Speed-of-sound anisotropy estimation using reflector-based pulse-echo ultrasound

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ABSTRACT

Speed-of-sound (SoS) measurements in ultrasound imaging have a promising diagnostic value for tissue characterization. They allow, for instance, the quantification of fat content in muscles, which is essential for musculoskeletal disease diagnosis. Fiber-rich tissues such as muscles, however, show anisotropic behavior, leading to direction-dependent propagation velocities of ultrasonic waves. Estimating anisotropy in SoS could potentially offer a new quantitative ultrasound biomarker that correlates to microstructural alignment as currently measured with magnetic resonance diffusion tensor imaging sequences. As a first step, this work presents a method to estimate average anisotropy in SoS of soft tissue using pulse-echo ultrasound. In particular, our setup includes a passive acoustic reflector located opposite to the ultrasound probe, with tissue in between. This enables the generation of strong reflections from which we measure their traveltimes. We use ray-based approaches to derive the forward problem that relates observed traveltimes with SoS anisotropy parameters. These include the maximum and minimum SoS values in the direction of the anisotropy symmetry axes, and the tilt angle of these with respect to the probe direction. We use numerical wave propagation simulations to verify the accuracy of our forward modelling of traveltimes. For the specific case in which the tilt angle is zero, the forward problem becomes linear, and the anisotropy parameters can be estimated using linear regression. Finally, we show the occurrence of anisotropy in gastrocnemius muscle tissue using in-vivo data. Observed average SoS values vary between 1483 m/s (perpendicular to muscle fibers) and 1520 m/s (23° towards fibers direction).

Keywords: speed of sound, anisotropy, pulse-echo ultrasound, muscle tissue, inversion

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Supplemental Material

1. DESCRIPTION OF PURPOSE

Tissues with structured collagen fiber networks, such as brain, muscles or bone, are anisotropic, meaning that they exhibit direction-dependent properties. Progress in quantitative imaging has enabled quantifying fiber distributions (tractography) based on Magnetic Resonance Imaging - Diffusion Tensor Imaging (MRI-DTI) techniques, which have become highly popular amongst clinical researchers. In ultrasound imaging, anisotropy has been regarded as an angle-generated artifact encountered, for instance, in muscle and tendon examinations. The estimation of anisotropy in elastic tissue properties, however, has a promising diagnostic value. It has been observed that diseases in muscles (e.g., inflammation or sarcopenia) modify their cellular structural organization, resulting in changed diffusion properties and anisotropy.[?] Anisotropy estimation, therefore, can potentially be used to quantify muscle abnormalities and show muscle diseases before they become evident on conventional ultrasound.

Attempts have been made to measure anisotropy in shear waves using state-of-the-art ultrasound elastography, which quantifies tissue stiffness as an indicator of disease. Shear waves show maximum and minimum velocities in directions parallel and perpendicular to muscle fiber alignment, respectively. Yet, elastography shows poor lateral resolution, and accurate shear wave measurements may be challenging due to the sensitivity of stiffness to ultrasound probe compression and muscle activation state.[?]

The use of speed-of-sound (SoS) estimations in diagnostic applications is gaining popularity. Recent studies have shown that it can be used, for instance, to accurately quantify tissue composition. For example, muscle and adipose tissue show SoS values of 1585 m/s and 1440 m/s, respectively. This allows the quantification of the fat fraction in muscles with ultrasound, and it is of high-relevance for objective diagnostics of fatty musculoskeletal diseases (sarcopenia).[?] However, the anisotropy of longitudinal waves in soft tissue has been very scarcely explored, and to the best of our knowledge, no method for in-vivo estimations have been proposed so far. In this work, we present a quantitative method to estimate average anisotropy in SoS with clinical ultrasound probes.

2. METHOD

2.1 Theory: traveltime modelling in anisotropic media

Anisotropy in soft tissue leads to direction-dependent propagation velocities of ultrasonic waves. Traveltimes of different arrivals, therefore, can potentially be used to estimate average SoS anisotropic parameters. For simplicity, let us consider a two-dimensional homogeneous anisotropic medium with a single source-receiver pair and the configuration illustrated in Figure 1(a). Here, we assume elliptic anisotropy, and c_1 and c_2 refer to the SoS values of the medium along the anisotropy symmetry axes, which are tilted at an angle φ from the reference x-y coordinate system. For instance, they may represent the SoS parallel c_1 and perpendicular c_2 to the tissue fibers. In a first approximation, the velocity $c(\theta)$ in an arbitrary direction θ can be derived from the equation of the ellipse

$$\frac{c^2(\theta)}{c_1^2}\cos^2(\theta-\varphi)+\frac{c^2(\theta)}{c_2^2}\sin^2(\theta-\varphi)=1. \tag{1}$$

By using trigonometric identities for θ, the traveltime t_{SR} of waves propagating from the source at $\mathbf{r}_{\mathrm{S}}$ to the receiver at $\mathbf{r}_{\mathrm{R}}$ can be computed as

$$t_{\mathrm{SR}}^2=\frac{1}{c_2^2}\left[(x_{\mathrm{R}}-x_{\mathrm{S}})\cos\varphi-(y_{\mathrm{R}}-y_{\mathrm{S}})\sin\varphi\right]^2+\frac{1}{c_1^2}\left[(y_{\mathrm{R}}-y_{\mathrm{S}})\cos\varphi+(x_{\mathrm{R}}-x_{\mathrm{S}})\sin\varphi\right]^2. \tag{2}$$

This is the forward model that relates traveltime observations with parameters describing tissue anisotropy, i.e., c_1, c_2, and φ. Because hand-held ultrasound systems use relatively high frequencies (1-10 MHz), Eq. (2) is derived using ray theory, which assumes infinite frequencies and infinitely thin ray paths. In this study, we moreover make straight-ray assumptions.

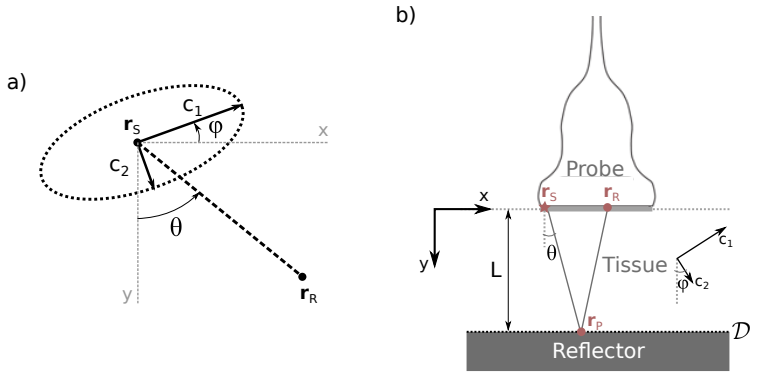

Figure 1. (a) Schematic representation of emitter-receiver configuration and anisotropy of speed-of-sound (SoS). (b) Illustration of reflector-based pulse-echo ultrasound system.

2.1.1 Reflector-based setup

In this study, we consider the pulse-echo ultrasound system shown in Fig. 1(b). A flat reflector is located opposite to the ultrasound probe with tissue in between. It generates strong echos visible in the recorded signals. We use their corresponding arrival times as our observed data. We refer the reader to Ref. **?** for a more detailed description of the system.

In this setup, the traveltimes can be modelled using Fermat's principle and Eq. (2) as

$$\min_{\mathbf{r}_\mathrm{P}\in\mathcal{D}} t_\mathrm{SR}(\mathbf{r}_\mathrm{P}), \quad \text{where} \quad t_\mathrm{SR}(\mathbf{r}_\mathrm{P}) = t_\mathrm{SP}(\mathbf{r}_\mathrm{P}) + t_\mathrm{PR}(\mathbf{r}_\mathrm{P}), \tag{3}$$

where $\mathcal{D}$ refers to the set of points at the reflector-tissue interface. For general anisotropic media, Eq. (3) is numerically solved by discretizing the interface $\mathcal{D}$. Equation (3) describes the forward problem addressed in this study. In general, the relationship between traveltimes and anisotropic parameters is nonlinear, and one could apply probabilistic inverse theory to infer these parameters.**?**

2.1.2 Special case: linear problem

When the anisotropy symmetry axes are aligned with the reference coordinate system, i.e., $\varphi = 0$ in Fig. 1(b), the forward problem in Eq. (3) becomes linear. In this case, the reflection point $\mathbf{r}_\mathrm{P}$ lies at the horizontal midpoint between $\mathbf{r}_\mathrm{S}$ and $\mathbf{r}_\mathrm{R}$, and $\mathbf{r}_\mathrm{P} = \left(\frac{1}{2}(x_\mathrm{R} - x_\mathrm{S}), L\right)$ with L being the probe-reflector distance. Thus, the traveltime t_SR is given by

$$t_\mathrm{SR}^2 = (x_\mathrm{R} - x_\mathrm{S})^2/c_1^2 + (2L)^2/c_2^2. \tag{4}$$

By representing measured traveltimes t_SR^2 as function of emitter-receiver offsets $(x_\mathrm{R} - x_\mathrm{S})^2$, we can use linear regression to estimate c_1 and c_2 from the slope m and intercept b of the linear model: $c_1 = 1/\sqrt{m}$ and $c_2 = (2L)/\sqrt{b}$.

2.2 Numerical simulations

To validate our forward model, we numerically simulate ultrasound wave propagation using the spectral-element waveform modelling software Salvus.**?** We approximate the wave propagation in soft tissue using the elastic anisotropic wave equation with shear modulus $\mu = 0$, i.e.,

$$\rho\partial_t^2 u(\mathbf{r}, t) - \nabla\cdot(\mathbf{D}\nabla u(\mathbf{r}, t)) = f(\mathbf{r}_\mathrm{S}, t). \tag{5}$$

Here, u is the scalar displacement potential, f is the external source generated from emitting transducers at $\mathbf{r}_\mathrm{S}$, ρ denotes the density distribution of the medium, and $\mathbf{D}$ is a second-order symmetric positive tensor describing the direction dependent SoS c. For instance, if the anisotropy is aligned with the coordinate system, $\mathbf{D}$ is a diagonal matrix with elements $D_{11} = \rho c_1^2$ and $D_{22} = \rho c_2^2$. In the general case of an anisotropic medium with tilted symmetry axes, one can use the rotation matrix to derive the elements of $\mathbf{D}$.

3. RESULTS

3.1 Synthetic study: proof-of-concept

First, we validate Eq. (4) using a two-layered medium representing soft tissue ($\rho = 1000$ kg/m^2) and reflector ($\rho = 1180$ kg/m^2, $c = 2670$ m/s). We simulate various c_2/c_1-ratio values of tissue with c_1 being fixed to 1515 m/s. The ultrasound probe consists of a 128-element linear array with an aperture of 40 mm. The probe-reflector distance is 37 mm. We use the left-most element as emitter, with a frequency of 1 MHz, and all elements act as receivers. We pick the traveltimes of the reflections from the tissue-reflector interface by cross-correlating the signals with the recordings for the isotropic medium $c_2 = c_1 = 1515$ m/s. Figure 2(a) illustrates the wavefronts in isotropic and anisotropic media. These become elliptical in the later case, thereby affecting the traveltimes (see Fig. 2(b)). To estimate c_1 and c_2, we represent the picked traveltimes as function of emitter-receiver offset (Fig. 2(c)) and apply Eq. (4). The results are summarized in Table 1. The maximum and minimum values of c_2/c_1 correspond to values reported in the literature for bone[?] and muscle,[?] respectively. Our approach successfully estimated anisotropy parameters, with increasing accuracy for smaller c_2/c_1-ratios. This may be due to finite-frequency effects that ray theory neglects. We therefore expect higher accuracy for higher frequencies.

Table 1. True and estimated values of anisotropy parameters c_1 and c_2, and their ratio.

True parameters			Estimated parameters		
$c_1\,[m/s]$	$c_2\,[m/s]$	Ratio	$c_1\,[m/s]$	$c_2\,[m/s]$	Ratio
1515	1818	1.2	1512.6 ± 0.2	1818.1 ± 1.4	1.202 ± 0.001
1515	1666.5	1.1	1512.3 ± 0.3	1666.6 ± 1.7	1.102 ± 0.001
1515	1590.75	1.05	1514.4 ± 0.1	1590.8 ± 0.4	1.0504 ± 0.0003
1515	1530.15	1.01	1515.1 ± 0.1	1530.1 ± 0.3	1.0099 ± 0.0002
1515	1522.575	1.005	1515.1 ± 0.1	1522.5 ± 0.3	1.0049 ± 0.0002

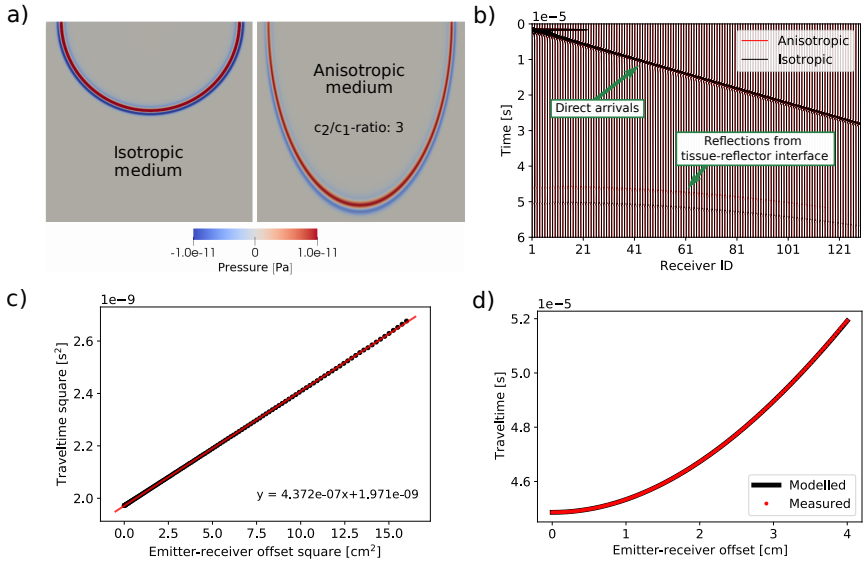

Figure 2. (a) Comparison of pressure wavefield propagation in isotropic and anisotropic media. (b) Simulated shot gather for reflector-based pulse-echo system. (c) Measured traveltimes square as function of emitter-receiver offset square (black) and the corresponding linear regression (red). (d) Comparison of measured (red) and modelled (black) traveltimes using Eq. (3) with $\varphi = 20°$. Anisotropy in figures (b), (c), and (d) is c_2/c_1-ratio = 1.1.

As a second step, we validate the general forward model in Eq. (3). Figure 2(d) compares measured and predicted traveltimes for a medium with $\varphi = 20°$, $c_1 = 1515$ m/s, and c_2/c_1-ratio = 1.1. It shows that Eq. (3) accurately models traveltimes of tissue-reflector interface reflections.

3.2 In-vivo data

To illustrate the occurrence of anisotropy in muscle tissue, we show in-vivo results for calf muscles (gastrocnemius) of a healthy volunteer. The study was approved by the local ethics committee, and informed consent was collected. We used a 5 MHz 128-element linear probe with an aperture of 38 mm (UF-760AG, Fukuda Denshi Inc.). With a probe-reflector distance of 45 mm, we picked traveltimes between the left-most element and each receiver. We then computed average SoS values by dividing geometric propagation distances with measured traveltimes. Figure 3 shows SoS values in muscle as function of θ that ranges between 0° and 23°. An experiment in water (isotropic) is also shown as a reference. As expected, SoS in water is isotropic within a measurement uncertainty of 5 m/s. SoS in muscle, however, presents anisotropic behavior, showing lowest values in the direction perpendicular to muscle fibers (1483 m/s at $\theta = 0°$) and larger values in directions more parallel to these (1520 m/s at $\theta = 23°$).

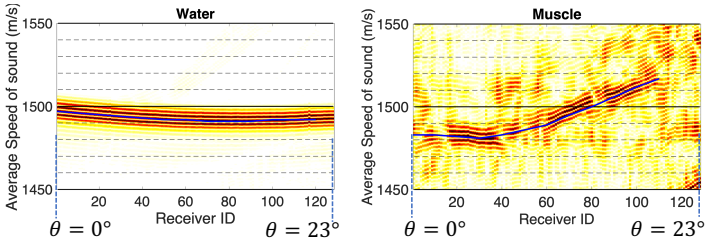

Figure 3. Experimental SoS values as function of emitter-receiver offset in (a) water, and (b) gastrocnemius muscle.

4. NEW OR BREAKTHROUGH WORK TO BE PRESENTED

We present a non-invasive quantitative method to estimate average anisotropy in SoS of soft tissue with clinical ultrasound systems. This approach has the potential to introduce new quantitative biomarkers to measure tissue microstructual alignment that pave the way for MRI DTI-analogue sequences based on ultrasound imaging.

5. CONCLUSIONS

We derived the forward problem that relates observed traveltimes with SoS anisotropy of soft tissue for pulse-echo ultrasound. Using a passive reflector, our approach has the potential to accurately estimate average anisotropy parameters of tissue. This has been demonstrated using numerical wave propagation simulations. Our numerical model is flexible to include different probe-reflector geometries. Future work will be focused on the inverse problem to robustly retrieve c_1, c_2, and φ from noisy patient data.

None of this work has been submitted elsewhere for publication or presentation.