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● *Original Contribution*

MULTIDIRECTIONAL ESTIMATION OF ARTERIAL STIFFNESS USING VASCULAR GUIDED WAVE IMAGING WITH GEOMETRY CORRECTION

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Abstract—We previously found that vascular guided wave imaging (VGWI) could non-invasively quantify transmural wall stiffness in both the longitudinal (r–z plane, 0°) and circumferential (r–θ plane, 90°) directions of soft hollow cylinders. Arterial stiffness estimation in multiple directions warrants further comprehensive characterization of arterial health, especially in the presence of asymmetric plaques, but is currently lacking. This study therefore investigated the multidirectional estimation of the arterial Young's modulus in a finite-element model, *in vitro* artery-mimicking phantoms and an excised porcine aorta. A longitudinal pre-stretch of 20% and/or lumen pressure (15 or 70 mm Hg) was additionally introduced to pre-condition the phantoms for emulating the intrinsic mechanical anisotropy of the real artery. The guided wave propagation was approximated by a zero-order antisymmetric Lamb wave model. Shape factor, which was defined as the ratio of inner radius to thickness, was calculated over the entire segment of each planar cross section of the hollow cylindrical structure at a full rotation (0°–360° at 10° increments) about the radial axis. The view-dependent geometry of the cross segment was found to affect the guided wave propagation, causing Young's modulus overestimation in four angular intervals along the propagation pathway, all of which corresponded to wall regions with low shape factors (<1.5). As validated by mechanical tensile testing, the results indicate not only that excluding the propagation pathway with low shape factors could correct the overestimation of Young's modulus, but also that VGWI could portray the anisotropy of hollow cylindrical structures and the porcine aorta based on the derived fractional anisotropy values from multidirectional modulus estimates. This study may serve as an important step toward 3-D assessment of the mechanical properties of the artery. (E-mail: wnlee@eee.hku.hk) © 2018 World Federation for Ultrasound in Medicine & Biology. All rights reserved.

Key Words: **Anisotropy, Artery, Dispersion, Guided wave, Phase velocity, Shear modulus, Ultrasound.**

INTRODUCTION

Arterial stiffness plays a central role in the function of arteries and is highly relevant to various cardiovascular diseases. Arterial stiffness directly affects the capacity of arteries to accommodate the pulsatile blood ejected from ventricles. Stiffened arteries therefore induce an increase in pulse pressure and may thereby impose an excessive afterload (Chirinos and Segers 2010; Nichols et al. 2011; Segers and Verdonck 2002) and penetration damage to peripheral target organs, such as the kidney and the brain (O'Rourke and Safar 2005; Vermeersch et al. 2008). Various biological process and risk factors, such as aging, smoking, obesity and hypertension, may affect arterial stiffness and thus cause cardiovascular diseases (Payne et al. 2010). Arterial stiffness has therefore emerged as an independent indicator of cardiovascular diseases and has been the focus of considerable investigations in the past few decades (Avolio 2013).

Several non-invasive techniques have been proposed for the quantitative measurement of arterial stiffness, including global pulse wave velocity techniques (Caro and Harrison 1962), regional pulse wave imaging (Luo et al. 2012; Taviani et al. 2010; Vappou et al. 2010) and shear wave imaging (SWI) (Bernal et al. 2011; Couade et al. 2010). The pulse wave-based techniques quantify arterial stiffness in the circumferential direction based on the velocity of the longitudinally propagating intrinsic pulse wave, which is generated by the ejection of blood from the left ventricle, *via* the Moens–Korteweg equation. Either a global value derived from the long-range measurement (Caro and Harrison 1962) or the regional value derived from the piecewise measurement (Luo et al. 2012; Taviani

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et al. 2010; Vappou et al. 2010) could be provided. Because of the low temporal sampling rate, that is, typically one intrinsic pulse wave per heartbeat, pulse wave-based techniques cannot quantify the variation in arterial stiffness over each cardiac cycle.

Recently, substantial efforts have been extended to apply SWI to arterial stiffness estimation. Since it was proposed in medical ultrasound imaging, SWI (Bercoff et al. 2004; Sarvazyan et al. 1998; Tanter et al. 2008) has been used for bulk soft tissues, such as in the characterization of the breast (Tanter et al. 2008) and liver (Muller et al. 2009). The group velocity (c_g) of the shear wave, which is generated using either an external vibrator or focused acoustic beams from a conventional ultrasound probe, is directly related to the stiffness of the underlying homogeneous, isotropic, incompressible and linearly elastic medium through

$$\mu = c_g^2 \times \rho \tag{1}$$

where μ and ρ are the shear modulus and the density of the medium, respectively. For arterial stiffness estimation using SWI, the thin-walled structure of the artery has been found to act as a wave guide and modify the propagation of the generated shear waves. The phase velocity c_{ph} of the shear wave is linked to μ by the zero-order antisymmetric Lamb wave model (Bernal et al. 2011) formulated as

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

where h is the thickness of the arterial wall, $k_L = \omega / c_{\mathrm{ph}}$ is the Lamb wavenumber, ω is the angular frequency, $\beta = \sqrt{k_L^2 - k_s^2}$ and $k_s = \omega\sqrt{\rho/\mu}$. The variation in *in vivo* arterial stiffness over the entire cardiac cycle has been reported (Couade et al. 2010). Subsequent studies have further reported SWI-estimated arterial stiffness in various conditions, such as thickness (Widman et al. 2016) and coupling medium (Chang et al. 2017), and validated its reliability by mechanical testing (Maksuti et al. 2016).

However, all the aforementioned studies assumed isotropy and reported arterial stiffness either in the circumferential direction by pulse wave-based techniques or in the longitudinal direction by the SWI. Arteries, which are composed of three layers with fibrous structures orienting along specific directions, cannot be simply regarded as an isotropic material. The structural and, thus, mechanical anisotropy was regarded as a direction-dependent response to loading. Assessment in one single direction is insufficient to fully evaluate the mechanical function of arteries. Moreover, plaque formation outside the imaging plane may thus be overlooked (Hansen et al. 2015).

In the investigation of arterial anisotropy and cross-segmental plaque characterization, there have been several recent studies that have employed arterial SWI in the circumferential direction (Guo et al. 2017; Hansen et al. 2015; He et al. 2017; Li et al. 2017; Shcherbakova et al. 2013, 2014; Urban et al. 2013). Guided circumferential wave (GCW), which was first proposed in non-destructive testing (NDT) (Liu and Qu 1998a, 1998b; Qu et al. 1996) to describe the guided wave propagation in the circumferential direction of hollow cylindrical structures, was introduced for the estimation of circumferential arterial stiffness (Guo et al. 2017; He et al. 2017; Li et al. 2017). These studies verified that the GCW could be approximated as a Lamb wave in eqn (2) when the shape factor p, which was defined as the ratio of the inner radius to the thickness, was larger than 1.5 from the finite-element-model simulations (Li et al. 2017). A new method based on coordinate transformation and directional filter was proposed for radial displacement estimation in the circumferential cross segment to derive the dispersion curve *ex vivo* and *in vivo* with significant improvement (He et al. 2017). Separately, we employed the Lamb-type wave model and reported biplanar estimation of the arterial stiffness across the wall (Guo et al. 2017). Although the other studies quantified wall stiffness either at the midwall or at the outer wall, we found that accurate estimation of circumferential stiffness was achieved in the vicinity of the inner boundary of the artery-mimicking phantoms whose shape factor was chosen to approximate that of large human arteries (Guo et al. 2017).

The biplanar estimation is, however, insufficient for fully understanding the relationship between arterial stiffness and its function, particularly in disease. The material properties of arteries under variant lumen pressure over the entire cardiac cycle in three dimensions has never been reported. Furthermore, investigating the influence of pathologic alterations, such as plaque formation (Tang et al. 2005), on arterial stiffness also requires the multidirectional estimation to identify any regional changes in the mechanical properties of arteries. In clinical practice, exact biplanar measurement in a free-hand scanning scenario may not be standardized. *A priori* knowledge about the scanning view and the estimation direction of the derived stiffness may thus be required for a more reliable clinical diagnosis.

Therefore, this study was aimed at investigating guided wave propagation in three dimensions within a thin-walled hollow cylindrical structure and proposing a method to estimate the multidirectional arterial Young's modulus. A finite-element model of isotropic thin-walled tubes, controlled artery-mimicking phantoms with either mechanical