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Reconstruction of Viscosity Maps in Elastography using Ultrasound Shear Wave Attenuation

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Abstract— **Changes in viscoelastic properties of biological tissues may be symptomatic of a dysfunction that can be correlated to tissue pathology. Past magnetic resonance imaging studies suggest that tumors have higher viscosity than normal tissues, and fatty organs might also correlate with higher viscosity. In this study, a frequency-shift method to compute attenuation was utilized to reconstruct viscosity maps by analyzing spectral properties of induced shear waves. The feasibility of viscosity reconstructions in animal tissue samples is investigated. Experiments were performed in an *in vitro* phantom, as well as in *ex vivo* and *in vivo* animal tissue samples of healthy and fatty livers. Quantitative values of viscosity obtained for two porcine liver tissues, two fatty duck liver samples, and one goose fatty liver imaged *in vivo* are 0.61 ± 0.21, 0.52 ± 0.35; 1.28 ± 0.54, 1.36 ± 0.73, and 1.67 ± 0.70 Pa.s, respectively.**

Keywords— Shear wave elastography, viscoelasticity, viscosity reconstruction, shear wave attenuation, spectral shift, fatty liver.

I. Introduction

Ultrasound shear wave elastography is a technique developed in the last two decades to noninvasively assess viscoelastic properties of the soft tissues such as breast or liver. Shear waves are generated inside the biological tissues with a conventional ultrasonic probe via a focused acoustic radiation force [1-3]. The objective is to indirectly measure the viscoelasticity of biological tissues by monitoring shear wave propagation in the target area. Shear waves propagate faster in stiffer media and slower in softer media. Shear wave elastography has clinical applications in the diagnosis of several soft-tissue diseases, such as non-alcoholic fatty liver diseases (NAFLD). Different stiffness scores for diagnostic interpretation of pathological conditions have been proposed for clinical use [4-6].

The stiffness, or Young's modulus (Y), of a purely elastic medium can be related to the shear wave speed (c) and mass density (ρ) through the relation $Y = 3\rho c^2$. Several methods to reconstruct tissue viscoelastic properties have been developed in the last decade but these are often limited to the reconstruction of elasticity maps only, or elasticity and viscosity but the latter being assessed according to a rheology model of the tissue [7, 8]. A preliminary magnetic resonance elastography study proposed that tumors and fibroadenomas have higher viscosity than typical breast tissues [9]. This study focuses on retrieving viscosity information from biological tissues for applications in clinical diagnosis.

Past studies suggest that retrieving viscosity of biological tissues is an important clinical information that may be useful in prognosis of several diseases [10-12]. An important step for viscosity reconstruction is to accurately compute the shear wave attenuation. In this study, we utilized a frequency-shift method to compute the shear wave attenuation by analyzing spectral properties of induced shear waves [13]. Experimental validations were performed to reconstruct viscosity maps of heterogeneous samples in an *in vitro* gelatin phantom with an inclusion, *ex vivo* porcine liver samples, *ex vivo* fatty duck liver samples, and in an *in vivo* fatty goose liver. We envisage that these results will indicate usefulness of viscosity as an important biomarker and open new perspectives in diagnostic clinical applications.

II. Methods

A. Frequency-shift method for shear wave attenuation computation

This method was recently developed by our group [13] to describe shear wave attenuation in soft tissues considering the amplitude spectral distribution. Briefly, if a shear wave has a frequency spectrum $S(f)$ at a location x_0,

then at a distance $x_0 + \Delta x$ the frequency spectrum, $R(f)$, can be expressed as

$$|R(f)| = G_s(f,x) \cdot H(f,\Delta x) \cdot |S(f)| \ , \quad (1)$$

where f is the frequency, $G_s(f,x)$ relates to the geometrical spreading of the propagating wave and $H(f,\Delta x)$ corresponds to the viscous attenuation effect on the wave amplitude. This method overcomes the geometrical spreading effects by assuming $G_s(f,x) = G_s(x)$. A linear attenuation model with respect to frequency is considered, which can be given as,

$$H(f,\Delta x) = e^{-\alpha_0 f \Delta x} \ , \quad (2)$$

where α_0 is the linear attenuation coefficient (in units Np .m^{-1}/Hz) and $\alpha = \alpha_0 \times f$ [13]. The amplitude spectrum of the travelling wave is assumed to be proportional to a gamma probability density distribution,

$$|S(f)| \propto f^{k_0 - 1} e^{-f\beta_o} \ , \quad (3)$$

where k_0 and β_0 are shape and rate parameters, respectively. Thus, the amplitude spectrum at a location $x = x_0 + \Delta x$ can be expressed as

$$|R(f)| \propto f^{k_0 - 1} e^{-f(\beta_o + \alpha_0 \Delta x)} \ . \quad (4)$$

A nonlinear least-square algorithm (such as Levenberg–Marquardt) can be used to estimate the shape and rate parameters of the gamma distribution model at each lateral position (x_0). The rate parameter from Eq. (4) at $x = x_0 + \Delta x$ is $\beta(\Delta x) = \beta_o + \alpha_0 \Delta x$. The curve $\beta(\Delta x)$ is then fitted to a straight line in the lateral direction, *i.e.*, from x_0 to x_0+Δx. The slope of the fitted straight line is the linear shear wave attenuation coefficient α_0.

The phase velocity (c), defined as the speed of the wave propagating at a constant phase, can be estimated by measuring the phase shift $\Delta\varphi$ along a distance Δx:

$$c = \omega \Delta x / \Delta\varphi. \quad (5)$$

Finally, the viscosity (η) can be retrieved from a linear viscoelasticity hypothesis using [14]:

$$G'' = 2c^2\omega^2\alpha \frac{\rho\omega c}{(c^2\alpha^2 + \omega^2)^2} \ , \quad (10)$$

and, $$\eta = \frac{G''}{\omega} \ . \quad (11)$$

B. Preparation of samples

The study was performed on a tissue mimicking phantom with an irregular inclusion, as well as on *ex vivo* and *in vivo* animal tissue samples. The phantom was prepared using basic mixtures of gelatin (5%), sigmacell cellulose (1.5%), and xanthan gum (0.5% for inclusion material and 0.1% for surrounding material).

The recipe to prepare the tissue-mimicking phantom material is as follows [15]. A mixture of 5% w/w gelatin and 0.1% xanthan gum in powder form was dry mixed and added to water at room temperature. This solution was then heated up to 90 °C while continuously stirring to completely dissolve the solvents. Once the solvents were completely dissolved, the mixture was allowed to gradually cool down. Sigmacell cellulose powder was added at 40 °C. A quantity of 0.1% graphite was also added in the inclusion material. The inclusion was embedded using a 3D printed mould. Once the phantom was cast in a rectangular box, it was kept in a refrigerator at a temperature of 4 °C for 16 hours to ensure uniform gelation and was later allowed to return to room temperature (22 °C) before making ultrasound measurements.

Two fresh porcine liver pieces were purchased from a grocery store for measurements on a healthy (not fatty) *ex vivo* liver tissue. Two packaged pieces of fresh fatty duck liver samples were bought from a specialized grocery store for fatty liver tissue measurements. *In vivo* viscoelastic ultrasound measurements on a fatty goose liver (steatosis grade unknown), that was being raised for *foie-gras* production, were performed at a farmhouse in the presence of a veterinarian. The protocol was approved by the ethical animal health care committee of the University of Montreal Hospital Research Centre.

C. Ultrasound measurements

An acoustic radiation force beam was implemented on a research ultrasound system (Verasonics V1, Verasonics Inc., Redmond, WA, USA) that worked similar to a supersonic imaging (SSI) sequence [14]. A linear array probe (ATL L7-4, Philips, Bothell, WA, USA) was used at a central frequency of 5 MHz to remotely generate shear waves inside the samples using the ultrasound radiation force. Three acoustic pushes spaced 5 mm apart were focused inside the sample. Each individual beam had a pushing velocity of 40 m/s for a duration of 100 µs, with a delay of 125 µs between two consecutive pushes. The same probe recorded the plane-wave imaging radio-frequency data at a 4-kHz frame rate immediately after generating the radiation force. These experiments are described in details in the Ref. [15].

The experiments were repeated for animal tissue samples with exactly the same procedure. The *in vivo* measurements of the goose liver were performed by a veterinarian.

III. Results and Discussion

Figure 1 displays the reconstruction maps for shear wave phase velocity, shear wave attenuation, and viscosity in the gelatin phantom. The mean values (mean ± standard deviation) of phase velocity, attenuation, and viscosity inside the inclusion were 2.08 ± 0.15 m/s, 0.32 ± 0.05

Np/m/Hz, and 0.39 ± 0.08 Pa.s, respectively; and outside the inclusion these measures were 1.90 ± 0.11 m/s, 0.23 ± 0.08 Np/m/Hz, and 0.22 ± 0.07 Pa.s, respectively.

Animal tissues are often heterogeneous and variations can be observed in their viscosity maps. Figure 2 shows viscosity maps inside a manually selected region of interest in an *ex vivo* normal porcine liver, *ex vivo* fatty duck liver, and in an *in vivo* fatty goose liver. The quantitative values of viscosity obtained from porcine animal tissues

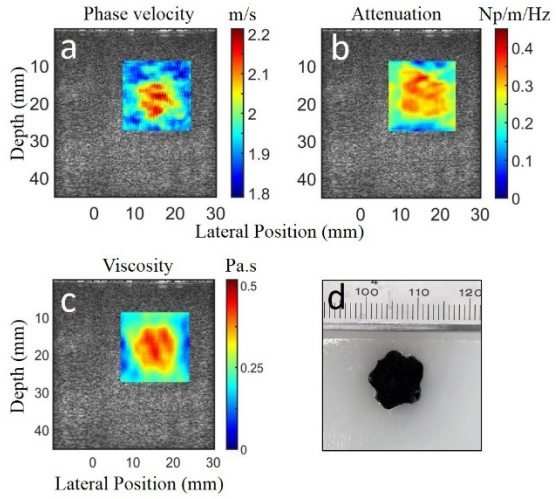

Fig. 1. Reconstruction of (a) shear wave phase velocity, (b) shear wave attenuation, and (c) viscosity in a phantom with irregular shape. (d) The photograph of the inclusion is shown.

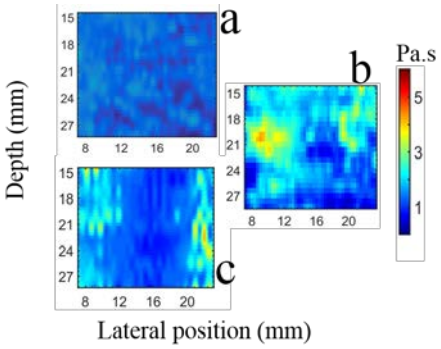

Fig. 2. Reconstruction of viscosity in (a) the *ex vivo* normal porcine liver #1, (b) the *ex vivo* fatty duck liver #1, and (c) the *in vivo* fatty goose liver.

were 0.61 ± 0.21 Pa.s and 0.52 ± 0.35 Pa.s. The viscosity of duck tissue samples were found to be 1.28 ± 0.54 Pa.s and 1.36 ± 0.73 Pa.s; and for *in vivo* goose liver the viscosity was 1.67 ± 0.70 Pa.s. It can be noticed that fatty duck liver and fatty goose liver tissues resulted in higher viscosities than porcine liver tissues. The *ex vivo* fatty duck and *in vivo* goose liver results revealed higher shear wave attenuation *in vivo*. The potential limitation of this method is the influence of measurement noise that can affect the reconstruction performance. The noisy situations may occur due to anisotropic anatomy, presence of air bubbles *ex vivo*, organ motion during the ultrasound scan, and upper harmonics generated inside the tissue due to non-linear properties.

IV. Conclusion

Successful viscosity maps were reconstructed in a phantom with an embedded mechanical inclusion having an irregular shape and a viscoelasticity contrast, and in animal tissue samples. The method is independent of any assumption on the wavefront geometry. The viscosity maps can provide more diagnostic information during early screening of diseases in soft tissues like liver or breast. Fatty animal liver tissue samples were found to be more viscous than normal liver tissue samples. Such viscosity information may provide several applications in clinical diagnosis such as in fatty liver disease, characterization of breast cancers, or rheological assessment of blood clots.

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