PREDICTING MECHANICAL PROPERTIES OF HUMAN TENDON USING QUANTITATIVE ULTRASOUND MEASURES

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INTRODUCTION
Ultrasound is a common imaging modality used to evaluate musculoskeletal tissues non-invasively and dynamically [1]. Tissue geometry can be assessed objectively, but determining tissue quality is largely subjective. As a result, clinical ultrasound examinations have low repeatability between examiners [1]. Previous studies have proposed the use of quantitative ultrasound measures (QUS) to objectively evaluate tissue quality using ultrasound imaging [1,4,5,6]. In addition, studies have shown that better tendon quality is correlated with QUS measures including higher values of echogenicity and variance and lower values of skewness and kurtosis [4]. However, the relationship between these QUS measures and mechanical properties of musculoskeletal tissues, representative of tissue quality, are poorly understood.

OBJECTIVE
The objective of this study is to relate mechanical properties of human tendon with QUS measures to be able to quantify tendon tissue quality.

HYPOTHESIS
It was hypothesized that high values of echogenicity and variance and low values of skewness and kurtosis are related to higher mechanical properties representing better tissue quality.

METHOD
Nine fresh frozen cadaveric long head of biceps tendon (LHBT) were harvested from intact shoulder specimens (59.8 ± 9.6 years old). The LHBT was then dissected into a “dog-bone” shape approximately half the width of the tendon to ensure failure in the mid-substance [2,3]. Two rubber band markers were superglued to the tendon at the ends of the “dog-bone” region to provide a point of reference to ensure repeatability between ultrasound images (Fig. 1). Using a laser scanner (Next Engine, Desktop 3D Scanner, Santa Monica, CA, USA), the cross-sectional area of the “dog-bone” region of the tendon was measured [2]. The LHBT was then secured to the materials testing machine (Instron Model 5965, Norwood, MA, USA) for uniaxial tensile testing using soft tissue clamps. A layer of skin was wrapped around the tendon to allow for ultrasound imaging during mechanical testing.

For mechanical testing, a 1N preload was applied to the LHBT, followed by preconditioning from 1-10N for 20 cycles at 10 mm/min. After preconditioning, the LHBT was loaded from 1-30N for 50 cycles at 10 mm/min. The maximum load of a loading set was then increased by 20N until tendon failure occurred (ie. 1-30N, 1-50N, etc.). Following each loading set, three ultrasound images (GE, LOGIQ S8, Fairfield, CT, USA) were taken at the maximum load of each loading set by a single experienced ultrasound examiner using a rig designed to ensure repeatable placement of the ultrasound probe.

For each ultrasound image, a region of interest (ROI) was selected as a box centered between the rubber band markers (Fig. 1). Tissue quality was measured using QUS measures (Skewness, Kurtosis, Variance, Echogenicity) which were calculated from a grayscale distribution produced from the ROI [1,4,5]. QUS measures from each of the three ultrasound images taken for a loading set were adjusted to account for baseline QUS measures of surrounding, unloaded fat tissue. The strength of the tissue was measured using mechanical properties including toe region tangent modulus and linear region tangent modulus, which were determined using the last cycle of the stress strain curve for each loading set, as well as percent creep, which was determined using the last and initial cycles of the stress strain curve for each loading set.

A backwards stepwise linear regression was performed to test the influence of QUS measures on predicting mechanical properties of the tendon. Significance was set at p < 0.05.

Figure 1: Typical ultrasound images of long head of biceps tendon. A) Image in the toe region of the stress-strain curve. B) Image in the linear region of the stress-strain curve. (ROI = Region of Interest)
RESULTS
A significant multiple linear regression model was found for each mechanical property determined in this study involving the interaction of at least two QUS measures as predictors (Table 1). Each mechanical property was predicted by variance, with toe region tangent modulus and percent creep inversely related and linear region tangent modulus directly related. The correlation coefficients for the linear region tangent modulus ($r^2 = 0.565$) and percent creep ($r^2 = 0.596$) regression models were higher than the correlation coefficient for the toe region tangent modulus regression model ($r^2 = 0.208$). There were no other significant multiple linear regression models between the mechanical properties (Percent Creep, Toe Region Tangent Modulus, Linear Region Tangent Modulus) and the QUS measures (Skewness, Kurtosis, Variance, Echogenicity).

<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>Linear Regression Equation</th>
<th>Correlation Coefficient</th>
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</thead>
<tbody>
<tr>
<td>Toe Region Tangent Modulus</td>
<td>$(248.1)(\text{Skewness}) + (-91.2)(\text{Kurtosis}) + (-0.2)(\text{Variance}) + 306.6$</td>
<td>0.208</td>
</tr>
<tr>
<td>Linear Region Tangent Modulus</td>
<td>$(0.4)(\text{Variance}) + (-16.9)(\text{Echogenicity}) + 1544.3$</td>
<td>0.565</td>
</tr>
<tr>
<td>Percent Creep</td>
<td>$(-5.8)(\text{Kurtosis}) + (-0.05)(\text{Variance}) + (0.3)(\text{Echogenicity}) + 17.2$</td>
<td>0.596</td>
</tr>
</tbody>
</table>

DISCUSSION
The results partially support our initial hypothesis, since the type of relationship observed between some of the QUS measures and mechanical properties are as expected: toe region tangent modulus was found to be inversely related with kurtosis, linear region tangent modulus was found to be directly related to variance, and percent creep was found to be inversely related to variance. Additionally, the direction of the linear relationships between tendon mechanical properties and QUS measures are consistent with the direction of correlations found between same QUS measures and other measures of tissue quality [1,6]. An inverse relationship between toe region tangent modulus and kurtosis indicates that an increase in the peakedness of the grayscale histogram produced from the tendon ROI relates to a decrease in the slope of the initial region of the stress strain curve. A direct relationship between linear region tangent modulus and variance indicates that an increase in the spread of the grayscale histogram produced from the tendon ROI, perhaps indicating higher tendon fiber alignment, relates to an increase in slope of the linear region of the stress strain curve. Likewise, an inverse relationship between percent creep and variance indicates that an increase in the spread of the grayscale histogram produced from the tendon ROI relates to a decrease in percent creep. These changes in the skewness, kurtosis, variance, and echogenicity of the grayscale histogram produced from the tendon ROI can be attributed to structural changes within the tendon [1,7].

A limitation of this study is that the tendon was covered with skin during mechanical testing, which limited the methods of tracking elongation in the tendon to determine strain. Tendon elongation was approximated by measuring the distance between the soft tissue clamps in order to calculate strain. Additionally, there is significant variation between each ultrasound image, so to minimize this variability, a single ultrasound examiner was used, gain and frequency parameters were kept constant for each ultrasound image, and each ultrasound image was adjusted to account for baseline grayscale values of the surrounding, unloaded fat tissue in the image.

CONCLUSION
Overall, the results of this study show that QUS measures can predict the mechanical properties of musculoskeletal tissue. Clinicians will be able to use QUS measures to better assess mechanical properties of musculoskeletal tissue, representative of tissue quality, with ultrasound, a common, inexpensive, and dynamic imaging modality, to improve treatments. Specifically, clinician can use these QUS measures to gain insight about the level of tissue pathology and better determine whether surgical intervention is needed. These QUS measures will provide clinicians with a repeatable tool to predict the strength of musculoskeletal tissue using ultrasound, providing insight on tissue quality and microstructure. In the future, other musculoskeletal tissues, including rotator cuff tendons, will be assessed using QUS measures to determine tissue quality, as well as gain a better understanding of how these QUS measures relate to tissue quality.

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REFERENCES