Estimation of mechanical properties of gelatin using a microbubble under acoustic radiation force

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Abstract. This paper is concerned with observations of the translation of a microbubble (80 μm or 137 μm in radius) in a viscoelastic medium (3 w% gelatin), which is induced by acoustic radiation force originating from 1 MHz focused ultrasound. An optical system using a high-speed camera was designed to visualize the bubble translation and deformation. If the bubble remains its spherical shape under the sonication, the bubble translation we observed can be described by theory based on the Voigt model for linear viscoelastic solids; mechanical properties of the gelatin are calculated from measurements of the terminal displacement under the sonication.

1. Introduction
It is desirable to obtain mechanical properties of ocular tissues in ophthalmic diagnostics and surgeries. A bubble-based acoustic radiation force technique has been developed to determine mechanical properties of viscoelastic tissues [1]. In principle, a bubble in viscoelastic media can translate under the action of the radiation force that arises from interaction, via acoustic impedance mismatching, between ultrasound and the bubble. We may model the translational motion based on the Voigt model (for linear viscoelastic solids); existing theories assume the case with a spherical bubble to relate the radiation force and evolution of the resulting bubble translation [2]. In the experiment of Yoon et al. [1], the elasticity of gelatin was inferred by fitting their acoustic measurement to the theory. However, optical visualization of ultrasound-induced bubble translation (and deformation) has not been provided in previous studies.

In this study, we design an optical system to visualize translation and deformation of a microbubble in gelatin under megasonic wave irradiation and estimate the mechanical properties of the gelatin.

2. Theory
Supposing that a spherical bubble in a linear viscoelastic solid is subjected to constant acoustic radiation force applied in step-wise manner from time \( t = 0 \), the transient motion of the spherical bubble can be derived based on the Voigt model [2]:

\[
x(t) = x_{max}\left[1 - \exp\left(\frac{t}{\tau}\right)\right]
\]  

(1)
where $x$ is the displacement from the original position before applying the radiation force, $x_{\text{max}}$ is the terminal displacement, and $\tau$ is the time constant that can be related to the ratio of viscosity to the elasticity of the surrounding medium. Note that the application of the Voigt model implies sufficiently small $x_{\text{max}}$ (or equivalently small strain in the medium) for its linear assumption to hold in experiments.

The bubble under constant radiation force eventually reaches a (static) mechanical equilibrium at which the radiation force is balanced with restoring force from elasticity of the surrounding medium. At the static equilibrium, the terminal displacement in Eq. (1) is given by [3]

$$x_{\text{max}} = \frac{F}{4\pi RG} \quad (2)$$

where $F$ is the (constant) acoustic radiation force, $R$ is the variable radius of the deformed bubble, and $G$ is the shear modulus of the viscoelastic solid surrounding the bubble. Now that acoustic waves of intensity $I$ are exerted on the projected area $\pi R^2$, the radiation force $F$ is calculated as

$$F = \frac{2I \pi R^2}{c} \quad (3)$$

where $c$ is the speed of sound in the viscoelastic solid and the prefactor 2 on the right-hand side means perfect wave reflection at the bubble wall (with no waves transmitted into the bubble). Assuming that the bubble deformation is negligible, we may normalize the terminal displacement by the initial bubble radius $R_0$. That is,

$$\frac{x_{\text{max}}}{R_0} = \frac{F}{2\pi c G} \quad (4)$$

It follows from Eq. (4) that the shear modulus may be estimated only from measurements of the maximum bubble displacement, provided the bubble keeps its spherical shape.

3. Experimental methods

A gelatin phantom was selected as a (tissue-like) viscoelastic solid; the phantom was prepared with 3 w% gelatin (G2500, Type-A, Sigma-Aldrich) mixed with water. A spherical microbubble in the gelatin phantom can be produced by focusing an infrared laser pulse (ULTRA 50 GRM, Quantel) according to [4]; after vapor condenses back into the surrounding medium, noncondensible gas contents (air) are left as a spherical cavity whose radius is varied around 100 $\mu$m for observations.

The experimental setup is depicted in Fig. 1. The gelatin phantom containing a spherical microbubble was placed inside an acrylic case filled with tap water ($23^\circ$ C). Acoustic radiation
force acting on the microbubble was generated by a 1.0 MHz, focus-type transducer (IZ30I R30, JAPAN PROBE) located at the case bottom, which is connected to a function generator (WF1973, NF Corporation) driven at 10 V, a delay generator (DG535, Stanford Research Systems Inc.), and an amplifier (GAIN ×10, HSA4011, NF Corporation). The microbubble was located in the focal zone in which the constant acoustic intensity was achieved soon after the irradiation starts and the pressure amplitude was recorded as 1.82 ± 0.03 MPa (HPM02/1, Precious Acoustics Ltd.). The focal zone is confirmed to be larger than the bubble size, so that the pressure may be assumed to act uniformly on the bubble. Since the forced frequency is much higher than the natural frequency of bubbles of our concern, the applied acoustic force is expected to drive the translation of the bubble, not oscillation in the bubble volume. To minimize wave reflections from boundaries, an acoustic absorber (EUA201, EASTEK) was placed at the top of the gelatin phantom. The ultrasound was irradiated from time $t = 0.5$ ms to 8.5 ms in Figs. 2 to 3. The motion of the microbubble was illuminated by LED light (SLG-150V, REVOX) and recorded through 8× magnification by a high-speed camera (FASTCAM SA-X2, Photron) whose frame rate and exposure time are 40,000 frames/s and 1/42105 s, respectively. The MATLAB image processing was used to extract the bubble information such as displacement of the centroid and trasverse radius of the deformed bubble [4].

4. Results and Discussion

Figure 2 shows an example of sequential images of the translation of a bubble with $R_0 = 137$ μm in the gelatin under the megasonic irradiation. As expected, the translation of the bubble is induced in the direction of the megasonic wave propagation. After the sonication, the bubble returns to its original position due to the gelatin elasticity, as seen in the last frame of Fig. 2. In this example, the bubble seems sufficiently small, meaning that surface tension and elasticity of the surrounding medium are large enough to keep its spherical shape against the acoustic radiation force.

A typical example of the temporal evolution of the translation for the case of $R_0 = 87$ μm (where the surface tension and elasticity are expected to be even stronger than in the previous example of $R_0 = 137$ μm) is presented in Fig. 3 (see the left vertical axis). To examine deviation from the spherical shape, that of the traverse radius $R_{\text{trav}}$ (defined in Fig. 2) normalized by the initial radius $R_0$ is also plotted in Fig. 3 (see the right vertical axis). The initially spherical bubble is found to be flattened under sonication. In particular, the non-sphericity is emphasized by encountering unsteady motion when the sonication is turned on or off and inertia of the surrounding medium plays a more important role. However, the increase in the transverse radius is bounded within a few percents from the unperturbed value, meaning that surface tension defeats pressure and inertial forces, which make the bubble non-spherical, in the overall process.

![Figure 2](image.png)

Figure 2. Translation of the microbubble ($R_0 = 137$ μm) in the gelatin. The megasonic waves propagating upward are applied from $t = 0.5$ ms to 8.5 ms.
Now that the bubble remains spherical in Fig. 3, the measured evolution of the bubble translation is fitted to the theory based on the Voigt model represented by Eq. (1); the fitting is denoted by the red line in Fig. 3. The good agreement between the measurement and the theory means that the deformation of the gelatin surrounding the translating bubble is sufficiently small for the linear Voigt assumption to be valid. It follows from the fitting that the shear modulus is predicted to be $650 \pm 20 \text{ Pa}$, which agrees with values reported in the previous study [5].

5. Conclusions
In this study, the experimental technique has been developed to visualize the bubble translation and deformation under acoustic radiation force in a viscoelastic solid (gelatin). The observed evolution of bubble translation where the bubble remains its spherical shape was well explained by the theoretical model for spherical bubbles in the (linear) Voigt solid. The comparison between the measurement and theory leads to an estimate of the gelatin shear modulus, which agrees well with the previous study.

In future, a series of the experiment with varying $R_0$ will be conducted to see how the bubble size affects the assumption of spherical shape based on dimensionless numbers including the Weber number.

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