Estimation of mechanical properties of a viscoelastic medium using a laser-induced microbubble interrogated by an acoustic radiation force^{a)}

Sangpil Yoon

Department of Mechanical Engineering, The University of Texas at Austin, Austin, Texas 78712-1063

Salavat R. Aglyamov, Andrei B. Karpouk, Seungsoo Kim, and Stanislav Y. Emelianov^{b)}

Department of Biomedical Engineering, The University of Texas at Austin, Austin, Texas 78712-0238

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An approach to assess the mechanical properties of a viscoelastic medium using laser-induced microbubbles is presented. To measure mechanical properties of the medium, dynamics of a laser-induced cavitation microbubble in viscoelastic medium under acoustic radiation force was investigated. An objective lens with a 1.13 numerical aperture and an 8.0 mm working distance was designed to focus a 532 nm wavelength nanosecond pulsed laser beam and to create a microbubble at the desired location. A 3.5 MHz ultrasound transducer was used to generate acoustic radiation force to excite a laser-induced microbubble. Motion of the microbubble was tracked using a 25 MHz imaging transducer. Agreement between a theoretical model of bubble motion in a viscoelastic medium and experimental measurements was demonstrated. Young's moduli reconstructed using the laser-induced microbubble approach were compared with those measured using a direct uniaxial method over the range from 0.8 to 13 kPa. The results indicate good agreement between methods. Thus, the proposed approach can be used to assess the mechanical properties of a viscoelastic medium. © 2011 Acoustical Society of America. [DOI: 10.1121/1.3628344]

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I. INTRODUCTION

In laser-based ophthalmic microsurgery, micrometer-size bubbles are used to precisely cut tissue in the eye.^{1–5} During the laser-tissue interaction, the focused laser radiation in tissue is absorbed, and a microbubble is formed where the intensity of the electromagnetic field exceeds the threshold of optical breakdown.^{5,6} One of the applications of laser-induced microbubbles in ophthalmology is refractive vision correction surgery to correct myopia, hyperopia, and astigmatism.^{5,7} Accurate corneal flaps can be created by using laser-induced microbubbles, providing a better surgery outcome.^{8,9}

While laser-tissue ablation and associated formation of microbubbles play an increasingly important role in laser-based microsurgery, microbubbles could also be used to obtain information about elastic properties of ocular tissues.^{10,11} According to the most widely accepted theory of presbyopia, the age-related loss of accommodation is attributed to gradual loss of lens elasticity. Furthermore, there is evidence that nuclear cataract lenses are generally harder than normal lenses.^{12–14} Thus, observing the changes of tissue properties may be used as a tool to diagnose disease and improve the outcome of treatment. Due to high acoustic reflectivity on the bubble surface, a microbubble-based acoustic radiation force technique can provide greater radiation force than an absorption-based acoustic radiation force technique.^{15–17} Therefore, displacement variations inside tis-

sue can be effectively generated by the combined method. External local excitation permits the estimation of the local mechanical properties of tissue based on the analysis of the motion of a laser-induced microbubble because the dynamics of the motion of a microbubble are defined by the properties of the surrounding tissue.¹⁸

A number of methods have been developed to estimate the mechanical properties of lenses: ultrasonic characterization of the lens using ultrasound wave attenuation;¹⁴ compression tests;¹⁹ application of radial force;^{20,21} hydrostatic or automated guillotine tests;^{13,22} uniaxial test;²³ cone penetration test;²⁴ and dynamic mechanical analysis.^{25–27} The results of these measurements demonstrate that elasticity of the whole lens increases with age and the nucleus becomes stiffer than the cortex. It is reported that the lens has a Young's modulus of several tens of Pa to tens of kPa.^{10,11,20,21,24,27} However, most of these techniques to measure lens elasticity assume direct mechanical testing and usually can be used only *in vitro*. Among various techniques to measure mechanical properties of tissues noninvasively, radiation force has investigated greatly during last few decades as a means of a palpation tool for imaging soft tissues where external forces cannot reach. Recent applications have opened a variety of areas including shear wave elasticity imaging,¹⁵ acoustic radiation force impulse imaging,^{28–34} supersonic shear imaging,^{35–37} sonorheometry,^{38–42} and vibroacoustography.^{43–48}

By combining microbubbles created by laser-induced optical breakdown and acoustic radiation force, microbubble-based acoustic radiation force was introduced as a technique to remotely measure the localized viscoelastic properties of the lens.^{10,11,49–51} In that approach, laser-induced microbubbles were displaced using a long acoustic pulse to interrogate

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^{b)}Author to whom correspondence should be addressed. Electronic mail: emelian@mail.utexas.edu

the mechanical properties of *ex vivo* porcine and human lenses.^{10,11} Elastic properties were evaluated based on the amplitude of the bubble displacement from an equilibrium position. Such an approach assumes that the acoustic radiation force on the bubble surface is known or deduced by experiments or analytical calculations. For example, the radiation force can be estimated by matching the measured displacement of a laser-induced microbubble in a human lens with the same displacement observed in a phantom study.^{10,11} However, the evaluation of the magnitude of radiation force is generally a challenging task due to the attenuation of ultrasound waves in tissue and unknown differences in acoustic impedances between tissue and the microbubble. In this paper, we propose to use a short acoustic impulse to estimate elasticity using time characteristics of the microbubble's motion.

In our previous studies we theoretically investigated the motion of round objects such as solid spheres and bubbles within a viscoelastic medium subjected to an acoustic radiation force.¹⁸ Static and transient responses of these round objects were obtained using linear approximation and analysis in both the frequency-domain and time-domain. The developed theoretical model was verified using experimental measurements on various solid spheres. The local elastic properties of the surrounding material were estimated from the temporal characteristics of the sphere's motion and were found to be in good agreement with direct measurements.^{52,53}

In this paper, we extend our research by employing laser-induced microbubbles as targets for acoustic radiation force in order to assess the mechanical properties of tissue-mimicking phantoms. We measured the maximum displacement as well as the time it took to reach that value of a laser-induced microbubble under the acoustic radiation force. Reconstruction of the Young's modulus of the phantom was performed by comparing experimentally measured times of maximum displacement of a microbubble with the values derived from a theoretical model of microbubble motion. When comparing the two, the scaling factor of acoustic radiation force was chosen to induce the best fit between the theoretical and measured data. Using this method, there was no need to measure the acoustic radiation force delivered to a laser-induced microbubble. Experiments were performed on tissue-mimicking phantoms with Young's moduli from 0.8 to 13 kPa, which approximately corresponds to the elastic properties of the crystalline lens obtained from literature.^{10,11,19,27,54,55}

II. THEORY

In our theoretical model, we assume that the surrounding medium is linear, viscoelastic, homogeneous, and isotropic. We further assume that the medium is incompressible as is the case for most soft tissues.⁵⁶ The problem at hand is axisymmetric and no force dependence in the azimuthal direction exists. Therefore, the deformation of microbubble is symmetric along the axial direction.

The equation of motion for the incompressible medium⁵⁷ in time-domain is

$$-\nabla P + \mu \nabla^2 \mathbf{U} + \eta \nabla^2 \frac{\partial \mathbf{U}}{\partial t} = \rho \frac{\partial^2 \mathbf{U}}{\partial t^2}, \quad (1)$$

where P is internal pressure, $\mathbf{U}$ is the displacement vector, μ and η are shear elastic modulus and viscosity, respectively, ρ is medium density, and t is time. Young's modulus (E) and shear elasticity modulus (μ) have a simple relation for homogeneous isotropic materials such that $E = 2\mu(1 + \nu)$, where ν is Poisson's ratio. For an incompressible medium where Poisson's ratio is 0.5, Young's modulus is three times larger than the shear modulus. The polar axis of the spherical system of coordinates (r, θ, ϕ) is along the force vector (i.e., an angle θ is between a radius vector and displacement), and $\mathbf{U} = (U_r, U_\theta, 0)$. The external force applied to the displaced spherical object is¹⁸

$$\mathbf{F}^{(ext)} = -2\pi R^2 \int_0^\pi (\sigma_{rr} \cos \theta - \sigma_{r\theta} \sin \theta) \sin \theta d\theta, \quad (2)$$

where σ_{rr} and $\sigma_{r\theta}$ are stress tensor components at the surface of the object:

$$\begin{aligned} \sigma_{r\theta} &= \left(\mu + \eta \frac{\partial}{\partial t} \right) \left(\frac{\partial U_\theta}{\partial r} - \frac{U_\theta}{r} + \frac{1}{r} \frac{\partial U_r}{\partial \theta} \right), \\ \sigma_{rr} &= -P + 2 \left(\mu + \eta \frac{\partial}{\partial t} \right) \frac{\partial U_r}{\partial r}. \end{aligned} \quad (3)$$

The boundary conditions at the bubble surface ($r = R$) are

$$\sigma_{r\theta} = 0, -\sigma_{rr} + P_r = P_0, \quad (4)$$

where R is the radius of bubble, P_r is acoustic radiation pressure acting on the surface of the bubble, and P_0 is an internal gas pressure.¹⁸ Since pressure P and, consequently, σ_{rr} are defined up to a constant, the internal gas pressure P_0 may be set equal to zero.

The solution of Eqs. (1) and (3) is found in the frequency domain, and displacement of a microbubble in time domain is obtained by taking inverse Fourier transform from the spectral solution. The frequency-domain representation of Eq. (1) is given by

$$-\nabla p + (\mu - i\omega\eta) \nabla^2 \mathbf{u} = -\rho\omega^2 \mathbf{u}, \quad (5)$$

where p and $\mathbf{u}$ are the Fourier transforms of P and $\mathbf{U}$, ω is an angular frequency.

In this study we consider that the external force applied to the bubble $\mathbf{F}^{(ext)}$ is impulsive:

$$\mathbf{F}^{(ext)} = \begin{cases} F_0 & 0 \leq t \leq t_0, \\ 0 & t \geq t_0, \end{cases} \quad (6)$$

where t_0 is the duration of acoustic radiation pulse. The frequency domain representation of Eq. (6) is

$$\mathbf{F}_w^{(ext)} = -\frac{iF_0}{\omega} (e^{i\omega t_0} - 1). \quad (7)$$

We consider u_ω as a spectral component of low frequency displacement and are looking for the bubble surface displacement components (for $r = R$) in the form

$$\begin{aligned} u_r &= u_w \left(1 - \frac{1}{3} ikR \right) \cos \theta, \\ u_\theta &= -\frac{1}{2} u_w \left(1 + \frac{1}{3} ikR \right) \sin \theta, \end{aligned} \quad (8)$$

where $u_w = [-(ik/R)\tilde{a}e^{ikR}]$ is the low frequency displacement,¹⁸ k is the wave number of the shear wave and defined as $k = \omega/(c_t\sqrt{1 - i\omega\eta/\mu})$ and $c_t = \sqrt{\mu/\rho}$. The sign of k is defined by the condition $\text{Im}(k) > 0$ because displacement of medium must approach zero away from the bubble. The constant $\tilde{a}$ is defined by the boundary conditions in Eq. (4). Taking into account the boundary conditions in Eq. (4) as well as equations Eq. (2) and Eq. (3), the relationship between the spectral components of the displacement and force is

$$F_w^{(ext)} = 4\pi(\mu - i\omega\eta)Ru_w \left(1 - ikR - \frac{1}{6}k^2R^2 + \frac{1}{18}ik^3R^3 \right). \quad (9)$$

By combining algebraic equations (7) and (9), the solution in terms of u_w is given by

$$u_w = -\frac{iF_0(e^{i\omega t_0} - 1)}{4\pi\omega(\mu - i\omega\eta)R(1 - ikR - \frac{1}{6}k^2R^2 + \frac{1}{18}ik^3R^3)}. \quad (10)$$

By taking inverse Fourier transform, time domain components U_r and U_θ are obtained:

$$\begin{aligned} U_r &= -\frac{iF_0 \cos \theta}{12\pi R} \mathcal{F}^{-1} \left[\frac{(e^{i\omega t_0} - 1)(3 - ikR)}{\omega(\mu - i\omega\eta)(1 - ikR - \frac{1}{6}k^2R^2 + \frac{1}{18}ik^3R^3)} \right], \\ U_\theta &= \frac{iF_0 \sin \theta}{24\pi R} \mathcal{F}^{-1} \left[\frac{(e^{i\omega t_0} - 1)(3 + ikR)}{\omega(\mu - i\omega\eta)(1 - ikR - \frac{1}{6}k^2R^2 + \frac{1}{18}ik^3R^3)} \right], \end{aligned} \quad (11)$$

where $\mathcal{F}^{-1}[f(\omega)] = \frac{1}{2\pi} \int_{-\infty}^{\infty} f(\omega) e^{-i\omega t} d\omega$ denotes inverse Fourier transform. To compare the theoretical model and experimental data the displacements should be transformed from spherical to Cartesian coordinates:

$$\begin{aligned} U_z &= U_r \cos \theta - U_\theta \sin \theta, \\ U_x &= U_r \sin \theta + U_\theta \cos \theta, \end{aligned} \quad (12)$$

where θ is the angle between z -axis and r -axis and increases in the counterclockwise direction. The displacement is not constant on the bubble surface as the bubble could be deformed by acoustic radiation force. Thus, U_x is the displacement in the normal direction with respect to the force vector and U_z is the displacement along the force direction. If the ultrasound imaging transducer and the excitation transducer are aligned in the z -axis, then U_z corresponds to axial displacement of the microbubble. There is some freedom in the choice of the angle θ , but in our calculations, it is assumed that $\theta = 0$. Thus, the theoretically predicted U_z of microbubble is used to find the best fit between theory and experimental measurements.

It is important to note that the problem has been formulated in linear approximation, assuming that the displacements of the bubble does not exceed one and half times the bubble radius.¹⁸ Otherwise, the deformation of the bubble becomes significant and the influence of surface tension should be taken into account. Surface tension reduces the bubble deformation, especially for small bubbles and makes the bubble behave more like a solid sphere with zero density.

III. MATERIALS AND METHODS

To verify the theoretical model, the experiments were performed using laser-induced microbubbles in tissue-mimicking phantoms, containing 3% by weight gelatin (300 Bloom, type-A, Sigma-Aldrich, Inc., St. Louis, MO). In addition, cylindrical samples of 35 mm diameter and 16–18 mm height were made out of the same gelatin solution to be used in direct mechanical measurements with portable benchtop uniaxial tester In-Spec 2200 (Instron, Inc., Morwood, MA). Prior to measurements, the phantoms and samples were kept together and followed the same experimental protocol to minimize any differences between the materials.

To validate the proposed approach experimentally, an experimental system was designed and built (Fig. 1). The overall system combined pulsed laser, objective lens, microscope, water cuvette, excitation transducer, and imaging transducer.

A pulsed Nd:YAG laser (Polaris II, Fremont, CA) with 5 ns pulse duration, 532 nm wavelength, and 0.3 mJ energy was focused by a custom-built objective lens [1.13 numerical aperture (NA) and 8.0 mm working distance] to produce a microbubble inside the gelatin phantom. A high NA guaranteed that a laser-induced microbubble would be small and nearly spherical.³

The size of the microbubble was monitored by an optical microscope (Dino-Lite AM411T, Wirtz, VA) operating at 230 × magnification. Example optical images of microbubbles

FIG. 1. (Color online) A schematic view of the experimental setup. A microbubble is produced by a focused laser beam. An excitation transducer generates acoustic radiation force on a microbubble. The motion of a microbubble is tracked by an imaging transducer. The size of the microbubble was monitored by an optical microscope.

FIG. 2. (Color online) Typical microbubbles generated by pulsed laser (5 ns pulse duration, 532 nm wavelength, and 0.3 mJ energy). Pulsed laser was focused by using a 1.13 numerical aperture (NA) objective. Bubble radii are from 13 ± 2 to 258 ± 2 μm .

captured during the experiments are presented in Fig. 2. The radii of microbubbles ranged from 13 ± 2 to 258 ± 2 μm .

A water cuvette with a hole for laser beam delivery was fixed to the standing post and the gelatin phantom attached to a translation stage was placed inside the water cuvette. The gelatin phantom was moved during the experiments to generate laser-induced microbubbles at different locations in the phantom. A 3.5 MHz transducer (Valpey Fisher, Hopkinton, MA) and a 25 MHz imaging transducer (Olympus-NDT, Waltham, MA) with focal lengths of 25.4 mm were located at the top of the water cuvette with an angle of 20° with respect to a vertical line. Thus, the angle between 3.5 and 25 MHz transducers was 40° . The foci of both transducers were aligned at the location of the microbubble.

The 3.5 MHz excitation transducer ($F/\# = 4$ and bandwidth = 60%), connected to RF power amplifier (ENI model 240L, ENI, Rochester, NY) with 50 dB gain, was used to generate pulsed acoustic radiation force to displace a laser-induced microbubble. The duration of the acoustic radiation pulse (t_0) was varied from 29 to 571 μs .

The 25 MHz imaging transducer ($F/\# = 4$ and bandwidth = 51%), connected to a pulser/receiver (DPR 300 Pulser/Receiver, JSR Ultrasonics, Pittsford, NY), was operated at pulse repetition frequency of 25 kHz in pulse-echo mode. Pulse-echo ultrasound signals were saved at the data acquisition card (CompuScope 12400, GaGe, Inc., Montreal, Canada) with 200 M samples/s for off-line processing. Therefore, radio frequency (RF) raw data were comprised of trains of backscattered ultrasound echoes started 120 μs before the acoustic radiation pulse was launched. Arrival time of the first echo defined the initial location of the micro-

bubble and changes in the arrival times of the following echoes determined microbubble displacement. RF raw data were used to define displacement of a microbubble by a cross correlation speckle tracking method.⁵⁸ The kernel size and search window for cross correlation tracking were 375 and 1125 μm , respectively.

Comparison between theoretical calculations and experimental measurements of the motion of a laser-induced microbubble in the gelatin phantom was made to verify the developed theoretical model. Then, this model was used to reconstruct the elasticity of tissue-mimicking phantoms.

Theoretically calculated values of maximum displacement (U_{max}) and time required to reach the maximum displacement (t_{max}) of a laser-induced microbubble were compared with those obtained by experimental measurements for different values of acoustic radiation pulse duration (t_0) and various radii of a microbubble (R). Young's modulus (E), measured by uniaxial tester, was used in theoretical calculations. The value of the scaling factor of acoustic radiation force (F_0) was chosen to match experimentally observed displacements with theoretically calculated displacements. The shear viscosity was found by comparing decaying profiles of microbubble displacements from theory and experiments. The estimated value was 0.06 Pa s which was used in all theoretical calculations. The value corresponded to the results of our previous work, which was 0.1 Pa s.^{52,53} The elastic properties were found to be almost independent from the shear viscosity in the measured range. Shear viscosity of porcine and human lens was investigated by another group and the values varied from 0.16 ± 0.1 to 0.33 Pa s.^{59,60}

In reconstruction, the Young's modulus was varied by gelatin concentrations. The gelatin concentrations used in the experiments were 1.4%, 2.0%, 3.0%, 4.0%, 5.0%, 6.0%, 7.0% by weight. Young's modulus of a viscoelastic medium was estimated using a laser-induced microbubble under acoustic radiation force by measuring the time of maximum displacement (t_{max}).^{52,53} Then, it was compared to the Young's modulus measured by the uniaxial tester.

IV. RESULTS AND DISCUSSION

A. Experimental validation of the theoretical model

Theoretically calculated and experimentally obtained displacements of a laser-induced microbubble with a radius of 258 ± 2 μm are shown in Figs. 3(a) and 3(b), respectively.

FIG. 3. (a) Theoretically calculated and (b) experimentally obtained displacements of the microbubble in response to various durations of the acoustic pulse. The arrows represent the end of acoustic pulse. Bubble radius is 258 ± 2 μm .

FIG. 4. (Color online) Comparison of theoretically predicted and experimentally measured (a) maximum displacement (U_{max}) vs duration of acoustic pulse (t_0) and (b) time needed to reach maximum displacement (t_{max}) vs duration of acoustic pulse (t_0). Four measurements were done using four different laser-induced microbubbles for every t_0 . Error bars mean one standard deviation.

The durations of applied radiation pulses were 29, 143, 286, and 571 μs . The arrows indicate the time when the force was turned off (i.e., the end of the acoustic pulse). The Young's modulus of the phantom measured using uniaxial test was 4.37 ± 0.26 kPa. As evident from Eq. (11), microbubble displacement was scaled with the scaling factor of acoustic radiation force (F_0). Therefore, F_0 in our model was chosen to match the experimentally observed displacements.

Calculated and measured displacements of the microbubble in response to the applied radiation force are in good agreement. The displacement profile and maximum displacement of a microbubble (U_{max}) depend on acoustic radiation pulse duration (t_0) (Fig. 3). Increase of U_{max} does not have linear relationship with t_0 . Increase of U_{max} gradually slows down as t_0 reaches values that induce steady-state displacement. Reaching steady-state displacement under certain t_0 means that elasticity of a medium is hard enough to push a microbubble in response to the bubble's motion and a microbubble does not have enough inertia to overcome the reaction of the medium after the applied external force is removed. Arrows in Fig. 3(a) indicate the end of acoustic pulses. When matching theory and experimental measurements, the scaling factor of acoustic radiation force (F_0) used here is 45 mN.

The comparison of theoretical and experimental dependences of maximum displacement (U_{max}) and time of maximum displacement (t_{max}) on acoustic radiation pulse durations (t_0) is shown in Figs. 4(a) and 4(b), respectively. The scaling factor of acoustic radiation force (F_0) was 35

mN in the same phantom and this value comes from the best fit between the displacement profiles obtained from theoretical model and experimental measurements. The mean and standard deviation of radii of the four microbubbles are 75 and 2 μm . Theory and experiments have reasonable agreement. Figure 4(a) depicts that the maximum displacement of the microbubble increases as radiation pulse duration becomes longer. Figure 4(b) shows that at the end of a short pulse (under 120 μs) the bubble continues to move away from the excitation transducer until it reaches a maximum displacement ($t_{max} > t_0$) while at the end of a long pulse the bubble starts to move back almost immediately ($t_{max} \approx t_0$) as shown by the identity line. Note that the same data was used for analysis of U_{max} and t_{max} in Figs. 4(a) and 4(b). Four measurements were done (one measurement on four different laser-induced microbubbles in different locations within the same gelatin phantom) for every t_0 .

The dependences of maximum displacement (U_{max}) and time of maximum displacement (t_{max}) on microbubble radius (R) for the duration of acoustic radiation pulse (t_0) of 43 μs are shown in Figs. 5(a) and 5(b), respectively. Figure 5(a) indicates that a large microbubble moves larger distances and takes a longer time to reach its maximum displacement as shown in Fig. 5(b). Indeed, the surface area of a larger microbubble is bigger than that of a smaller microbubble. Because the diameter of the focus of the 3.5 MHz transducer is about 800 μm , microbubbles in the experiments are always inside the focal area. Thus, under the same acoustic radiation pressure, a larger microbubble experiences larger acoustic

FIG. 5. (Color online) Comparison of theoretical and experimental dependences of (a) maximum displacement (U_{max}) and (b) time of maximum displacement (t_{max}) on bubble radius (R). At each point, three to five different measurements were made. Error bars mean one standard deviation.

FIG. 6. (Color online) Theoretical analysis. Maximum displacement (U_{max}) and time of maximum displacement (t_{max}) under different acoustic radiation force amplitudes (F_0). t_{max} is an invariant parameter under different acoustic radiation forces. Acoustic radiation pulse duration (t_0) for this evaluation is $28 \mu\text{s}$ and arrow indicates the end of t_0 .

radiation force. The measured values of bubble radii are 49 ± 3 , 60 ± 1 , 66 ± 3 , 74 ± 3 , 85 ± 3 , 92 ± 3 , 98 ± 2 , and $110 \pm 3 \mu\text{m}$ and corresponding scaling factor of acoustic radiation forces (F_0) of each microbubble are 30, 46, 54, 68, 90, 106, 120, and 151 mN after displacements of theoretical model and measurements were matched. The measurements were performed at least on three different microbubbles in the same gelatin phantom but at different locations.

The difference between time of maximum displacement (t_{max}) and acoustic radiation pulse duration (t_0) increased for short t_0 as shown in Fig. 4(b) and large microbubble radius (R) as shown in Fig. 5(b). The large difference between t_{max} and t_0 was due to the increased inertial effect of the surrounding tissue. Furthermore, if the difference was large, more accurate measurements of t_{max} were possible, otherwise t_{max} could be hardly distinguished from t_0 .

We could select durations of acoustic radiation pulse (t_0) based on microbubble radius (R) to perform effective Young's modulus reconstruction. To maximize the difference between time of maximum displacement and t_0 , a short t_0 was used to reconstruct the elastic properties of the medium.

B. Reconstruction

The results of previous subsection A demonstrate that the developed theoretical model can predict mechanical response of microbubble under radiation force in a viscoelastic medium. In this subsection, an inverse problem is considered, i.e., reconstruction of the elastic properties of a medium.

Different strategies could be used to reconstruct elasticity. For example, an approach based on the value of maximum displacement was considered in several studies.^{10,11,49–51} The disadvantage of this method is the challenge in estimation of the acoustic energy delivered to the bubble as has been discussed previously. However, elasticity may be evaluated from the temporal characteristics of the bubble motion. While the amplitude of a laser-induced microbubble displacement is proportional to the amplitude of acoustic radiation force, the time of maximum displacement (t_{max}) remains the same as shown in Fig. 6.

FIG. 7. (Color online) Comparison of Young's modulus values reconstructed using microbubble-based method and measured using the uniaxial load-displacement test. Two measurements were performed on five different microbubbles in all phantoms. Error bars represent one standard deviation.

Gelatin-based phantoms with the gelatin concentrations of 1.4%, 2.0%, 3.0%, 4.0%, 5.0%, 6.0% and 7.0% by weight were used to vary elastic properties of the phantoms at the reconstruction process.⁶¹ To estimate elasticity of a medium, a microbubble was created in a phantom using a single laser pulse. Then, the microbubble was perturbed by an impulsive radiation force. We chose durations of acoustic radiation pulse as short as possible to maximize the inertial effect. In addition, experimentally meaningful durations were used to induce a noticeable displacement. The values of a laser-induced microbubble radius (R) and acoustic radiation pulse durations (t_0) were from 50 ± 2 to $142 \pm 5 \mu\text{m}$ and $43 \mu\text{s}$, respectively. The measurements were performed twice for five different microbubbles created at various locations in every phantom.

Figure 7 demonstrates the comparison of Young's modulus (E) reconstructed using the laser-induced microbubble approach and measured by using uniaxial tester. The solid line represents the ideal match between measurements. The Young's modulus reconstructed by the laser-induced microbubble technique and that directly measured by uniaxial test agree well with one another. For stiffer materials, the uniaxial tests provide higher accuracy of elasticity measurements. This is the result of a small difference between time of maximum displacement (t_{max}) and duration of acoustic radiation pulse (t_0) for stiffer materials. Thus, the errors of t_{max} measurements induced larger error in the Young's modulus reconstruction. To measure elastic properties of stiff materials, higher pulse repetition frequency (PRF) of the ultrasound measurements are required. The increase of PRF is one of the major direction of our future work.

V. CONCLUSIONS

Assessment of the mechanical properties of a viscoelastic medium using laser-induced microbubbles under acoustic radiation force was developed. The measured displacements of microbubbles demonstrated good agreement with the theoretical predictions. Moreover, the phantom studies demonstrated good agreement between the Young's

modulus reconstructed using remote microbubble-based measurements and that measured using the uniaxial tests. Thus, the Young's modulus of a medium can be measured using a laser-induced microbubble with typical sizes of tens of micrometers up to a hundred micrometers using acoustic radiation force.

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