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Design and Testing of a Single-Element Ultrasound Viscoelastography System for Point-of-Care Edema Quantification

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Abstract

Management of fluid overload in patients with end stage renal disease represents a unique challenge where clinical practice still lacks accurate and objective measurement methods. Currently, peripheral edema is subjectively assessed by palpation of the patient's extremities, ostensibly a qualitative indication of tissue viscoelastic properties. New robust quantitative estimates of tissue fluid content would allow clinicians to better guide treatment, minimizing reactive treatment decision making. Ultrasound viscoelastography (UVE) can be used to estimate strain in viscoelastic tissue, deriving material properties that can help guide treatment. We are developing and testing a simple, low-cost UVE system using a single-element imaging transducer that is simpler and less computationally demanding than array-based systems. This benchtop validation study tested the UVE system feasibility by measuring the mechanical properties of a tissue-mimicking material under large strains. We generated depth-dependent creep curves and viscoelastic parameter maps of time constants and elastic moduli for the Kelvin model of viscoelasticity. During testing, the UVE system performed well with mean UVE-measured strain matching standard mechanical testing with maximum absolute errors less than or equal to 4%.

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Motion tracking showed high correlation and signal-to-noise ratios, indicating that the system is reliable.

Keywords

Creep experiment; edema; ESRD; point-of-care; poroelasticity; speckle tracking; strain imaging; ultrasound; viscoelastography

Introduction

End stage renal disease (ESRD) affects over 615,000 Americans with over 115,000 new cases in 2011 alone and costs totaling \$49.3 billion (U.S. Renal Data System 2013). There is no cure for ESRD, and the median wait time for renal transplant is 2.6 years (U.S. Renal Data System 2013). During that time, patients must undergo regular hemodialysis treatments, and physicians must regularly intervene to control a number of important deficiencies brought on by the loss of kidney function. Because the kidneys can no longer properly control filtration and fluid balance, careful monitoring is necessary to prevent fluid depletion or fluid overload. In particular, fluid overload partially manifested as peripheral edema can accompany life-threatening congestive heart failure. As such, edema is part of the standard clinical assessment for patients. Current monitoring techniques of peripheral edema rely primarily on palpation. Typically, a clinician grasps and compresses an edematous extremity with his or her thumb. The observed indentation is then rated on a semi-quantitative scale from 0 to 4+ to classify the degree of edema. This method is highly imprecise and relies largely on the experience and expertise of the clinician.

Fully quantitative methods based on new technologies have the potential to substantially improve patient fluid balance monitoring by providing a more consistent, observer-independent measurement. A number of studies have proposed the use of ultrasound elastography as a potential tool for measuring the mechanical properties of edematous tissue (Adriaenssens et al. 2012; Berry et al. 2008; Kruger et al. 2012; Righetti et al. 2007a). Ultrasound elastography is an imaging technique that allows accurate estimation of internal tissue strain from ultrasound radiofrequency (RF) data (Ophir et al. 1991). Elastography has excelled at imaging the mechanical properties of linearly elastic gelatin phantoms. Biological tissues however are rarely linearly elastic. They can more accurately be described using more complex poroelastic (Armstrong et al. 1984), viscoelastic (Fung 1993), or nonlinear elasticity models (Hall et al. 2011). Elastography techniques aimed at measuring these types of properties generally fall into three groups based on the material model: poroelastography, viscoelastography, and nonlinear elastography.

Poroelastography estimates the local effective Poisson's ratio of a material under compression (Berry et al. 2006a; Berry et al. 2006b; Konofagou and Ophir 1998; Righetti et al. 2004; Righetti et al. 2005; Righetti et al. 2007b). The feasibility of using poroelastography to quantify the properties and strain response of edematous tissue has been demonstrated in lymphedema patients (Berry et al. 2008; Righetti et al. 2007a). Viscoelastography, which has primarily been applied to the imaging of breast tumors, relies on spring-dashpot viscoelastic material models (Insana et al. 2004; Qiu et al. 2008; Sridhar

et al. 2007). Standard elastography techniques are first used to estimate the strain field in a compressed medium. The strain data are then fit with an appropriate material model to obtain elastic moduli and viscoelastic time constants that describe the material. Studies employing these techniques have primarily focused on viscoelastic contrast rather than the actual values of the material properties. The notable exception is the 2007 study by Righetti et al. (2007b), which reported the viscoelastic moduli and time constants of a tissue mimicking material found using axial strain elastograms. Nonlinear elastography uses the measured strain field as an input into an inverse problem (Samani and Plewes, D. 2004). The forward mechanical compression problem is solved using nonlinear material models, and the solution process is iterated until the forward model matches the measured strain field.

The vast majority of elastography studies are performed using small strains, typically less than 2% (for example, Berry et al., 2006b; Righetti et al., 2007b). At these strain values, the behavior of tissue is often described as nearly linear. Larger strains could result in a more pronounced nonlinear strain response. In addition, larger strains result in increased decorrelation of the ultrasonic speckle pattern thus reducing the elastographic signal to noise ratio (Cespedes 1993; Varghese and Ophir 1997). These challenges however do not negate the usefulness of elastography imaging in the nonlinear regime. The standard clinical exam for edema relies on large strains to differentiate grades of edema, and this convention may be useful for quantifying edema using elastography. Furthermore, errors resulting from speckle decorrelation at large strains can be overcome. By generating a series of incremental strain images from sequential ultrasound frames and then summing these incremental strains, one can arrive at the total strain while minimizing decorrelation errors (O'Donnell et al. 1994).

Another common feature of most elastography studies is the use of array transducers. These transducers generate two-dimensional images of the tissue in real time. This simple fact makes them generally more useful than single-element transducers, which can only image along one line of sight at a time. Point-of-care applications such as edema monitoring, however, may benefit from the decreased hardware complexity and computational expense associated with single-element systems. This does limit the clinician's ability to image spatial variations within the tissue, but this is largely irrelevant for the purposes of edema quantification where the goal is to estimate bulk properties of the tissue. We have developed a simple, portable ultrasound system specifically for this application. In this paper, we investigate the use of this single-element system to quantify the viscoelastic properties of a tissue-mimicking material subjected to large strains.

Methods and Materials

To demonstrate the feasibility of using UVE measurements to estimate the fluid content of edematous tissue, we conducted two similar experiments. One experiment was a standard creep compression test; the other was a creep compression test with simultaneous UVE measurements. The standard creep compression test served as a gold standard comparison for our UVE measurements. In this section, we outline the procedure used to obtain and process data for each of these experiments.

In all experiments, we used cylindrical samples of extra-firm tofu (Nasoya, Ayer, MA) as an edematous tissue-mimicking phantom. Cylinders were cut from a single block of tofu using a 32 mm diameter tube of sharpened plastic at room temperature. Next, each cylinder was trimmed to a height of 20 ± 1 mm. This yielded a total of 12 samples per block of tofu. The samples were relatively uniform in structure although some macroscale variations in the structure (e.g. larger pores) were visibly present, as might be expected of a randomly porous material such as tofu. The samples were stored at room temperature for the course of the experiment (approximately 3 hours) in the original holes from which they were cut in the tofu block and submerged in the original preservation fluid from the tofu packaging. This ensured that the samples experienced constant structural and osmotic conditions when not in use.

During testing, individual tofu samples were submerged in a water tank and immediately subjected to a constant, step-like loading of 1.0 N (a mechanical creep test). A single-axis programmable test stand (ESM301L, Mark-10, Copiague, NY) and digital force gauge (Series 5, Mark-10, Copiague, NY) allowed for precise control of the loading. To create the step-like loading, the test stand subjected the samples to a steep ramp compression of 50 mm/min until the force gauge measured 1.0 N. After this point, the ramp loading ceased, and the test stand adjusted the loading to maintain a constant 1.0 N force for five minutes while data were collected. A schematic of the apparatus is shown in Fig. 1. A fixture containing a single-element, 8 MHz focused ultrasound transducer made contact with the tofu samples and distributed the load uniformly across the surface of the sample. For standard creep compression tests, we used MesurGauge software (Mark-10, Copiague, NY) to collect displacement data from the test stand. As a side note, the loading produced a steady state strain of approximately 10%. This constitutes a large strain at which nonlinear effects are not negligible. We accounted for this by using finite strain theory in our analysis.

Although all of our experiments used the same brand and type of tofu, we did notice large variations between different blocks. Because of this, we treated each pack as a separate data set and drew comparisons between standard creep compression and UVE tests for each block individually (3 total blocks). Because large strains can cause irreversible mechanical changes to the porous structure of the tofu and viscoelastic materials exhibit strong effects from loading history (Fung 1993), each tofu cylinder cut from a block was loaded only once. Half of the cylinders underwent the standard creep compression test, and the other half underwent the UVE test.

For UVE tests, we collected radio frequency (RF) ultrasound data using an in-house single-element ultrasound data acquisition system (Fig. 2). This system was designed with point-of-care applications in mind where conventional high frame rates are not required, and minimizing device complexity is desirable. The design of this ultrasound system minimizes the dedicated hardware necessary compared with typical ultrasound systems. A 32-bit MIPS microcontroller (MCU) running at 80 MHz controls all the high-level functions of the device, while a complex programmable logic device (CPLD) is responsible for low-level sequencing of the ultrasound sub-systems. The MCU is responsible for configuring the CPLD with the specific parameters necessary to create the required pulse-receive sequence, for initiating the pulse/acquisition sequence, and for reading the received RF data via an 8-

bit data bus interface. Specifically, the CPLD controls the transmit pulse duration and timing for the transmit circuit control and drivers consisting of a power amplifier (PA) and drivers. The system is configured to drive a single-element 8 MHz transducer (Acetara, Longmount, CO) at a frame rate of 16 kHz. The CPLD also controls the transmit/receive switch (T/R) as well as a programmable time-gain amplifier (TGA) and reads samples from the 3 MSPS 12-Bit ADC over a 48 MHz serial peripheral interface (SPI) bus. The MCU controls the demodulator (DeMod), which is followed by integrated low pass filters to provide noise removal and control of the RF signal acquired by the ADC.

In our experiments, we acquired the analog RF signal output from a low-pass filter following the transmit/receive switch. We then applied further filtering to the RF signal using an external analog filter board. The filter board consisted of a one-pole high pass filter with a 100 Hz cutoff frequency in series with a four-pole low pass Bessel filter with a 10 MHz cutoff frequency. The filtered RF signal was digitized at a sampling rate of 100 MHz using an oscilloscope (DSO7032B, Agilent Technologies, Santa Clara, CA). Data acquisition was controlled with a MATLAB (The Mathworks, Natick, MA) script on a Windows-based workstation. The MATLAB script triggered acquisitions of 1 ms windows of data from the oscilloscope via USB at a rate of approximately 4 Hz. Each 1 ms acquisition from the oscilloscope contained multiple ultrasound A-lines.

Following data collection, the digitized RF acquisitions were segmented into individual A-lines, and A-lines within each 1 ms window were averaged together. The averaged A-lines were then filtered with a second-order Butterworth band-pass filter with cutoff frequencies of 6 and 10 MHz. The final averaged and filtered RF signals were then converted to analytic signals using the Hilbert transform. These analytic signals were used to estimate the axial displacement of the tofu as a function of depth and time using an exhaustive-search speckle tracking algorithm with a normalized cross-correlation coefficient maximum likelihood estimator. The speckle tracking kernel was 1.5 mm in length, and adjacent kernels were overlapped 50%. The speckle tracking algorithm utilized a search region of 0.5 mm in both the positive and negative axial directions to coarsely estimate the most likely displacement of each kernel. Following coarse displacement estimation, the nearest zero crossing of the analytic signal phase was computed and defined as the final displacement estimate. The resulting displacement fields were cropped to include only depths of 5-15 mm (to exclude near field and far field), processed with a 2.3 mm local outlier filter (Westerweel and Scarano 2005), and smoothed with a 1 mm median filter along the axial direction. The differential Green-Lagrange strain was computed from an ensemble average of the displacement fields using a simple finite difference (Eq. 1). In Eq. 1, w_k^n denotes the axial displacement at position k for ultrasound frame n , and z_k^0 denotes the axial position k in the reference (uncompressed) configuration. The Green-Lagrange strain is a metric used to describe large strains, usually those greater than 5%. We chose to use this metric to analyze our data since the measured strains were on the order of 10-15%. By integrating the differential strain function in time, we obtained the time-dependent Green-Lagrange strain function (Ammann et al. 2005). Creep curves were generated for both standard creep compression data and UVE data. Standard creep curves were computed from the

displacement of the test stand, and UVE creep curves were generated by averaging the UVE strain function at all depths.

$$dE_k^n = \frac{\partial w}{\partial z} + \frac{1}{2} \left(\frac{\partial w}{\partial z} \right)^2 \approx \frac{w_k^n - w_{k-1}^n}{z_k^0 - z_{k-1}^0} + \frac{1}{2} \left(\frac{w_k^n - w_{k-1}^n}{z_k^0 - z_{k-1}^0} \right)^2 \quad (1)$$

The mechanical properties of the tofu were estimated by assuming that a modified version of the Kelvin (standard linear solid) viscoelastic model (Fig. 3) could describe the material (Fung 1993). This model is commonly used to model the behavior of viscoelastic materials in one dimension. The Kelvin model describes a solid as a combination of elastic (spring) and viscous (dashpot) elements. The strain ε in a Kelvin solid in response to a constant stress σ_0 applied impulsively at time $t = t_0$ is given by Eq. 2 (that is, applied as a Heaviside step function $H(t - t_0)$). The response depends upon three material properties: the elastic moduli E_0 and E_1 and the time constant $\tau = E_1/\eta_1$. Note that the time constant contains the viscous constant η_1 . In tissue, this means that the time constant carries information about fluid content and tissue porosity.

$$\varepsilon(t) = \sigma_0 \left[\frac{1}{E_0} + \frac{1}{E_1} \left(1 - e^{-\frac{t}{\tau}} \right) \right] H(t - t_0) \quad (2)$$

We have added a slight modification to the Kelvin model to account for the effect of the Boussinesq problem. This effect describes the decrease in stress along the depth of a compressed elastic material. The modification we use is to replace the instantaneous constant stress σ_0 with a depth-dependent stress $\sigma(z)$ given by

$$\sigma(z) = \sigma_0 \left(\frac{z^3}{(a^2 + z^2)^{3/2}} - 1 \right), \quad (3)$$

where a is the radius of the compressor and z is depth. The Boussinesq problem is discussed in more detail by Love (1929) in the general context, and elastography studies have previously used Eq. 3 to model its effects (Ophir et al. 1991; Ponnekanti et al. 1992).

The modified model (Eq. 4) was fit to the first 60 seconds of the UVE ensemble creep curves at each depth using a nonlinear least squares trust-region fitting procedure (MATLAB Curve Fitting Toolbox, The Mathworks, Natick, MA). We chose to only include the first 60 seconds in the fit since this is likely the longest possible time we would expect to apply compression in clinical settings. The fitting procedure yielded three material parameters for each data set – two elastic moduli (E_0 and E_1) and one time constant τ . The instantaneous elastic modulus E_0 was obtained from the center depth of the tofu ($z = 10$ mm) and used as a fixed value for all other fits, thus reducing the number of fit parameters to two (E_1 and τ).

$$\varepsilon(t, z) = \sigma(z) \left[\frac{1}{E_0} + \frac{1}{E_1} \left(1 - e^{-\frac{t}{\tau}} \right) \right] H(t - t_0) \quad (4)$$

Results

Fig. 4 shows the ensemble Green-Lagrange strain as well as the minimum correlation image for each of the three blocks of tofu used. The Green-Lagrange strain is displayed as a set of creep curves at various depths throughout the tofu. The minimum correlation images are displayed in an m-mode configuration with time on the horizontal axis and depth on the vertical axis. The ensemble strain shows clear depth dependence with larger strains closer to the upper surface (where the stress was applied) decaying to smaller strains nearer to the lower surface. This is expected as a result of the Boussinesq effect.

At each depth, we see that the creep curves generated resemble the rising exponential function modeled by the modified Kelvin model (Eq. 4). To illustrate this, Fig. 5 shows some examples of the UVE strain and corresponding curve fits at depths of 5, 7.5, 10, 12.5, and 15 mm from one tofu block (labelled C in Fig. 4). From these curve fits, we obtained time constants and elastic moduli for each depth (Fig. 6). The time constant τ remains relatively constant across the depth of the tofu sample with a mean value of approximately 7-10 s. The elastic modulus E_1 shows some depth dependence ($p < 0.01$) in all cases with a magnitude on the order of 5-15 kPa. The instantaneous elastic modulus E_0 for the three blocks of tofu tested were 137 MPa, 1.85 MPa, and 185 MPa, respectively.

To further describe the depth dependent strain and aid in validating this UVE system, it is useful to compare the steady state strain at each depth to a theoretical prediction (Equation 4). Figure 7 shows the mean steady state strain (at time $t = 300$ s) as a function of depth in each tofu block. For comparison, it also shows a theoretical prediction based on the Boussinesq effect. The theoretical prediction of the depth-dependent strain is similar to Equation 2, differing only in that it specifies the strain ε instead of the stress σ (Ponnekanti et al. 1992). Note that we have used the mean steady state strain obtained from the standard creep tests as the “applied strain” ε_0 in the theoretical model. The behavior of the UVE measured strain does differ somewhat from the theory, but this may be due to nonlinear effects from large strain and viscoelasticity, both of which violate some assumptions of the theoretical model. Overall, the UVE measurements and theoretical predictions seem to follow the same general trend, indicating that the depth-dependence is likely a result of the Boussinesq effect. This also justifies our use of the Boussinesq effect in our curve fitting.

$$\varepsilon(z) = \varepsilon_0 \left(\frac{z^3}{(a^2 + z^2)^{3/2}} - 1 \right) \quad (5)$$

The correlation coefficient produced at each point in space and time by the speckle tracking algorithm provides a useful quality metric for the strain estimation. Each tofu sample in an ensemble yielded a correlation image. The minimum correlation of all displacement

estimates included in an ensemble was chosen as a conservative quality metric (Fig. 4). Regions of low correlation, defined here as less than or equal to 0.9, are indicative of large changes in speckle characteristics between consecutive frames. In all experiments, we observed some low correlation during the initial compression. This is likely due to the higher strain rate causing larger changes in the speckle pattern between ultrasound frames. Speckle tracking of tofu block B resulted in noticeably lower correlations (shown in purple) throughout the experiment. Over the course of the experiments, tracking of tofu blocks A and C resulted in a mean estimated elastographic signal-to-noise ratio (SNR_s) (Lindop et al. 2008; Treece et al. 2011) of 30.6 and 30.5 dB, respectively, while tofu block B resulted in a mean SNR_s of 28.2 dB.

As a final metric of quality, we compared the creep curves obtained by standard creep tests to those obtained by averaging the UVE generated creep curves over all depths at each time point (Fig. 8). In all three cases, UVE underestimated the mean strain with a maximum absolute error of approximately 4% for tofu block B and 2% for tofu blocks A and C.

Discussion

The data suggest that our UVE method can accurately estimate strain, including depth dependence, in a viscoelastic tissue mimicking material. This is most clear when comparing the depth-averaged UVE generated creep curves with the results of standard mechanical creep testing (Fig. 8). The small errors (2-4%) show that in an average sense, we can accurately measure the compression-induced strain in tofu samples. More importantly though, we can also accurately quantify depth dependent changes in strain consistent with the Boussinesq effect. As shown in Fig. 7, the steady state strain in each tofu block decreased with depth at a rate similar to the theoretical predictions of the Boussinesq effect (Eq. 5). Given the assumptions of the Boussinesq problem (linear elasticity, small strains), we should treat it more as a general guide in analyzing our results. Specifically, we measured depth dependent strain in a viscoelastic material under large strains. In addition, the random porous structure of tofu could lead to spatial variations that cannot be predicted theoretically. While the UVE measurement shows much more variation and noise than the theoretical prediction, the same general trend is observed. This justifies our use of Eq. 3 in our curve fitting procedure and viscoelastic parameter estimates.

Our UVE method also performed well when considering two quality metrics: the speckle tracking correlation coefficient and the elastographic signal-to-noise ratio. As mentioned earlier, decreased correlation is indicative of changes in the speckle pattern and therefore less reliable displacement estimation. This manifests itself as errors in the strain field which will affect the viscoelastic curve fits. In Fig. 4, we observed that the high initial strain rates during the steep compression may have caused decreased correlation. As seen in Fig. 8, however, this initial decreased correlation did not seem to negatively affect the UVE measured strains, at least in tofu blocks A and C. We do see even lower correlation and SNR_s for tofu block B at all times, especially for depths below 10 mm. This is the most likely mechanism for the strain measurement errors we see in tofu block B (Fig. 8).

The decreased correlation in tofu block B also may explain some of the differences in the estimation of the instantaneous elastic modulus E_0 . When performed for data from tofu block B, the curve fitting procedure estimated a value of E_0 roughly two orders of magnitude smaller than blocks A and C (1.85 MPa versus 137 MPa and 185 MPa). The instantaneous elastic modulus describes the initial deformation of the material. As such, the decreased correlation seen in block B, especially during the early compression, is likely the source of the measured differences between tofu blocks. This error does not necessarily represent a lack of robustness in this UVE method. On the contrary, the method seems quite robust against differences in the instantaneous elastic modulus E_0 , as the time constants and elastic moduli E_1 obtained for all three tofu blocks are similar.

The previous analyses suggest successful benchtop validation for our point-of-care UVE system. We have shown that depth dependent maps of tissue strain and viscoelastic properties can be generated for a tissue mimicking material. Although our laboratory tests demonstrate the possible usefulness of our point-of-care UVE system, clinical studies must be able to show the system can be used to improve patient care. That is, UVE measurements of tissue time constants and elastic moduli must be able to guide clinical decision making by providing a consistent, quantitative metric for grading peripheral edema. Ideally, this would take the form of an estimated volume of mobilizable fluid that could be removed from the edematous limb to reach dry weight. Theoretically, the time constant should provide some insight into excess fluid volumes. Such an analysis was outside the scope of this study but will be the focus of future clinical studies that may investigate the correlation between UVE-measured time constants and elastic moduli and the degree of clinical edema observed in patients.

The transition from the controlled laboratory environment to the clinic raises a number of challenges for this imaging system. Perhaps chief among these is the sensitivity to poorly defined geometry within the edematous limb. In vivo, the lack of a 2D image from this single-element ultrasound system may make it difficult for clinicians to identify suitable regions of interest for UVE edema measurements. Additionally, the test geometry described in this study, where the tissue is compressed between two hard, parallel surfaces, may not always be available clinically. We envision this system being used to take UVE measurements on the lower calf of patients, where the tibia may provide a hard lower surface for the compression. In general, however, this will not provide a parallel surface to the upper compressor and may result in out-of-plane motion that may confound this one-dimensional measurement through large decorrelation errors. The two problems previously mentioned are likely surmountable provided the clinician receives adequate training in choosing a region of interest and applying the compression. Future clinical studies mimicking the image processing algorithms of our system (tracking motion along a single A-line) using an array transducer could clarify the extent of these challenges. Finally, tissue is not isotropic, and slip boundaries between different layers of tissue (skin, fat, fascia, muscle, bone, etc.) may lead to discontinuities in the speckle tracking process. This will likely manifest itself as errors in the depth-dependent creep curves. This can possibly be compensated for by a more clever integration of the differential Green-Lagrange strain field that integrates along material path lines defined by the displacement estimates. Future clinical studies will explore the impact of these challenges on our system for UVE measurements in vivo.

Other mechanical parameters may prove to be useful to classifying edema and may be less susceptible to errors when compared to elastic and viscous moduli. The compressibility of a material, defined as the volumetric response to a pressure change, naturally lends itself to a description of edematous tissue. In response to an applied stress, fluid movement out of edematous tissue leads to a volume change in the compressed region of interest. This volumetric response can be described as a function of Poisson's ratio or measured directly. Poroelastography methods provide a natural avenue for determining the Poisson's ratio and the Poisson's ratio time constant. The application of these methods to edema monitoring may therefore lead to useful metrics for tissue fluid content.

Conclusions

We are developing and testing a simplified single-element viscoelastography system for point-of-care edema monitoring. This system has the potential to reduce hardware complexity as well as computational expense. Using our system, we measured the viscoelastic properties of a tissue-mimicking material (tofu) in creep tests under large strains, as would be used clinically to diagnose edema. The Green-Lagrange strain creep curves generated for all depths in the tofu samples match the expected mechanical response described by the Boussinesq effect and could be described accurately by the Kelvin (standard linear solid) model. Using this model, we demonstrated that our UVE system was capable of generating depth-dependent maps of viscoelastic material parameters including time constants and elastic moduli. A quality analysis of our results showed that the speckle tracking algorithm produced a good estimate of the internal displacement field with high correlation and SNR_s. Estimates of the mean creep response were highly sensitive to tracking errors, and experiments with lower SNR_s showed poor agreement with the creep response measured using a standard creep compression test. The estimates of viscoelastic time constants and elastic moduli, however, were quite robust to these errors, producing similar estimates despite differences in SNR_s. Our results suggest successful benchtop validation of our UVE method. Future clinical studies will be required to fully establish the feasibility of using this method and ultrasound system for edema monitoring. This translation to the clinic will bring with it a number of challenges, but the results of this work provide a good foundation for future studies, which will investigate the relationship between UVE measurements and current methods of assessing peripheral edema.

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Fig. 1. Schematic of our ultrasound viscoelastography system showing the mechanical test stand, single-element ultrasound transducer, and a tofu sample under test as well as block diagrams for the electronics and acquisition hardware. Note that the mechanical test stand could be replaced with a portable or hand-held pressure source in the clinic.

Fig. 2. Block diagram of the portable ultrasound board used in our ultrasound viscoelastography experiments.

Fig. 3.

Spring-dashpot representation of the Kelvin (standard linear solid) viscoelastic model used to describe both the ultrasound viscoelastography and standard creep measurements.

Fig. 4.

Ensemble Green-Lagrange strain creep curves and minimum correlation images obtained from samples in three blocks (A-C) of extra firm tofu. Ensemble strain creep curves are computed from an ensemble mean of measured displacement fields ($n = 5, 6, 6$ for blocks A-C, respectively). These show a clear depth dependence in the mechanical response of the tofu samples. The minimum correlation images (rendered in an m-mode configuration) show the pointwise minimum of all computed correlation coefficients in each ensemble. In all cases (A-C), we found high correlation with slightly less quality in tofu block B.

Fig. 5.

Example UVE creep curves at depths of 5, 7.5, 10, 12.5, and 15 mm from tofu block C as well as curve fits using the Kelvin model of viscoelasticity. These curve fits were used to estimate the viscoelastic properties of the tofu samples at all depths.

Fig. 6.

Viscoelastic time constant and elastic modulus estimates obtained by fitting the Kelvin viscoelastic model to the Green-Lagrange strain creep curves at all depths in tofu blocks A-C. Time constants (black solid) remain relatively constant through the entire depth of the tofu with a mean value (gray dashed) of 8-10 s. The elastic modulus E_1 showed a depth dependence, increasing slightly with depth with values on the order of 5-15 kPa. Outliers, defined as points at which the R^2 value of the fit was less than 0.9, are shown as lone points with their locations indicated on the x-axis as well.

Fig. 7.

Comparison of the steady state strain as measured using UVE (black) to the theoretical depth dependence expected from the Boussinesq effect (gray). Despite some variation, which may be due to the viscoelastic properties and nonlinear strains used, we see that our results follow the general trend of the theory. This justifies our use of the Boussinesq effect in our analysis.

Fig. 8.

Comparison of mean creep curves from the standard creep compression test (black dashed) with those obtained by averaging the UVE measured strain over the depth of the sample (black solid) for tofu blocks A-C. The individual realizations ($n = 6$) of the standard creep measurements for each tofu block are shown as well (gray dashed).