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Young's Modulus Measurements of Soft Tissues with Application to Elasticity Imaging

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Abstract— **Ultrasound elasticity imaging is a promising method that may eventually allow early detection of many tissue pathologies. However, before elasticity imaging can be applied to its numerous potential clinical applications, the quantitative accuracy of tissue elasticity measurements must be established. Simple 1-D ultrasound elasticity measurements were performed on muscle and liver and compared with independent and established mechanical measurements to investigate both the accuracy and consistency of ultrasound elasticity measurements. In addition, some interesting properties of soft tissue and aspects of the measurement process which should be considered in elasticity measurements are discussed.**

I. Introduction

The goal of this work is threefold: 1) To establish the accuracy of ultrasound elasticity measurements under simple test conditions, 2) to provide elasticity values for two important tissues (muscle and liver), and 3) to investigate several interesting aspects of the measurement process that should be considered in elasticity measurements. Tissue elasticity imaging has direct relevance in the early detection of breast and prostate cancers and liver cirrhosis; diseases which are believed to significantly alter tissue elasticity. There is also significant potential for commercial applications in animal sciences and in food science [1]–[5].

Previous measurements of tissue elastic properties are limited and have spanned a wide range of values. Elasticity measurements have been reported for tendon, heart, skin, and cartilage; however, quantitative values for muscle, liver, and fat are still lacking [6]–[8]. There does exist a large body of meat science literature involving measurements of closely related muscle mechanical properties such as tenderness, tangent modulus, and chewiness. However, most if not all of these studies focused attention on the correlation between measured mechanical parameters and human sensory parameters and not on the accuracy of the measured mechanical parameters or the degree of consistency or correlation between the various measurement methods [3], [8]–[12].

To test both the accuracy and consistency of ultrasound measurements, Young's modulus (YM) values for muscle and liver are compared with independent mechanical measurements made using the Instron load cell device. The results of this study have two major implications. First, they contribute to the limited quantitative data currently available on muscle and liver elastic properties. Second, by comparing ultrasound elasticity measurements with established mechanical measurements, we have a basis for determining the quantitative accuracy of ultrasound elasticity values. It should be noted that the measurements reported here can help establish the accuracy of elastography [13], but not necessarily other elasticity imaging methods.

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II. Materials and Methods

A. Ultrasound Elasticity Measurements

Three bovine muscle and three bovine liver samples were obtained from the Meat Sciences Laboratory, Department of Animal Sciences, the University of Illinois. Muscle samples were excised from the beef longissumus dorsi (LD) muscle of a U.S.D.A. select grade animal and were approximately 4 cm × 4 cm in length and width, with thicknesses ranging from 1–2 cm. Tissue samples were packed in ice and transported to the Bioacoustics Research Laboratory for experiments within 48 h of death. Muscle samples had an angled fiber orientation leaving fibers neither parallel nor perpendicular to the sides.

Previous studies indicate that muscle fiber orientation can strongly influence elasticity measurements [8], [14]. When samples are measured with fibers perpendicular to the direction of compression, both muscle fibers and connective tissue contribute to resistance, while only muscle fibers contribute to resistance when fibers are parallel to the direction of compression. Since all of the muscle samples used in this study had an angled fiber orientation, with fibers neither parallel nor perpendicular, the measured YM values should fall between these extremes. Since the same samples with the same fiber orientation were used for both sets of measurements (ultrasound, Instron), fiber orientation should not produce inconsistency between measurement techniques.

Three samples of ultrasound tissue mimicking gel standoff material were also used in test measurements. Gel standoff samples were made of plasticized poly-vinyl-chloride (PVC) shor value #4. Sample A was cut into a rectangular block with dimensions (length, width, thickness) of 2.0 cm × 2.0 cm × 2.5 cm. Sample B was cut into a rectangular block with dimensions of 2.5 cm × 3.5 cm × 2.5 cm. Sample B2 was cut into a rectangular block with dimensions of 2.5 cm × 2.5 cm × 3.5 cm.

Ultrasound elasticity measurements were made using a single transducer setup. Samples were placed on the pad of a Taconic Farms model YG-700 rat scale. A 2.5-MHz circular, unfocused Panametrics transducer with 3.18 cm diameter was attached to the robotic arm of a Daedal motorized positioning system and aligned to perform uniaxial compressions. The system is computer controlled and has five degrees of freedom. The transducer was positioned to be in light contact with the sample. Precise axial compressions were made in 0.5-mm increments until a total deformation of approximately 7.0% was reached. The Daedal system compressions were made at a speed of approximately 1 cm/s. After each incremental compression, a 1025-point A-line was digitized at 50 MHz using a model 11401 Tektronix digitizing oscilloscope. Incremental tissue strains were computed from time-of-flight (TOF) measurements of an ultrasonic pulse using (1), where t_i represents the round trip TOF of the pulse after the ith compression.

$$\epsilon_i = \frac{\Delta L}{L} = \frac{t_0 - t_i}{t_0}. \tag{1}$$

Scale readings were used to compute the force applied to samples after each incremental compression. The equivalent stress on samples was computed by dividing the force by the surface dimensions of individual samples. By measuring the strain for several different applied stresses, the stress–strain behavior of samples was characterized and the Young's modulus was estimated from the slope of the curve in the linear region of sample stress–strain curves. YM values of samples were calculated from the initial linear region (up to 5% strain for tissue samples and 10% strain for PVC) of the curves using a least squares fit. YM values were calculated from a larger strain range for the PVC samples since they exhibited a larger linear elastic region.

All measurements were made at room temperature (22°C) after Aquasonic coupling gel was applied to lubricate contact between the transducer punch, the scale pad, and muscle samples.

B. Instron Load Cell Measurements

Precise load-deflection measurements of all samples were made using an Instron universal testing instrument, model 1122. Samples were axially compressed by a circular 5.7 cm diameter aluminum punch cross head with cross head velocity set to 5 cm/min, chart speed set to 500 cm/min, and full scale deflection on the chart set to 1 kg. The Instron cross head was set to reverse direction when the punch reached a deformation equivalent to approximately 15.0% of the sample thickness. The surface dimensions of all samples allowed the samples to fit completely under the Instron aluminum punch cross head which had a 5.7 cm diameter. This enabled a uniform stress to be applied and reduced the possibility of stress nonuniformities at sample edges. Instron punch and sample surfaces were lightly lubricated with Aquasonic coupling gel to prevent bonding between the sample and punch. All measurements were made at room temperature (22°C).

C. Constrained Young's Modulus

In elasticity measurements it is important that samples remain unconfined or unconstrained laterally as they are compressed axially. If samples are constrained laterally then the constrained YM (Y_b) will be larger than the unconstrained YM (Y_0). The constrained YM, Y_b, is related to the unconstrained YM, Y_0, according to

$$\frac{Y_0}{Y_b} = 1 - \frac{2\nu^2}{1-\nu} = C \tag{2}$$

where ν represents the Poisson ratio of the material. Therefore, C represents a correction factor between the constrained and unconstrained cases.

D. Soft Tissue Poisson Ratio

The Poisson ratio, ν, represents the degree to which a material expands laterally as it is strained (compressed) axially.

$$\nu = \left| \frac{\textit{lateral strain}}{\textit{axial strain}} \right|. \tag{3}$$

The Poisson ratio is limited to values between $0.0 < \nu < 0.5$ [15]. Materials with $\nu = 0$ are termed completely compressible, while materials with $\nu = 0.5$ are termed incompressible. Compressibility roughly represents the degree to which the material obeys a conservation of volume. When completely compressible materials are compressed axially, they do not expand laterally. When incompressible materials are compressed axially, their volume must remain constant and they expand laterally. Most soft tissues are considered as roughly incompressible materials and are assumed to have a Poisson ratio in the range of $0.45 < \nu < 0.49$ [6]. Intuitively, this means that if the tissue is compressed by one unit axially (in the z direction), then it must expand by roughly 0.5 unit laterally in both the x and y directions.

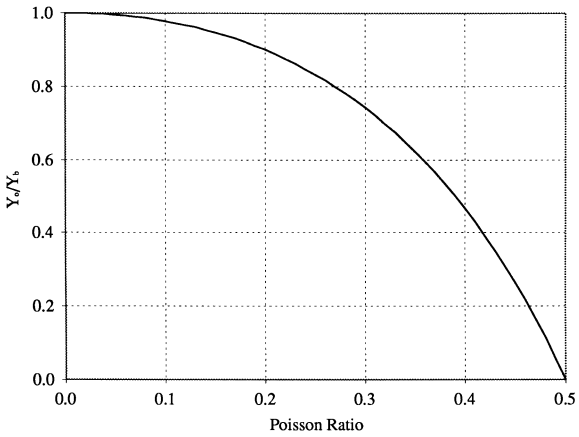

Fig. 1. Correction factor for constrained and unconstrained cases for different values of Poisson ratio.

E. Numerical Analysis

Since the ultrasound and Instron methods used different diameter punches, a numerical analysis needs to be performed to approximately account for the difference in punch sizes. For Instron measurements, the 5.7 cm diameter punch was always larger than any sample. Therefore, a uniform stress is assumed and no correction is needed. For the ultrasound measurements, the 3.18 cm diameter transducer does not completely cover all samples. Therefore, these measurements are modeled as the case of a small compressor above a large or semi-infinite medium.

In the Instron measurements all samples remained unconstrained laterally as they were compressed. In the ultrasound measurements, the tissue directly below the transducer is constrained by the surrounding tissue. Therefore, the ultrasound measurements can be equivalently modeled as the case of uniform compression with lateral confinement of samples. The ratio of Y_0 to Y_b is plotted in Fig. 1 for various values of ν. *In vivo* elasticity measurements will more closely resemble the constrained case.

Equation (2) provides a valid correction factor between the constrained and unconstrained cases assuming a small (point) compressor. As the compressor diameter increases relative to the sample dimensions, the correction factor approaches 1.0 and is equal to 1.0 when the compressor completely covers the sample surface. Equation (4) provides a correction between the constrained and unconstrained cases based on the ratio of compressor and sample diameters.

$$C(r) = 17 \exp^{-\frac{(r-1)}{35}}. \tag{4}$$

In (4), $1 < r < 100$ represents (in percent) the ratio of the compressor diameter to the sample diameter. The case $r = 100$ indicates that the compressor diameter and sample diameter are equal. Equation (4) was derived to satisfy the boundary conditions of $C(1) = 17$ and $C(100) = 1$. $C(1) = 17$ is the correction factor for a small (point) compressor assuming $\nu = 0.49$, while $C(100) = 1$ indicates no correction when the compressor diameter equals that of the sample.

For ultrasound measurements, a numerical analysis was performed using (2) and (4) to approximately account for the smaller diameter of the transducer. Although samples were rectangular, for the purposes of the numerical analysis, samples were assumed to be circular, with diameter equal to the largest surface dimension of individual samples. A Poisson ratio of 0.49 was assumed for these calculations.

III. Results

Typical Instron stress–strain curves from bovine LD muscle and liver and PVC sample A are shown in Fig. 2. This result was

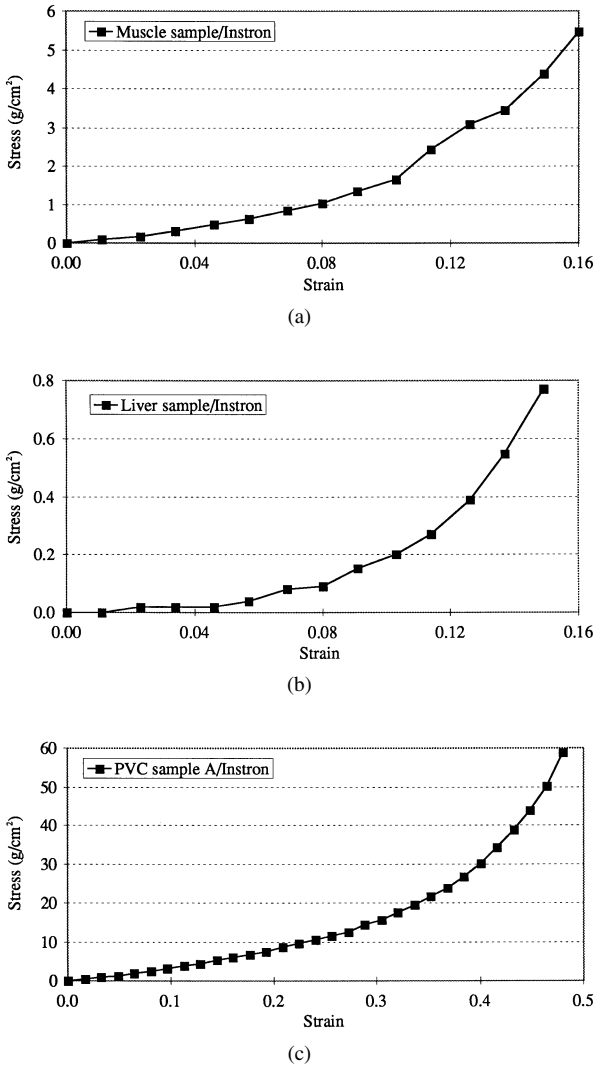

Fig. 2. Instron stress–strain curves for (a) muscle, (b) liver, and (c) PVC samples. YM values for samples were estimated from the slope of the linear region of curves (up to 5% strain for tissue samples and 10% strain for PVC) using a linear least squares fit.

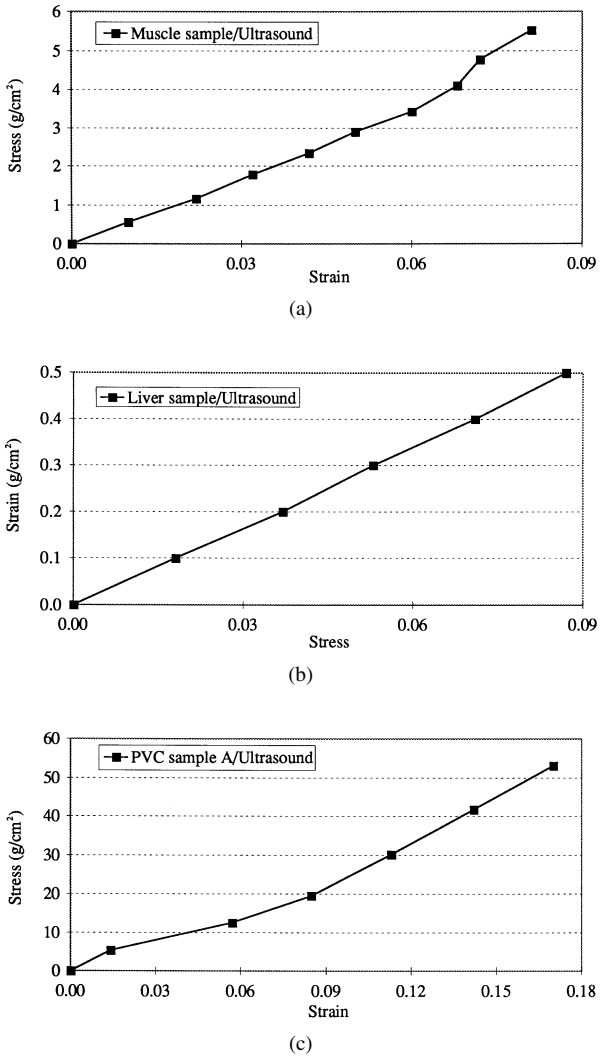

Fig. 3. Ultrasound stress–strain curves for (a) muscle, (b) liver, and (c) PVC samples. YM values for samples were estimated from the slope of the linear region of curves (up to 5% strain for tissue samples and 10% strain for PVC) using a linear least squares fit.

representative of all samples measured. The raw data produced by the Instron load cell are a plot of load (kg) versus displacement of punch (mm). The axes in Fig. 2 have been normalized to represent stress (g/cm^2) versus strain (dimensionless). The stress–strain curve obtained from ultrasound measurements of the same muscle, liver, and PVC samples is shown in Fig. 3.

The YM values for all samples measured are shown in Table I. All ultrasound YM values are unconstrained values calculated using the numerical analysis described in Section II-E. The average ultrasound and Instron YM of muscle samples was 2.12 $\pm$ 0.91 kPa and 1.53 $\pm$ 0.31 kPa, respectively, with an average relative error of 35%. The average ultrasound and Instron YM of liver samples was 0.62 $\pm$ 0.24 kPa and 0.94 $\pm$ 0.65 kPa with an average relative error of 29%. The average ultrasound and Instron YM of PVC samples was 33.77 $\pm$ 5.49 kPa and 39.97 $\pm$ 12.09 kPa with an average relative error of 16%.

TABLE I
YOUNG'S MODULUS VALUES OF SOFT TISSUES MEASURED USING ULTRASOUND AND INSTRON METHODS

Sample Type	Sample #	strain range for YM	Ultrasound YM (kPa)	R^2	Instron YM (kPa)	R^2	Relative Error
muscle	LD-122I	1-5%	3.15	0.981	1.80	0.986	75%
muscle	LD-122J	1-5%	1.74	0.995	1.60	0.985	9%
muscle	LD-122K	1-5%	1.46	0.984	1.20	0.994	22%
liver	125A	1-5%	0.35	0.988	0.43	0.770	19%
liver	126A	1-5%	0.79	0.993	0.72	0.847	10%
liver	117A	1-5%	0.72	0.949	1.68	0.927	57%
PVC	A	1-10%	30.9	0.957	33.7	0.998	9%
PVC	B	1-10%	30.7	0.932	32.3	0.973	5%
PVC	B2	1-10%	40.1	0.988	53.9	0.990	34%

IV. DISCUSSION

The exponential shape of the stress–strain curves in Fig. 2 is characteristic of many materials including soft tissues [7]. An initial linear elastic region of tissue stress–strain curves was observed for strains up to 5%. For tissue strains exceeding 10%, the deformation enters the nonlinear elastic region of the stress–strain curve. As the load is increased, the exponential stress–strain behavior suggests a strain hardening effect. This strain hardening has also been observed in elasticity measurements of anterior cruciate ligaments, the aorta, psoas major tendon, and pericardium [6], [7]. If the sample is compressed further, then it will eventually pass the elastic limit of the sample (largest applied stress for which the material will behave elastically) and enter the plastic region of the curve. At this point, it

has been observed that compression of samples can result in plastic deformation of the sample (sample does not return to its original shape even after the load is removed).

Relative errors in YM measurements were typically on the order of 25% (Table I). These errors were reduced significantly (nearly a factor of two) by performing a numerical analysis to account for differences in the measurement geometry (compressor diameters) of both methods. It should be remembered that differences in the YM of different tissues can span an extremely large dynamic range of elasticities [6], [16], so even with large errors, differential diagnosis based on elasticity imaging may still be useful. In addition, YM measurements of muscle, liver, and PVC showed agreement between the two methods as to which samples were the hardest (PVC) and softest (liver). Ultrasound elasticity measurements thus appear to provide reasonable consistency (high R^2 values indicating consistent YM estimates at different strain levels and ability to differentiate materials with one order of magnitude difference in YM, i.e., tissue and PVC), using Instron measurements as a reference. Nonlinear behavior of tissue samples may also contribute to differences in YM values. For example, PVC samples exhibited much larger linear elastic regions and relative errors for these samples was significantly lower (Table I). The true limits of the linear stress–strain region regions of the curves may also be influenced by the measurement geometry and sample sizes. The numerical analysis only approximately accounts for the difference in punch sizes. In addition, for Instron measurements, tissue samples may not be completely covered by the punch after some deformation since the samples expand laterally. Differences in measured YM values may also simply indicate a systematic difference or systematic experimental error between the two methods. For example, the Instron device exhibited poor sensitivity and resolution in measuring the lower stresses and strains of the tissue samples. In addition, it was difficult to reproduce exactly initial conditions (initial deformation or strain on samples at contact, etc.) for both sets of measurements.

We have observed that YM values computed by averaging measurements from multiple strain levels seem to significantly reduce uncertainties in YM values. Since the present ultrasound measurements are a simple case of elastography [13], where the Young's modulus is estimated from a single point on the stress–strain curve, it may be useful to perform elastography type measurements using multiple compression levels, taking care to maintain strains within the linear elastic region of tissue samples.

It is clear that the strain level applied in elasticity measurements is very important. Because of the strain hardening effect observed for soft tissues, strains outside the linear elastic region may not provide information about intended tissue material properties. YM values for large strains will tend to be positively biased and largely stress dependent. Previous studies have shown that large strains may be required in order to achieve a reasonable strain SNR [16]. In addition, clinical application of elasticity imaging and palpation will likely involve high strains. It should be understood that high strain elasticity measurements will provide information only about tissue pseudo-elastic properties [6] (elasticity of tissue at a specific stress or strain level). Lepetit *et al*. [8] indicate that whatever the measurement configuration (fibers transverse or parallel to compression), there is a critical compression ratio (CCR) which corresponds to the strain at which all fibers of collagen (connective) tissue are strained due to compression. However, for strains below the CCR, only myofibers contribute to resistance. Thus, the strain level also plays an important role in determining which structural properties of tissue are measured.

It is also important to consider the effect of preconditioning on tissue elasticity measurements. When cyclic loading/unloading tests are performed on soft tissues (ligament and tendon), hysteresis of tissue stress–strain curves can occur [6]. YM measurements performed on unconditioned tissue may be indicative of tissue pseudo-elastic properties and subject to large uncertainties since they are representative of tissue elastic properties during a particular loading cycle. By subjecting muscle and liver tissue to a specified preconditioning cycle (cyclic loading and unloading), the hysteresis effect can be reduced [6]. It may thus be necessary to first precondition tissue in practical elasticity measurement situations.

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