alpha was 0.926. For day-to-day, ICC was 0.948 (95% CI=0.884–0.976) with a Cronbach's alpha of 0.955 [40]. If more subjects had been used intra-day in the present study, with day-to-day session comparisons, it is expected that SWE would present similar repeatability for the ACL.

The high re-injury rate after ACLR, particularly for young athletes, suggests that the procedure is unable to fully restore the stiffness of the ligament. In the future, SWE should also be used to evaluate individuals who have undergone ACL reconstruction. The difference in stiffness between their healthy and injured knees could offer valuable insight into the high post ACLR re-injury rate. The findings could determine the difference between the shear modulus of a healthy ACL and that of a graft ACL. Different graft sources should also be noted in this future study, because different tendons would very likely exhibit different stiffness values from each other, ACL allografts, and a true ACL. This could also potentially indicate which graft source can be used for optimal ACL replacement stiffness.

Because of the nature of non-contact ACL injury, it is possible that individuals participating in athletics may experience some degree of ACL degradation which increases their susceptibility to injury. SWE should also be used to compare healthy subjects with athletes who participate in high level training. The data from regular individuals of the same age and gender would serve as a control to observe the impact of athletic training. Previous SWE studies have evaluated the muscles of cross country runners before, immediately after, and a week after a race [38]. A similar study on the ACL could reveal when athletes are most susceptible to ACL injury. This could lead to discovery of the effect of athletic training on the stiffness of the ACL.

The most significant limitation of this study was the low number of subjects. A sample size of at least 20 subjects was initially intended, as well as a group of post-ACLR subjects, yet was unfulfilled due to the ongoing COVID-19 pandemic. This data would have produced more reliable values and offered some early insight into the mechanical differences between a natural ACL and a graft ACL *in vivo.* Another limitation of the study is the difference in quality between the Verasonics B-mode images and the Siemens clinical system at Hershey. While the elastography system was able to successfully locate the ACL, the image clarity was still noticeably diminished. Refining the technique and improved equipment could lead to increased image quality in the future. However, the clarity of images produced with simply a Verasonics system and MATLAB setup was deemed sufficient for this study and future work.

Shear Wave Elastography is an emerging method for evaluating biological tissue. More studies on various tendons, muscles, and ligaments should be carried out in order to determine baseline shear modulus and shear wave speed values. This data could serve as biomarkers for both injury susceptibility and rehabilitation progress. The ACL is highly susceptible to injury, and more studies with healthy individuals, athletes, and post ACLR patients should be carried out in the future. Better understanding of ACL failure and rehabilitation could offer mitigation of an incident that is particularly devastating for young adults and athletes.

Appendix A

Individual ACL Data

Table 3. Subject #1 shear wave speed data.

									AVG	STD
Shear Wave Speed (m/s)	**Left Leg**	11.3	9.00	11.4	5.56	9.67	10.43	9.35	9.530	1.980
	Right Leg	8.43	9.53	15.01	10.91	9.84	12.73	9.53	10.85	2.281

Table 4. Subject #2 shear wave speed data.

									AVG	STD
Shear Wave Speed (m/s)	**Left Leg**	8.58	8.13	9.03	4.40	14.05	9.36	11.9	9.350	3.035
	Right Leg	9.24	12.81	7.59	7.48	11.0	8.57	8.52	9.316	1.940

Table 5. Subject #3 shear wave speed data.

									AVG	STD
Shear Wave Speed (m/s)	**Left Leg**	10.27	9.39	11.71	9.53	11.99	9.15	10.97	10.43	1.149
	Right Leg	12.65	11.0	8.21	9.19	9.06	8.57	9.69	9.767	1.556

BIBLIOGRAPHY

[1] Griffin, L. Y., Albohm, M. J., Arendt, E. A., Bahr, R., Beynnon, B. D., Demaio, M., et al. (2005). “Understanding and preventing noncontact anterior cruciate ligament injuries: a review of the Hunt Valley II meeting, January 2005.” *Am. J. Sports Med.*, 34(9), pp. 1512–1532.

[2] Buller, L. T., Best, M. J., Baraga, M. G., & Kaplan, L. D. (2014). Trends in Anterior Cruciate Ligament Reconstruction in the United States. *Orthop. J. Sports Med.*, 3(1).

[3] Gottlob, C. A., Baker, C. L. Jr., Pellissier, J. M., et al. Cost effectiveness of anterior cruciate ligament reconstruction in young adults. (1999). *Clin. Orthop. Relat. Res.*, (367), pp. 272–282.

[4] Herzog, M. M., Marshall, S. W., Lund, J. L., Pate, V., & Spang, J. T. (2017). Cost of Outpatient Arthroscopic Anterior Cruciate Ligament Reconstruction Among Commercially Insured Patients in the United States, 2005-2013. *Orthop J of Sports Med*, 5(1).

[5] Yu, B., & Garrett, W. E. (2007). Mechanisms of non-contact ACL injuries. *Br. J. Sports Med.*, 41(SUPPL. 1), pp. 47-51.

[6] Gamada, K., & Kubota, S. (2014). The Mechanism of Non-contact Anterior Cruciate Ligament Injury in Female Athletes: Is the Injury Mechanism Different between the Genders? *Int. J. Phys. Med.*, 2(6).

[7] Joseph, A. M., Collins, C. L., Henke, N. M., Yard, E. E., Fields, S. K., & Comstock, R. D. (2013). A multisport epidemiologic comparison of anterior cruciate ligament injuries in high school athletics. *J. Athl. Train.*, 48(6), pp. 810-817.

[8] Serpell, B. G., et al. (2012). Mechanisms and Risk Factors for Noncontact ACL Injury in Age Mature Athletes Who Engage in Field Or Court Sports. *J. Strength Cond. Res.*, 26(11), pp. 3160–3176.

[9] Waldén, M., Krosshaug, T., Bjørneboe, J., et al. (2015). Three distinct mechanisms predominate in non-contact anterior cruciate ligament injuries in male professional football players: a systematic video analysis of 39 cases. *Br. J. Sports Med.*, 49(22), pp. 1452-1460.

[10] Grindem, H., Eitzen, I., Engebretsen, L., Snyder-Mackler, L., & Risberg, M.A. (2014). Nonsurgical or Surgical Treatment of ACL Injuries: Knee Function, Sports Participation, and Knee Reinjury: The Delaware-Oslo ACL Cohort Study. *J. Bone Joint Surg. Am*., 96(15), pp.1233-1241.

[11] Barber-Westin, S. D., & Noyes, F. R. (2011). Factors Used to Determine Return to Unrestricted Sports Activities After Anterior Cruciate Ligament Reconstruction. *Arthroscopy*,, 27(12), pp. 1697–1705.

[12] Turner, C. (2014). “ACL Implant.” *Surgical Implants*, Medical Illustration Sourcebook, 29 Sept. 2014.

[13] Wiggins, A. J., Grandhi, R. K., Schneider, D. K., Stanfield, D., Webster, K. E., & Myer, G.D. (2016). Risk of Secondary Injury in Younger Athletes After Anterior Cruciate Ligament Reconstruction: A Systematic Review and Meta-analysis. *Am. J. Sports Med.*, 44(7), pp. 1861–1876.

[14] Thomas, A. C., et al. (2017). Epidemiology of Posttraumatic Osteoarthritis. *J. Athl. Train.*, 52(6), pp. 491–496.

[15] Holm, I., Øiestad, B. E., Risberg, M. A., Gunderson, R., & Aune, A. K. (2012). No Differences in Prevalence of Osteoarthritis or Function After Open Versus Endoscopic Technique for Anterior Cruciate Ligament Reconstruction: 12-Year Follow-up Report of a Randomized Controlled Trial. *Am. J. Sports Med.*, 40(11), pp. 2492–2498.

[16] Thompson, S. M., Salmon, L. J., Waller, A., Linklater, J., Roe, J. P., & Pinczewski, L. A. (2016). Twenty-Year Outcome of a Longitudinal Prospective Evaluation of Isolated Endoscopic Anterior Cruciate Ligament Reconstruction With Patellar Tendon or Hamstring Autograft. *Am. J. Sports Med.*, 44(12), pp. 3083–3094.

[17] Ajuied, A., et al. (2014). Anterior Cruciate Ligament Injury and Radiologic Progression of Knee Osteoarthritis. *Am. J. Sports Med.*, 42(9), pp. 2242–2252.

[18] Culvenor, A. G., Lai, C. C. H., Gabbe, B. J., et al. (2014). Patellofemoral osteoarthritis is prevalent and associated with worse symptoms and function after hamstring tendon autograft ACL reconstruction. *Br. J. Sports Med.*, 48(6), pp. 435-439.

[19] von Porat, A., et al. (2004). High Prevalence of Osteoarthritis 14 Years after an Anterior Cruciate Ligament Tear in Male Soccer Players: a Study of Radiographic and Patient Relevant Outcomes. *Ann. Rheum. Dis.*, 63(3), pp. 269–273.

[20] Foran, J. R. H., & Grelsamer, R. P. (2011). Patellofemoral Arthritis. *Am. Academy Orthop. Surg.*,

[21] Hewett, T. E., Lindenfeld, T. N., Riccobene, J. V., & Noyes, F. R. (1999). The Effect of Neuromuscular Training on the Incidence of Knee Injury in Female Athletes. *Am. J. Sports Med.*, 27(6), pp. 699–706.

[22] Agel, J., Arendt, E. A., & Bershadsky, B. (2005). Anterior cruciate ligament injury in National Collegiate Athletic Association basketball and soccer: A 13-year review. *Am. J. Sports Med.*, 33(4), pp. 524-530.

[23] Arendt, E., & Dick, R. (1995). Knee Injury Patterns Among Men and Women in Collegiate Basketball and Soccer: NCAA Data and Review of Literature. *Am. J. Sports Med.*, 23(6), pp. 694–701.

[24] Mihata, L. C. S., Beutler, A. I., & Boden, B. P. (2006). Comparing the Incidence of Anterior Cruciate Ligament Injury in Collegiate Lacrosse, Soccer, and Basketball Players: Implications for Anterior Cruciate Ligament Mechanism and Prevention. *Am. J. Sports Med.*, 34(6), 899–904.

[25] Girgis, F. G., Marshall, J. L., & Monajem, A. (1975). The cruciate ligaments of the knee joint. Anatomical, functional and experimental analysis. *Clin. Orthop. Relat. Res.*, (106), pp. 216-231.

[26] Markolf, Keith L., et al. (1995). Combined Knee Loading States That Generate High Anterior Cruciate Ligament Forces. *J. Orthop. Res.*, 13(6), pp. 930–935.

[27] Fleming, B. C., et al. (2001). The Effect of Weightbearing and External Loading on Anterior Cruciate Ligament Strain. *J. Biomech.*, 34(2), pp. 163–170.

[28] Pandy, M. G., & Shelburne, K. B. (1997). Dependence of cruciate-ligament loading on muscle forces and external load. *J. Biomech.*, 30(10), pp. 1015–1024.

[29] Cortes, N., Onate, J., & Van Lunen, B. (2011). Pivot task increases knee frontal plane loading compared with sidestep and drop-jump. *J Sports Sci*., 29(1), pp. 83–92.

[30] Fujie, H. Mechanical Properties and Biomechanical Function of the ACL. *ACL Injury and Its Treatment*, Springer Verlag, Japan, 2018, pp. 69–77.

[31] Butler, D. L., Guan, Y., Kay, M. D., Cummings, J. F., Feder, S. M., Levy, M. S. (1992). Location-dependent variations in the material properties of the anterior cruciate ligament. *J. Biomech.*, 25(5), pp. 511–518.

[32] Woo, S. L., Hollis, J. M., Adams, D. J., Lyon, R. M., Takai, S. (1991). Tensile properties of the human femur-anterior cruciate ligament-tibia complex. The effects of specimen age and orientation. *Am. J. Sports Med.*, 19(3) pp. 217–225.

[33] Kwak, J. Y., & Eun-Kyung, K. (2014). Ultrasound elastography for thyroid nodules: recent advances. *Ultrasonography*, 33(2), pp. 75-82.

[34] Cortes, D. H., Suydam, S. M., Silbernagel, K. G., Buchanan, T. S., & Elliott, D. M. (2014). Continuous Shear Wave Elastography: A New Method to Measure Viscoelastic Properties of Tendons in Vivo. *Ultrasound Med. Biol*., 41(6), pp. 1518–1529.

[35] Nowicki, A., & Dobruch-Sobczak, K. (2016). Introduction to Ultrasound Elastography. *J. Ultrason.*, 16(65), pp. 113-124.

[36] Botanlioglu, H., Kantarci, F., Kaynak, G., et al. (2013). Shear wave elastography properties of vastus lateralis and vastus medialis obliquus muscles in normal subjects and female patients with patellofemoral pain syndrome. *Skeletal Radiol*., 42(5), pp. 659-666.

[37] Chen, X-M, Cui, L-G, He, P., Shen, W-W, Qian, Y-J, & Wang, J-R. (2013). Shear Wave Elastographic Characterization of Normal and Torn Achilles Tendons. *J. Ultrasound Med.*, 32(3), pp. 449-455.

[38] Newman, C. (2017). Change in Skeletal Muscle Stiffness After Running Competition Is Dependent on Both Running Distance and Recovery Time. *The Pennsylvania State University*.

[39] Aubry, S., Nueffer, J. P., Tanter, M., Becce, F., Vidal, C., & Michel, F. (2015). Viscoelasticity in Achilles Tendonopathy: Quantitative Assessment by Using Real-time Shear-Wave Elastography. *Radiology*, 274(3), pp. 821-829.

[40] Lin, C-Y, Sadeghi, S., Bader, D. A., Cortes, D. H. (2018). Ultrasound Shear Wave Elastography of the Elbow Ulnar Collateral Ligament: Reliability Test and a Preliminary Case Study in a Baseball Pitcher. *J. Eng. Sci. Med. Diagnostics Ther*., 1(1), 10.1115.

[41] "ACL Injury." Mayo Foundation for Medical Education and Research, 30 Mar. 2019.

[42] Chen, P-T, et al. (2013). Sonography of the Normal Anterior Cruciate Ligament: A Preliminary Report. *J. Med. Ultrasound*, 21(1), pp. 16-20.

[43] Murphy, A., Nadrlijanski, M., et al. Ultrasound Frequencies: Radiology Reference Article. *Radiopaedia Blog RSS*.

[44] "The Anatomy of the Elbow." *Washington University Orthopedics*.

[45] "Structure and Function of Ligaments and Tendons." *Biological Systems Engineering*, Washington State University.

ACADEMIC VITA

Academic Vita of Rachel Heller
Rbh5218@psu.edu

Education

The Pennsylvania State University, Schreyer Honors College
B.S. Mechanical Engineering
French Studies Minor
Honors in Mechanical Engineering

Thesis Title: Shear Wave Elastography of the Anterior Cruciate Ligament
Thesis Supervisor: Daniel Cortes

Work Experience

May 2019 – August 2019
Operations Engineering / Manufacturing Support Intern
Lockheed Martin Aeronautics
F-35 Program

May 2018 – August 2018
Systems Engineering Intern
Lockheed Martin Rotary Mission Systems
Training and Logistics Solutions

Awards

Louis A. Harding Memorial Scholarship, AFCEA Captain John & Angie Skinner

Merit Scholarship, Taylor Waltman Memorial Scholarship

Professional Memberships

American Society of Mechanical Engineers, Society of Women Engineers

Community Service Involvement

Penn State Panhellenic Dance Marathon Dancer Relations Committee