Waveguide Magnetic Resonance Elastography of the Left Ventricle in a Pressure Varying Model

Ria Mazumder[1], Bradley D. Clymer[1], Richard D. White[2], Anthony J. Romano[3], and Arunark Kolipaka[2]

[1]*Department of Electrical and Computer Engineering, The Ohio State University, Columbus, OH, United States,* [2]*Department of Radiology, The Ohio State University, Columbus, OH, United States,* [3]*Department of The Navy, Naval Research Laboratory, Washington, DC, United States*

Targeted Audience: Biomedical and biomechanical engineers, cardiologists, radiologists, researchers.

Purpose: Increased myocardial stiffness (MS), abnormal left ventricular (LV) filling and delayed relaxation has been associated with heart failure with preserved ejection fraction (HFPEF) also known as diastolic heart failure[1] wherein the ejection fraction (EF) of the LV stays normal (>50%). Hence, conventional determinants of heart failure such as LV EF do not indicate the true pathophysiology underlying HFPEF. Therefore, there is a need to develop an alternative diagnostic tool. Since, MS is elevated as a result of HFPEF, quantifying MS may reveal pathophysiological conditions which might assist in diagnosis and prognosis of HFPEF patients. Recently, magnetic resonance elastography (MRE) has emerged as a non-invasive tool to estimate the shear stiffness of myocardium[2-5]. However, the current established MRE technique[6] assumes the myocardium to be an infinite homogenous isotropic structure; which is not true. Previous studies have shown that the myocardium exhibited anisotropy and passive MS changed nonlinearly[7,8]. Romano et al. has demonstrated a novel technique known as waveguide MRE to quantify anisotropic stiffness of soft tissues[9, 10]. Therefore, the purpose of this study was to estimate anisotropic myocardial stiffness using waveguide MRE in an ex-vivo porcine model with varying LV pressure.

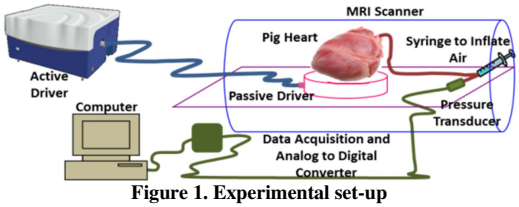

Figure 1. Experimental set-up

Methods: ***Experimental Set-Up***: Three juvenile Yorkshire (~80 lbs) pigs were used for this study. After the animals were euthanized, their hearts were extracted, flushed and stored in Ringer's solution at 4°C till the scanner was available (i.e. ~5 hrs). A balloon was inserted through the aortic opening into the LV chamber via a plastic tube (Figure 1). A syringe was attached to the end of the tube via a T-connection and was used to inflate the balloon with air at two different pressure points (Pressure range for all the three hearts: Lower (50-70mm of Hg) and higher (80-110mm of Hg)). A pressure transducer (PX26-005GV, Omega Engineering, Stamford, CT) was connected to the other end of the T-connection to measure the real-time pressure in the heart using a computer at a sampling rate of 1kHz. ***Acquisition:*** In order to estimate anisotropic stiffness, prior information of the fiber directions is necessary which was achieved using diffusion tensor imaging (DTI). DTI and MRE were performed on ex-vivo pig hearts in a 3T MRI scanner (Tim Trio, Siemens Healthcare, Erlangen, Germany). Short axis views covering the entire myocardium were imaged at an isotropic resolution of 2x2x2mm (imaging matrix: 128x128 mm^2; FOV: 256x256mm^2). ***DTI:*** Imaging parameters included: 30 diffusion encoding directions; 4 averages; TE/TR=90/5000ms; b-values=0,1000s/mm^2; ***MRE:*** Imaging parameters included: TE/TR=23.3ms/33.33ms; $\alpha=22^o$; mechanical vibration frequency=60Hz; 4 MRE time offsets; and motion encoding gradients of 16.67ms duration (60Hz) was applied in all the three directions (x, y, z) to encode the in-plane and through plane motion. ***Analysis:*** The acquired MRE and DTI images were masked to segment the LV. Custom-built software written in Matlab (Mathworks, Natick, MA) was used to obtain the principal eigenvectors. A spatial spectral filter based on the principal eigenvector was applied on the first harmonic displacement data to identify waves traveling in particular directions defined by a local coordinate system[9, 10]. Simultaneously, a Helmholtz decomposition was performed to separate the total field into its longitudinal and transverse components. Finally an orthotropic inversion was implemented to evaluate the compressional (C_{11}, C_{22}, C_{33}) and shear (C_{44}, C_{55}, C_{66}) complex stiffness values along the fiber (C_{33}), sheet (C_{11}) and sheet normal (C_{22}) directions of the heart[10]. Additionally, isotropic stiffness was measured using MRE Lab (Mayo Clinic, Rochester, MN). A 3D local frequency estimation inversion[6] (LFE) was performed by applying a directional filter in 8 directions (to remove the reflected waves) and a band-pass filter (to remove the longitudinal motion). The mean anisotropic and isotropic stiffness values and their standard deviation (SD) from all the slices were reported. Paired student's t-test was performed to determine the significant difference in stiffness value between the two pressure points with the two different inversion techniques.

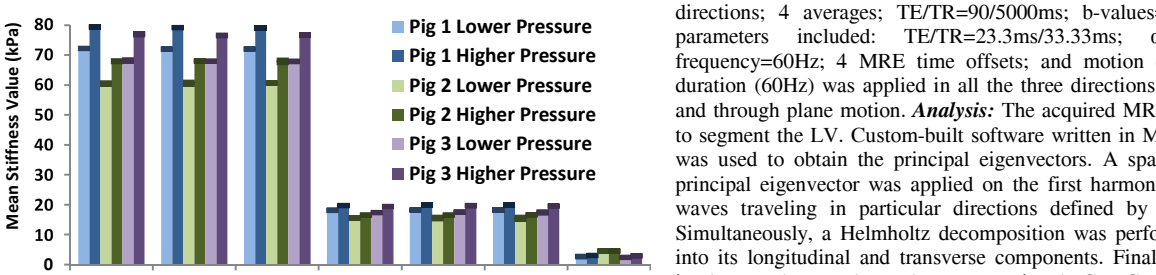

Figure 3. 1st 6 Cols: Mean anisotropic compressional (C_{11}- C_{33}) and shear (C_{44}- C_{66}) stiffness with SD. Last Col: Mean isotropic shear stiffness and their SD measured using LFE.

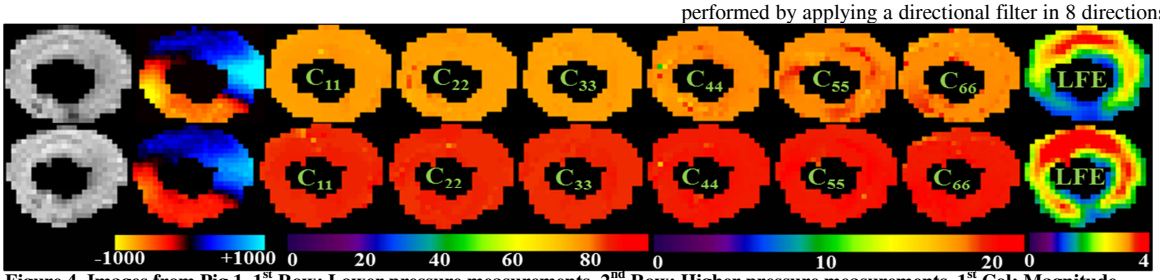

Figure 4. Images from Pig 1. 1st Row: Lower pressure measurements. 2nd Row: Higher pressure measurements. 1st Col: Magnitude Image. 2nd Col: Wave propagation in X-direction. 3rd – 5th Col: Compressional (C_{11}- C_{33}) stiffness maps (anisotropic inversion). 6th – 8th Col: Shear (C_{44}- C_{66}) stiffness maps (anisotropic inversion). 9th Col: Isotropic stiffness maps (LFE inversion).

Results: Figure 3 shows the mean stiffness values and their SD obtained from both the anisotropic (C_{11}-C_{66}) and isotropic inversion (LFE) algorithms in all the porcine hearts. Figure 4 represents the magnitude image, wave image and the corresponding stiffness maps (anisotropic and isotropic) for Pig 1 at two different pressure points.

Discussion & Conclusion: We have demonstrated that non-invasive measurement of anisotropic stiffness is feasible using waveguide MRE. As expected, stiffness increased with increasing pressure. Furthermore, we have seen that anisotropic stiffness estimation showed a significant difference between the two pressure points both in the compressional (P – Value = 0.0053) and shear (P – Value = 0.0015) stiffnesses. However, the isotopic stiffness measurements showed only slight increase in stiffness as a function of pressure with no significant difference (P – Value = 0.75).

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