SHEAR WAVE ELASTOGRAPHY FOR ASSESSING MYOCARDIAL MATERIAL PROPERTIES: AN IN VITRO, EX VIVO AND IN SILICO STUDY

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INTRODUCTION
Diastolic (dys)function is a major determinant of surgical decision making and clinical outcome in children with cardiac disorders. However, current diagnostic tools are not ideal as these measure surrogates for ventricular stiffness and compliance, and are either invasive or based on adult-specific guidelines [1].

Shear Wave Elastography (SWE) is a highly promising method for non-invasive assessment of cardiac muscle stiffness [2], as it derives stiffness from the propagation characteristics of the excited shear waves (SWs). We here focus on ultrasonic SWE with impulsive SW excitation, realized through a focused ultrasound beam generated by a conventional transducer. This technique has received wide recognition as a reliable, quantitative imaging tool for evaluating tissue stiffness in unbounded media, such as breast and liver tissue [3, 4]. However, its feasibility for evaluating cardiac stiffness remains to be investigated, as complex SW propagation (e.g. wave guiding, mode conversions, dispersion) is expected to arise due to the myocardium’s anisotropic material properties, and ventricular layered thin geometry.

The objective of this work was to investigate the feasibility of SWE in determining cardiac material properties by means of a combined experimental and modeling approach. More specifically, we investigated the effect of ventricular geometry and myocardial anisotropy on SW physics and characterization.

METHODS
Effect of ventricular geometry: We studied the effect of the curved and thin walled ventricular geometry on SW patterns and characterization through a generic left ventricular (LV) model tailored to 10-15 years old adolescents [5]. This model is replicated in (i) polyvinyl alcohol (PVA) for experimental purposes, to investigate the performance of different material characterization techniques and as validation for the numerical results, and (ii) in the finite element (FE) software Abaqus (Abaqus Inc., Providence, USA) for numerical purposes, to gain more profound insights into the complex SW physics (see fig. 1a). PVA’s stiffness was obtained via uniaxial mechanical testing, and served as a reference for our material model in Abaqus.

For the SWE experiments, SW’s were excited in the submerged PVA phantom via the Aixplorer system (SuperSonic Imagine, Aix-en-Provence, France) using the linear SL15-4 probe. This was done for two different cardiac zones (basal and apical) using four different probe orientations (0°, 30°, 60° and 90°). The obtained axial particle velocities were post-processed with two material characterization

![Figure 1](image-url)
methods: (i) a time-of-flight (TOF) method [6], conventionally used for bulk media without dispersion, tracking the SW’s position in time to estimate SW speed and subsequently shear stiffness and, (ii) phase velocity analysis [7], standardly applied for media with dispersion, estimating shear modulus through a theoretical fit to the measured frequency spectrum of the SW (via the 2D Fast Fourier Transform).

For the modeling part, we replicated numerically the experiment on the basal zone of the heart and 0° probe orientation. The acoustic pressures of the pushing beam were modeled in the ultrasound simulation software Field II [8]. These pressures are then converted into a time-averaged body force, which is applied on the numerical viscoelastic phantom for the experimental push duration (250 µs). With this model, we studied the effect of tissue surroundings (water) and acoustic loading (interface pressure) on SW physics in the LV.

Effect of myocardial anisotropy: The influence of myocardial anisotropy on SW characteristics was investigated by performing SWE experiments on a pig heart, obtained from a slaughterhouse. A rectangular slab was dissected from the left ventricle by cutting along the interventricular septum. This slab was uniaxially pre-stretched (5%, 10 % and 15%) during SWE acquisitions for 19 different probe directions – 0° to 180° in steps of 10° (see fig. 1b). Assuming the myocardium consists of transversely isotropic layers, the fiber orientation was estimated for each of these layers based on the angle of the tilted major axis of the ellipse fitted to the wave surface [9]. For validation purposes, the myocardial fiber architecture was also derived through a visual image analysis of the sliced myocardium [10].

RESULTS

Effect of ventricular geometry: The modeled SW propagation corresponded well with the experiment (fig. 2a), especially when the surrounding water and the surface radiation force, present at the phantom-water interfaces during SW excitation, were accounted for. In both cases, clear dispersion was present as the SW front has split into two (see arrows in fig. 2a). For stiffness characterization (fig. 2b), the TOF-method underestimated (11.6-20.8 kPa for all acquisitions) actual stiffness of 24.3 kPa whereas the phase velocity analysis or cF-method slightly overestimated (21.1-31.2 kPa for all acquisitions).

Effect of myocardial anisotropy: The resulting fiber orientation across myocardial thickness for 5% stretch is illustrated in fig. 3a. The SWE-derived fiber architecture corresponded well to the image based analysis (fig. 3b). Fig. 3b also shows a clear alignment of the myocardial fibers when stretching the LV slab.

Figure 3 – Effect of myocardial anisotropy: (a) SWE-derived fiber angles for 5% stretch, (b) Fiber orientation via SWE vs. image analysis results.

DISCUSSION

SWE experiments and simulations both improved our understanding of the factors influencing SW propagation and characterization in the LV setting, providing insights in the potential applicability and accuracy of the method in vivo.

In vitro assessment of shear moduli estimators revealed that phase velocity analysis better estimated true stiffness than the TOF-method, independent of the selected cardiac zone and probe orientation (representing LV settings with varying thickness and curvature). This demonstrates the importance of using a material characterization algorithm for dispersive wave regimes, instead of the machine-implemented method for non-dispersive SWs. This conclusion is in line with recent results from Maksuti [11] on models of arteries. Additionally, we presented the potential of SWE in non-invasively extracting myocardial fiber orientation during uniaxial loading, which is corresponding with previous studies [12]. SWE offers the advantages of using low cost ultrasound and acquiring data in a short time, making it an attractive alternative to the well-established Diffusion Tensor MRI [13] for visualizing the myocardial fiber architecture.

We conclude that the ventricular geometry and anisotropic composition of the myocardium pose extra challenges to the use of SWE-based characterization of myocardial stiffness in the clinical setting. Therefore, an important role for FE-modeling is foreseen to ultimately improve these soft tissue characterization techniques.

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