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Quantification of regional aortic stiffness using MR elastography: A phantom and ex-vivo porcine aorta study

Nan Zhang [a,b], Jun Chen [a,*], Meng Yin [a], Kevin J. Glaser [a], Lei Xu [b,**], Richard L. Ehman [a]

[a] Department of Radiology, Mayo Clinic, 200 First Street SW, Rochester 55905, MN, USA
[b] Department of Radiology, Beijing Anzhen Hospital, Capital Medical University, Chaoyang District Anzhen Road 2nd, Beijing 100029, China

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ABSTRACT

MR Elastography (MRE) is a noninvasive technique for measuring tissue stiffness that has been used to assess the average stiffness of the abdominal aorta. The utility of aortic MRE would be improved if it could provide information about local variations in aortic stiffness. We hypothesize that regional variations in aortic stiffness can also be measured with MRE and the purpose of this work was to demonstrate that MRE can measure regional stiffness variations in a vascular phantom and in ex vivo porcine aortas.

A vascular phantom was fabricated, containing two silicone tubes embedded in gel. A segment of one of the tubes was modified to increase its stiffness. MRE was performed on the phantom with a continuous flow of water through the tubes. The stiffness distribution along the modified tube was measured and compared to the reference tube. MRE was also performed in porcine aortas embedded in gel with segments treated with saline or formalin for 4 days. The stiffness difference between saline- and formalin-treated aortic segments was measured by MRE and mechanical tests. A positive correlation was found between the regional stiffnesses measured by MRE and mechanical tests.

The results indicate that MRE can be used to evaluate the local stiffness distribution in silicone tubes and ex vivo porcine aortas. It may therefore be possible to apply MRE to measure regional stiffness variations of the aorta in vivo.
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1. Introduction

Increased aortic stiffness has been proven to have a significant association to the onset and progression of cardiovascular diseases, such as hypertension [1], systolic hypertension, atherosclerosis [2–4], and aortic aneurysm [5,6]. Aortic stiffness is also a very important clinical indicator to predict future cardiovascular events and death, especially among hypertensive patients [7,8]. Thus, aortic stiffness assessment by using pulse wave velocity (PWV) has become a routine procedure in clinical practice.

Recent studies have demonstrated that regional variation of stiffness can provide more information for clinical diagnosis. From animal study, local pulse wave velocity (PWV) can provide early information about the local progression of atherosclerosis [3]. Higher regional aortic stiffness, especially at aortic root and ascending aorta, is associated with higher rates of surgical aortic replacement and aortic root dilation in children and young adults with connective tissue disorders [9]. Regional PWV was found to be correlated with different cardiovascular risk factors [10], different incidence and prognosis of various cardiovascular diseases in hypertensive patients [11].

PWV is one of the methods to evaluate global aortic stiffness [12]. However, because of the inaccurate estimation of aortic length from body surface anatomical landmarks, the accuracy of PWV assessment is controversial [13]. Regional aortic stiffness may better reflect the mechanical property distribution of the aorta. The local change in aortic diameter or area due to pressure along the aorta can be used to evaluate regional aortic stiffness, but the central pressure required for this analysis must typically be measured invasively by catheterization [14]. With the development of MR and ultrasound derived PWV, regional arterial stiffness of different aortic segments has shown the potential capability to evaluate the cardiovascular health and risk of patients [15–17].

MRE has been used in a few studies to assess aortic stiffness [18–20]. However, it has not been tested if MRE is capable of measuring regional aortic stiffness. In the present study, our aim was to investigate the feasibility of measuring regional differences in aortic stiffness using a silicone tube model of the aorta and ex vivo porcine aortas.

2. Materials and methods

2.1. Phantom study

A phantom study was first performed to assess wave propagation along an aorta with different elastic properties in two segments. Half

* Correspondence to: J. Chen, Department of Radiology, Mayo Clinic, 200 First Street SW, Rochester 55905, MN, USA. Tel.: +1 507 538 0758.
** Correspondence to: L. Xu, Department of Radiology, Beijing Anzhen Hospital, Capital Medical University, Chaoyang District Anzhen Road 2nd, Beijing 100029, China. Tel.: +86 133 7010 3592.
E-mail addresses: Chen.Jun@mayo.edu (J. Chen), leixu2001@hotmail.com (L. Xu).

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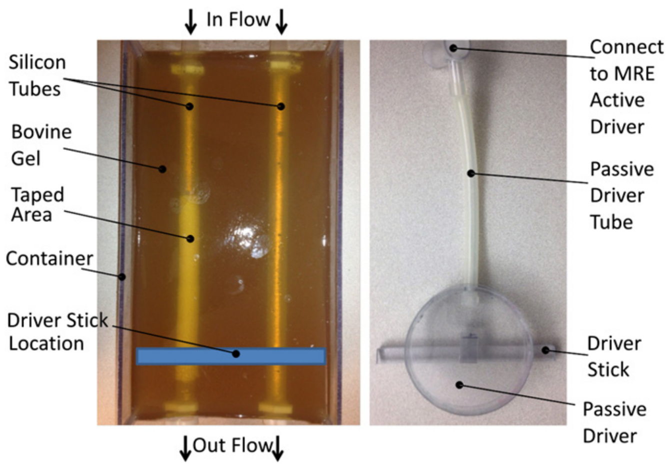

Fig. 1. Schematic of the driver and phantom setup.

of a 30-cm long silicone tube was wrapped with waterproof tape (Kendall™, Covidien) to simulate an aortic segment with higher wall stiffness. A tissue-simulating 10% B-gel (Bovine Skin Powder, Sigma-Aldrich, St. Louis, MO) was made in a rectangular container to mimic the abdominal tissue that mechanical vibrations normally pass through during in vivo MRE. The tube was embedded at the bottom of the gel phantom and another silicone tube of the same type but without tape was embedded as well to serve as a control. Tap water was circulated through the embedded tubes during the scans.

Fig. 1 shows the driver and phantom setup. A 10-cm-long plastic stick was attached to a plastic drum-like passive driver (6-cm diameter), which was connected to MRE active driver [19,21]. The driver stick was positioned on one side of the phantom where the tap water flew out of the two tubes; the stick was also perpendicular to the two tubes so that it tapped the phantom right above the two tubes simultaneously. Tape water was continuously flowing in the two tubes to maintain stable pressure in case of collapse of the lumen. The exact flow rate was not recorded during the experiments, but it was set closed to the blood flow velocity during diastolic phase in vivo.

The phantom with the attached passive driver was placed in a single-channel transmit–receive (T/R) head coil. Imaging was performed on a 1.5-T whole-body MR system (Signa HDxt, GE Medical Systems, Waukesha, WI). For localization, coronal images were first acquired using a T2-weighted single-shot fast spin echo (SSFSE) sequence. A 2D, non-gated, flow-compensated, gradient-echo MRE sequence was used to image the wave propagation in the phantom [22].

The data acquisition parameters for MRE were as follows: single 6-mm-thick coronal slice, repetition time/echo time (TR/TE) = 50.1/26.6 ms, 256 × 96 acquisition matrix with a 0.75 FOV in the phase-encoding direction (interpolated to a 256 × 256 matrix), flip angle = 30°, FOV = 40 cm, and bandwidth = 31.25 kHz. The imaging plane was oriented along the longitudinal axis of both tubes. One 16.7-ms, 1.6-G/cm, first gradient moment nulled motion-encoding gradient was applied in the slice direction (dominating motion direction in the tubes). Ten phase offset images were acquired equally spaced over one cycle of the motion.

The MRE wave images were analyzed using MRE-Lab (Mayo Clinic, Rochester, MN). The coronal images were masked to the region of the tubes for MRE data analysis, including the wall and lumen. A one-dimensional directional filter was applied to the wave data to isolate wave propagation in one direction along the tubes and to remove the reflected wave information (Fig. 2). The directional filter incorporated a 4th-order Butterworth bandpass filter with cutoff values of 1–40 waves/FOV to remove longitudinal waves and high-frequency noise [23]. The directionally filtered wave images were then processed using the local frequency estimation (LFE) and phase gradient (PG) inversion algorithms to obtain effective shear stiffness maps of the tube, μ_{MRE} [19,20].

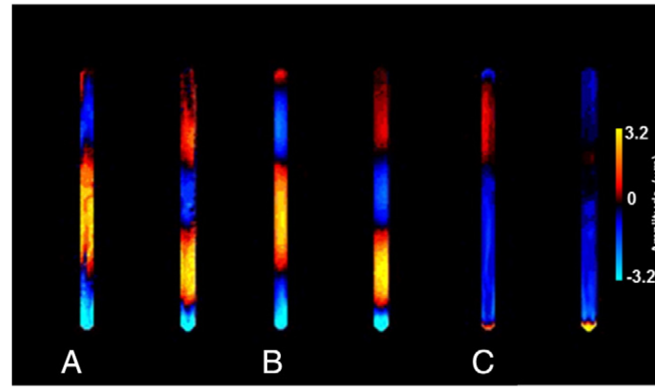

Fig. 2. Phantom MRE Wave Images. A) One offset of the acquired wave data in the phantom. B, C) The forward and reflected waves isolated using a 1D directional filter.

2.2. Ex vivo porcine aorta

4 ex vivo porcine aortas were obtained from seven-month-old male domestic healthy pigs (100–130 kg) within 15 min of slaughter from a local commercial slaughterhouse. The aortas were immersed in 0.9% saline solution (0.9% sodium chloride USP pH 5.0 (4.5 to 7.0) mEq/L solidum 154 chloride 154 osmolarity 308 mOsmol/L, Baxter Healthcare, IL, USA) and preserved at room temperature prior to examination. All the side branches were tied off. Fig. 3 shows a picture of one of the excised porcine aortas.

The porcine aortas were cut to about 28 cm in length and were embedded in 10% B-gel as was done for the phantom study described above. 3 aortas were embedded in a single gel, and the other aorta used for control was embedded in another gel phantom. Glass rod was placed in each aortic lumen before being embedded in the hot gel to prevent the collapse due to the weight; when the B-gel cooled down and solidified, the glass rod was removed from the aortic lumen for MRE experiments. MRE was performed on each porcine aorta with the same driver arrangement and MRE protocol as the phantom study. Similar to the phantom study, tap water was circulated through the aortas during the scans. The total time from death of the animal to completion of all examinations on the aortas was approximately 12 h.

After MRE scan, all the aortas were removed from the gel, and the 3 aortas were wrapped with 2 pieces of gauze, one piece covering each half of the length of the aorta. One piece of gauze was soaked with saline and the other was soaked with 10% neutral buffered formalin (NBF) (Fisher Scientific Company L.L.C., Kalamazoo, MI). The fourth aorta sample was wrapped with only saline gauze for standard reference. Aortic samples were reexamined using the same driver arrangement and MRE protocol two times at 2, 4 days. The aortas were embedded in gel 6 h before each reexamination with gauze removed. During the course of the study, saline and NBF were added to the gauze every 3 h to prevent evaporation.

All the images were analyzed with the same procedure that was used for the phantom study. The effective shear stiffness maps were used to report μ_{MRE} for all of the aorta samples.

Within 6 h after the last MRE scan, mechanical testing was performed on each aorta sample. We used disk geometries with 15-cm diameter and 2-mm thickness for all of our aorta samples that underwent RheoSpectris test (RheoSpectrisTM C500+, Rheolution Inc., Canada). Each sample was fixed horizontal on the circular cavity without visible curvature (Fig. 4). Optical beam was then focused at the center of the circular upper surface of the disk sample for mechanical testing at 60 Hz. 3 positions in the 3 treated aortas, including the saline segment, formalin segment and junctional part were chosen for mechanical testing, as well as two locations in the reference aorta.

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