Cardiac MR Elastography: Estimation of myocardial stiffness throughout cardiac cycle as a function of age

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Target Audience: Biomedical researchers, cardiovascular and radiology physicians, technologists

Purpose: Myocardial stiffness has been a significant biomarker for various cardiovascular disease processes, such as myocardial infarction, hypertension, diastolic dysfunction and tissue rejection in heart transplant patients [1-4]. Many factors contribute to stiffening of the myocardium, but it is important to understand its correlation to age. Pressure/volume based techniques are commonly used to measure left ventricular (LV) chamber stiffness, but are limited to global measurements, and do not provide true intrinsic properties of the myocardium [5]. Recently, a novel non-invasive method termed Cardiac MR Elastography (CMRE) was used to estimate stiffness of the myocardium [6,7]. However, earlier studies were performed in animals. Therefore, the aim of this study is to measure LV myocardial effective stiffness across the cardiac cycle as a function of age in healthy subjects.

Methods: All imaging was performed on a 1.5T MRI scanner (Avanto, Siemens Healthcare, Erlangen, Germany). Written informed consent was obtained from all volunteers. The study included volunteers with varying ages (age range: 21-70 y/o). A retrospectively cardiac gated, multi-phase gradient recalled echo CMRE sequence was used to obtain short axis slices of the LV covering the entire ventricle. The mechanical waves were introduced into the heart as shown in Figure 1. CMRE parameters included: TR/TE/flip angle=8.9/200ms/25°, matrix=128x64, FOV=400x400cm^2, slice thickness=10mm, # of slices=5, mechanical excitation=80Hz , # of cardiac phases=8, # of segments= 8 (+ and - motion encodings), motion encoding gradient of 160Hz (6.25 ms), which was applied separately in the x, y, and z directions to encode the motion in three directions in separate breatholds. CMRE wave images were sorted based on location within the RR-interval, and analyzed using MRE-Lab (Mayo Clinic, Rochester, MN) to obtain the stiffness of the LV myocardium.
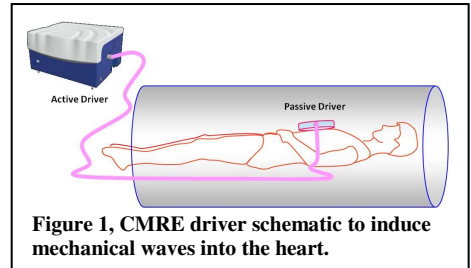

Figure 1, CMRE driver schematic to induce mechanical waves into the heart.
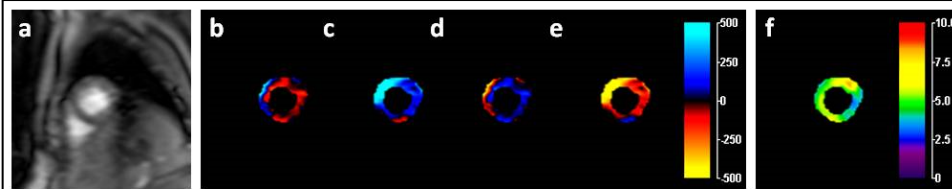

Figure 2, End-Diastolic short-axis magnitude image (a) and through plane wave images at four different time offsets (b-e), corresponding stiffness map (f).
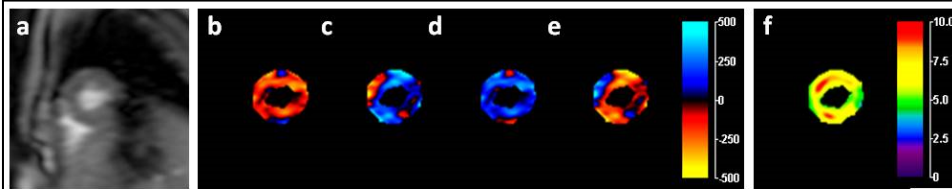

Figure 3, End-Systolic short-axis magnitude image (a) and through plane wave images at four different time offsets (b-e), corresponding stiffness map (f).

Results: Figures 2 and 3 display the magnitude (a) and four time-offset wave images (b-e) acquired on a 22 y/o male volunteer showing the LV myocardium, during end-diastole (ED) and end-systole (ES) respectively. MRE-derived stiffness maps of the myocardium were determined for all volunteers throughout the cardiac cycle using 3D local frequency estimation (see Figures 2 and 3 f). The behavior of the stiffness throughout the cardiac cycle is illustrated in Figure 4 in one of the volunteers, where a higher mean myocardial effective stiffness is measured at ES, and lower value during ED. No significant increase or decrease of ES and ED stiffness is observed as a function of age, as illustrated by the plot in Figure 6. However, a significant difference between mean ED and ES stiffness was observed (Figure 5) when pooling all the volunteers, where mean ES stiffness was 5.9±1.2 kPa and ED was 5.2±0.8 kPa (p<0.034, paired t-test).
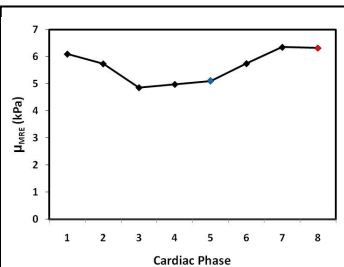
Discussion: Preliminary data show a distinct behavior across the cardiac phases, with significantly higher stiffness values during ES compared to ED. The preliminary data do not suggest a correlation with age. However, more studies are warranted to determine the correlation of LV stiffness to age.

References: *1.* Pislaru, C.J., et al, Circulation, 2004 109(23):2905-10; *2.* Badenhorst, D., et al, Cardiovas.Research, 2003 57(3):632-41; *3.* Zile, M.R., et al, Circulation, 2002 105(11):1387-93; *4.* Amrut V. Ambardekar and Peter M. Buttrick, Reverse Remodeling With Left Ventricula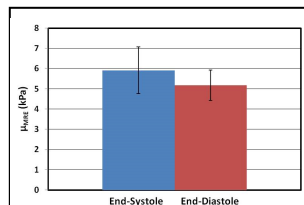r Assist Devices: A Review of Clinical, Cellular and Molecular Effects, Circ Heart Fail. 2011 4:224-233; *5.* Mirsky, I., et al, Prog. In Cardiovas. Diseases, Vol.32 No 4,1990 291-318; *6.* Kolipaka A, et al., J Magn Reson Imaging, 2012 Jul;36(1):120-7; *7.* Kolipaka A, et al., Magn Reson Med. 2010 Sep; 64(3):862-70.

Figure 4, MRE derived myocardial stiffness throughout the cardiac cycle, with a lower value at ED (blue) vs. ES (red).

Figure 5, Consistent and statistically significant differences between mean ES and ED stiffnesses were observed, with values of 5.9±1.2 vs. 5.2±0.8 kPa.

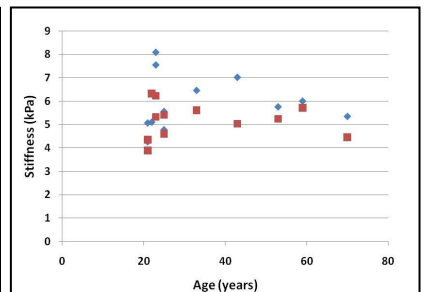**Figure 6, Plot of CMRE-derived ES stiffness (blue markers) and ED stiffness (red markers) as a function of age demonstrating no correlation.**