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● *Original Contribution*

CARDIAC SHEAR WAVE VELOCITY DETECTION IN THE PORCINE HEART

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Abstract—Cardiac muscle stiffness can potentially be estimated non-invasively with shear wave elastography. Shear waves are present on the septal wall after mitral and aortic valve closure, thus providing an opportunity to assess stiffness in early systole and early diastole. We report on the shear wave recordings of 22 minipigs with high-frame-rate echocardiography. The waves were captured with 4000 frames/s using a programmable commercial ultrasound machine. The wave pattern was extracted from the data through a local tissue velocity estimator based on one-lag autocorrelation. The wave propagation velocity was determined with a normalized Radon transform, resulting in median wave propagation velocities of 2.2 m/s after mitral valve closure and 4.2 m/s after aortic valve closure. Overall the velocities ranged between 0.8 and 6.3 m/s in a 95% confidence interval. By dispersion analysis we found that the propagation velocity only mildly increased with shear wave frequency. (E-mail: h.vos@erasmusmc.nl)

Key Words: **Echocardiography, Stiffness measurements, Shear wave elastography, High-frame-rate imaging, Valve closure.**

INTRODUCTION

Heart failure is a major public health problem in developed countries. Chronic heart failure is a highly disabling and life-threatening condition: Patients experience dyspnea and fatigue, and 1-y mortality rates range from 10% to 20%. The prevalence increases rapidly with age, reaching over >10% for those aged >75 y (Mosterd et al. 1999). In patients with heart failure with preserved ejection fraction, left ventricular stiffening is presumed to be one of the important causes responsible for the symptoms and poor prognosis. Currently, there is no accurate non-invasive method for diagnosing left ventricular stiffening, as blood biomarkers are non-specific and current ultrasound imaging methods have low specificity and sensitivity (Paulus et al. 2007; van Dalen et al. 2016). Yet, early recognition of the decreasing condition of the heart, for example, in diabetic or hypertensive patients, could facilitate prompt initiation of personalized medicine (*e.g.,* angiotensin-converting enzyme [ACE] inhibitors, beta blockers, diuretics) and/or a change in lifestyle ("good food, good movement, good sleep and good attitudes") and thereby prevent or delay the progression toward overt heart failure.

The literature over the past 15 y reports the use of shear waves for tissue stiffness measurements, so-called shear wave elastography, based on either magnetic resonance or ultrasound imaging. It is targeted mainly at radiology applications such as liver cirrhosis and breast cancer diagnosis (Parker et al. 2011). The suspected correlation between diastolic dysfunction and myocardial stiffness led to several ultrasound studies on the use of shear waves to measure the myocardial stiffness (Bouchard et al. 2009; Hollender et al. 2012; Kanai 2005; Song et al. 2013; Urban et al. 2013; Vos et al.

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2015), generally using minimally invasive approaches, such as intracardiac catheters, to highly invasive approaches, including measurements in open-chest animal models. The waves occur naturally after closing of the valves, which also leads to the regular heart tones (Brekke et al. 2014; Kanai 2009; Pernot et al. 2007). Moreover, the atrial-systolic wave (*i.e.,* atrial-kick wave), which occurs in late diastole, has been studied recently by Pislaru et al. (2014). They reported the propagation of a wave front along the anterior left ventricular wall with a propagation velocity that correlates well to the derived diastolic elasticity of the wall. Alternatively, the waves can be induced by external sources (Bouchard et al. 2009; Hollender et al. 2012; Song et al. 2013; Urban et al. 2013). Shear waves in soft biological tissue have a propagation velocity of 1–10 m/s, and this velocity is influenced by the stiffness of cardiac tissue (Couade et al. 2011; Kanai 2005; Urban et al. 2013).

During each heartbeat, shear waves are generated at two different time points: after mitral valve closure, and after aortic valve closure. The first occurs in early systole, the second in early diastole. This means that muscle stiffness can be measured in both the relaxed and contracted states, potentially providing relevance for both diastolic and systolic phases.

The limited length of the septal wall (~4 cm) and the propagation velocity of these waves imply that the events generally last 10–25 ms and 50 ms at most. Hence, to visualize the waves and accurately measure their propagation velocity by tracking the wave pattern on at least a few frames, the frame rate should reach >500 frames/s. Specialized ultrasound equipment is needed that can sustain a very high frame rate on the order of 1000–5000 frames/s, compared with the 20–100 frames/s of conventional ultrasound scanners. Such high-frame-rate detection techniques (Bercoff et al. 2011; Brekke et al. 2014; Hansen et al. 2014; Holfort et al. 2008; Kruizinga et al. 2012) are made possible by the more recent development of multichannel acquisition equipment, in which all data from the probe are digitized and made available for software-based image reconstruction.

To our knowledge, cardiac shear wave measurements immediately after closure of both the aortic and mitral valves have not been studied quasi-simultaneously and in a non-invasive manner, to date. In the work described here, we explored the naturally occurring shear waves in the porcine septal wall produced by aortic and mitral valve closure using high-frame-rate ultrasound recordings and subsequent shear wave imaging. Measurements were performed on a closed chest under light sedation. The primary aim was to estimate wave propagation velocity and frequency content, as a first step toward actual non-invasive stiffness measurements. In addition, we studied dispersive wave propagation effects of the shear wave and the implications of such dispersion on the accuracy of the methods used to extract the shear wave propagation velocity from the data.

METHODS

Concept

In a bulk elastic material the shear wave velocity C_s depends on the density of the material ρ and the shear modulus μ:

$$C_s = \sqrt{\mu/\rho} \tag{1}$$

Application of this equation to actual shear wave propagation in cardiac tissue is probably too simplistic. Cardiac fiber orientation varies across the septal wall, featuring two regions of different anisotropy (Jiang et al. 2007), which may result in anisotropic shear wave propagation as observed with radiation force-induced shear wave elastography (Couade et al. 2011). Furthermore, viscous loss will introduce dispersion (Bercoff et al. 2004b), and the finite wall thickness may lead to dispersive Lamb waves (Kanai 2005; Nenadic et al. 2011). Moreover, the shear modulus varies in time throughout the cardiac cycle (Couade et al. 2011), with presumably the strongest variation in early systolic and early diastolic phases, which mark the onset of contraction and relaxation. Nonetheless, the equation illustrates that shear modulus and shear wave propagation do have a monotonic relationship in which a higher propagation velocity is expected for a higher shear modulus (*i.e.,* stiffer material).

We extracted the shear waves on the septal wall after mitral valve and aortic valve closure. Shear waves have a particle displacement oriented perpendicularly to the direction of propagation. In soft biological tissue, the *propagation* velocity is on the order of 1–10 m/s. The *local particle* velocity of the shear waves is much lower, on the order of 0.1–3 cm/s. Tissue Doppler imaging is used to detect this local particle velocity. Because Doppler is most sensitive to axial motion, it can best detect shear waves propagating laterally in the field of view, at a tissue Doppler image (TDI) velocity scale adapted to match the local particle velocity. Translating these properties into clinical echocardiography, a TDI system would be most sensitive to shear waves traveling through the interventricular septal wall in a long-axis parasternal view, rather than in an apical view. Hence, we used the parasternal view to detect the waves after valve closure.

Animal model and preparations

The study was approved by the Erasmus MC Animal Experiments Committee (DEC 109-12-22), and all experiments were performed in accordance with the National Institutes of Health *Guide for the Care and Use of*