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## Original Contribution

# ISOVOLUMETRIC ELASTICITY ALTERATION IN THE HUMAN HEART DETECTED BY IN VIVO TIME-HARMONIC ELASTOGRAPHY

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Abstract—Time harmonic elastography (THE) has recently been introduced for measurement of the periodic alteration in myocardial shear modulus based on externally induced low-frequency acoustic vibrations produced by a loudspeaker. In this study, we propose further developments of cardiac THE toward a clinical modality including integration of the vibration source into the patient bed and automated parameter extraction from harmonic shear wave amplitudes, wall motion profiles and synchronized electrocardiographic records. This method has enabled us to evaluate the delay between wall motion and wave amplitude alteration for the measurement of isovolumetric times of elasticity alteration during contraction ( $\tau_{\rm C}$ ) and relaxation ( $\tau_{\rm R}$ ) in a group of 32 healthy volunteers. On average, the wave amplitudes changed between systole and diastole by a factor of 1.7  $\pm$  0.3, with a  $\tau_{\rm C}$  of 137  $\pm$  61 ms and a  $\tau_{\rm R}$  of 68  $\pm$  73 ms, which agrees with results obtained with the more time-consuming and expensive cardiac magnetic resonance elastography. Furthermore, because of the high sampling rate, elasto-morphometric parameters such as transition times and the area of wave amplitude-cardiac motion cycles can be processed in an automated way for the future clinical detection of myocardial relaxation abnormalities. (E-mail: ingolf.sack@charite.de) © 2013 World Federation for Ultrasound in Medicine & Biology.

Key Words: Cardiac elastography, Time-harmonic shear waves, Heart, Shear modulus alteration, Isovolumetric times, Cardiac magnetic resonance elastography.

### INTRODUCTION

The periodic alteration in myocardial shear modulus is vital to blood circulation. Measurement of the shear modulus of the heart wall would provide the primary biomarker of myocardial activity and dysfunction (Glantz and Kernoff 1975; Zile et al. 2004). Myocardial tissue characterization by echocardiography combines acoustic parameters such as ultrasonic attenuation (O'Donnell et al. 1979), propagation speed (O'Brien et al. 1995) and integrated backscatter (D'Hooge et al. 2000; Wickline et al. 1985). However, these parameters are related to the propagation of pressure waves and, thus, are governed by the myocardial bulk modulus, which is, other than the shear modulus, not the primary mechanical constant altered by muscle contraction.

For this reason, various strategies of cardiac elastography have been pursued by medical ultrasound or magnetic resonance imaging (MRI) researchers to assess the alteration in myocardial elasticity during the heart cycle non-invasively. Basically three concepts of mechanical activation of in vivo heart muscle for elastographic examinations have been realized: intrinsic activation of the myocardium (Kanai 2005, 2009; Konofagou et al. 2002; Luo et al. 2007; Pernot et al. 2007); internal stimulation of shear waves based on focused ultrasound impulses (Bouchard et al. 2009, 2011; Couade et al. 2011; Hsu et al. 2007; Pernot et al. 2011); and externally induced shear waves from a timeharmonic vibration source (Elgeti et al. 2008, 2012; Kolipaka et al. 2010). The last concept, time-harmonic elastography (THE), has been tested in animals, healthy volunteers and patients using MRI (Elgeti et al. 2010a; Kolipaka et al. 2011; Sack et al. 2009) and ultrasound (Tzschatzsch et al. 2012). Time-harmonic shear waves in the low audible frequency range 25 to 30 Hz, for example, can readily be introduced into the chest without

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significant attenuation. Moreover, the deposition of mechanical energy is negligible at low audio frequencies, as the continuous flux of shear wave energy through the tissue scales with the squared excitation frequency (Achenbach 1999). However, at low vibration frequencies, the heart wall is thinner or on the same order as the length of the shear waves being measured. In such finite geometries, the propagation speed and dispersion of shear waves depend on both intrinsic properties and the geometry of the medium (Graff 1991). To account for boundary conditions in the heart, several attempts have been made based on Lamb waves (Nenadic et al. 2011a, 2011b) or a model of 2-D waves in a spherical thin shell (Kolipaka et al. 2009a, 2009b). According to a simplified analysis of THE, shear wave amplitudes are altered because of the variation in shear modulus in an unbounded, linear elastic and isotropic medium (Sack et al. 2009). As a result, the relative variation in myocardial elasticity during the cardiac cycle was obtained. Although wave amplitude-sensitive THE is based on many elasto-dynamic assumptions, the method has been tested by our group in animals, healthy volunteers and patients with diastolic dysfunction (Elgeti et al. 2008, 2009, 2010a). Motivated by these MRI elastography (MRE) studies, we recently introduced the concept of cardiac THE into real-time ultrasound elastography and found that the wave amplitude variation (WAV) observed with this fast and cost-efficient technique agrees with MRE values (Tzschatzsch et al. 2012). However, the WAV factor is not the only potential diagnostic marker in cardiac THE. It has frequently been reported that wave amplitudes change before heart motion and that the delay between wall motion and WAV is related to isovolumetric times, which, other than the isovolumetric contraction

and isovolumetric relaxation times known from echocardiography, reflect the times of elasticity alteration during contraction ( $\tau_{\rm C}$ ) and relaxation ( $\tau_{\rm R}$ ) (Elgeti et al. 2010b). In the study described here, we aimed to measure these diagnostically important time intervals using a simple A-line ultrasound device in real-time with automated parameter extraction. To improve patient handling and consistency of wave excitation into the chest, an integrated vibration bed was proposed. The device is intended as proof-of-concept of cardiac THE as a modality potentially sensitive to pathologically increased diastolic stiffness of the left ventricular wall.

#### **METHODS**

**Patients** 

Institutional review board consent was obtained, and written informed consent was waived. None of the 32 volunteers (12 females, 22–52 y, mean = 29 y, standard deviation [SD] = 7 y, no significant age difference between women and men) was on any medication, nor had any history of cardiac events, hypertension, diabetes or hypercholesterolemia. One volunteer (male, 28 y) was investigated seven times on different days to assess the reproducibility of the method.

Mechanical stimulation of cardiac shear waves

The bed-type actuator with integrated vibration source and audio amplifier is illustrated in Fig. 1. The volunteers were investigated in expiration in a left lateral recumbent position so that the thoracic region of the patient was stimulated from the left lateral side of the chest. No further individual variation of heart anatomy or body shape had to be taken into account. The vibration

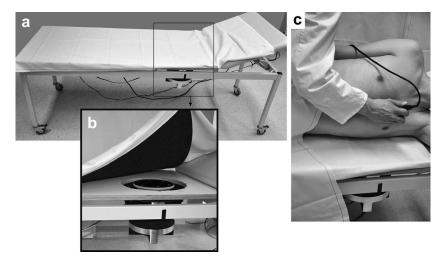


Fig. 1. Experimental setup for the vibration bed used in time-harmonic elastography. The loudspeaker underneath the patient's chest is driven by a continuous sinusoidal signal of 30-Hz frequency. In the prescribed position, the recumbent patient is prone to the left-lateral side of the thorax, while time-harmonic elastography is conducted along a parasternal line of sight with a window placed in the lateral wall of the left ventricle.

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