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● *Original Contribution*

ARTERIAL STIFFNESS ESTIMATION BY SHEAR WAVE ELASTOGRAPHY: VALIDATION IN PHANTOMS WITH MECHANICAL TESTING

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Abstract—Arterial stiffness is an independent risk factor found to correlate with a wide range of cardiovascular diseases. It has been suggested that shear wave elastography (SWE) can be used to quantitatively measure local arterial shear modulus, but an accuracy assessment of the technique for arterial applications has not yet been performed. In this study, the influence of confined geometry on shear modulus estimation, by both group and phase velocity analysis, was assessed, and the accuracy of SWE in comparison with mechanical testing was measured in nine pressurized arterial phantoms. The results indicated that group velocity with an infinite medium assumption estimated shear modulus values incorrectly in comparison with mechanical testing in arterial phantoms (6.7 ± 0.0 kPa from group velocity and 30.5 ± 0.4 kPa from mechanical testing). To the contrary, SWE measurements based on phase velocity analysis (30.6 ± 3.2 kPa) were in good agreement with mechanical testing, with a relative error between the two techniques of 8.8 ± 6.0% in the shear modulus range evaluated (40–100 kPa). SWE by phase velocity analysis was validated to accurately measure stiffness in arterial phantoms. (E-mail: elira.maksuti@sth.kth.se) **© 2016 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).**

Key Words: **Accuracy, Arterial phantom, Arterial stiffness, Group velocity, Lamb waves, Mechanical testing, Phase velocity, Poly(vinyl alcohol), Shear modulus, Shear wave elastography.**

INTRODUCTION

Arterial stiffness has been reported to be an independent risk factor for a wide range of cardiovascular diseases, such as hypertension, heart failure, stroke (Quinn et al. 2012; Vlachopoulos et al. 2010) and hypertensive complications of pregnancy (Coutinho 2014). Furthermore, elevated arterial stiffness is a marker for the development of atherosclerosis (Vlachopoulos et al. 2010) that may precede the onset of clinical apparent cardiovascular disease as well as be involved in the development of hypertension (Glasser 1997). Early detection of elevated arterial stiffness therefore has the potential to improve diagnosis and decrease morbidity and mortality rates.

Several methods have been suggested to estimate *in vivo* arterial stiffness globally and locally. The pulse wave velocity (PWV) technique is commonly used to estimate global arterial stiffness by measuring the velocity of the pulse wave generated by the heart while propagating through the arterial system. This PWV is then related to the arterial elastic modulus of the arterial wall. Other methods aim at estimating indices related to local arterial stiffness and are usually based on ultrasound imaging techniques. Among these methods, some common measures are distensibility (Hoeks et al. 1990), stiffness index (Kawasaki et al. 1987), local PWV imaging (Brands et al. 1998), arterial wall strain (Ribbers et al. 2007) and arterial wall strain–stress elastography (Khamdaeng et al. 2012). However, these are often combined with pressure measurements that are performed in peripheral arteries by tonometry and apply a transfer function to obtain the pressure waveform in the large central arteries (Kim and Braam 2013). Because of the limitations of the suggested methods, no gold standard for assessing arterial stiffness locally has been identified (Hamilton et al. 2007).

In the past few decades, there has been increased interest in the ultrasound technique shear wave

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elastography (SWE) (Sarvazyan et al. 2013). SWE is a non-invasive tool used to quantitatively assess local tissue stiffness that can be integrated into a conventional ultrasound device (Bercoff et al. 2004a). The technique takes advantage of the fact that the speed of shear waves is related to the elastic shear modulus of the material. SWE has so far been validated and clinically adapted for large and relatively homogeneous organs such as breast (Chang et al. 2011) and liver (Ferraioli et al. 2014). In these organs, the shear waves are assumed to travel in a purely elastic infinite medium. In such case, the linear elastic shear modulus μ can be derived from the density ρ of the tissue and the shear wave speed c_s by

$$\mu = \rho c_s^2 \tag{1}$$

Commercial SWE systems are based on these assumptions and, therefore, specifically developed for large organs. In these systems, the speed of the envelope of the propagating shear wave, also referred to as group velocity, is used to calculate the shear modulus. The assumption of a large, homogeneous, infinite, elastic medium does not hold for arteries, but, despite this, commercially available ultrasound SWE systems have been used in arterial applications both *in vitro* (Ramnarine et al. 2014) and *in vivo* (Garrard and Ramnarine 2014). Initial studies for clinical applications of ultrasound SWE in confined tissues, such as the arterial wall (Bernal et al. 2011; Couade et al. 2010), bladder (Nenadic et al. 2013) and cornea (Tanter et al. 2009), have recently been carried out.

Magnetic resonance elastography methods have also been developed to derive arterial stiffness from the speed of induced shear waves (Woodrum et al. 2006; Xu et al. 2012). Magnetic resonance elastography enables imaging of central arteries such as the aorta, which can be difficult to image with ultrasound, but has the disadvantage of lower spatial and temporal resolution compared with ultrasound. Also the arterial magnetic resonance studies have based their analysis on group velocity.

In a confined geometry, shear wave propagation is strongly affected by internal reflections at the medium's boundaries, resulting in guided wave propagation. These reflections generate dispersion (*i.e.*, waves at different frequencies travel at different speeds), such as seen in viscoelastic media, even if the medium itself is purely elastic (Chen et al. 2004). This guided wave propagation can be mathematically modeled. An analytical solution for wave propagation in a hollow cylinder, with geometry close to that of an artery, has previously been derived (Gazis 1959a). However, the solution includes a series of Bessel functions, which can only be determined numerically (Gazis 1959b). To reduce the complexity, while still taking the geometric dispersion phenomenon into account, adoption of a Lamb wave propagation model in a plate and approximation of the complex propagation in the artery with a zero-order anti-symmetric Lamb wave mode has been proposed (Bernal et al. 2011; Couade et al. 2010). This simplification can be justified by the fact that the dispersion curves (*i.e.*, phase velocity–frequency relationship) of the plate and the hollow cylinder converge at higher frequencies (Couade et al. 2010). The expression for the anti-symmetric Lamb wave mode for a solid plate submerged in a non-viscous incompressible fluid, assuming that the solid plate and surrounding fluid have similar densities and wavenumbers, is given by (Bernal et al. 2011)

$$4k_L^3\beta \cosh\left(k_L\frac{h}{2}\right)\sinh\left(\beta\frac{h}{2}\right) - \left(k_s^2-2k_L^2\right)^2 \sinh\left(k_L\frac{h}{2}\right)\cosh\left(\beta\frac{h}{2}\right) = k_s^4 \cosh\left(k_L\frac{h}{2}\right)\cosh\left(\beta\frac{h}{2}\right) \tag{2}$$

where $k_L = \omega/c_L$ is the Lamb wavenumber, $k_S = \omega\sqrt{\rho/\mu}$ is the shear wavenumber, $\beta = \sqrt{k_L^2-k_s^2}$, ω is the angular frequency, h is the plate thickness and c_L is the frequency-dependent Lamb wave velocity. Because k_s and β are functions of the elastic shear modulus, the latter can be derived by fitting the experimental data to the theoretical model.

Phase velocity analysis using eqn (2) has previously been applied to assess arterial stiffness in urethane tubes and excised porcine carotid arteries using a Lamb wave-based model (Bernal et al. 2011), as well as in arterial phantoms and *in vivo*, where an empirical formula derived from Lamb wave theory was used to estimate the shear modulus (Couade et al. 2010). However, comparison with an independent reference method was not reported in these studies. In addition, a study of the feasibility of using SWE for detection of arterial nonlinear behavior and anisotropy on a single equine aortic sample, with comparison with mechanical testing, was recently published (Shcherbakova et al. 2014). In this study, only group velocity analysis was performed, and the sample was cut longitudinally before ultrasound investigation, thereby losing its cylindrical geometry.

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