Published in final edited form as:

Magn Reson Med. 2016 May ; 75(5): 1920–1926. doi:10.1002/mrm.25719.

Quantification of Aortic Stiffness Using Magnetic Resonance Elastography: Measurement Reproducibility, Pulse Wave Velocity Comparison, Changes over Cardiac Cycle, and Relationship with Age

William E. Kenyhercz¹, Brian Raterman, B.S.R.T.¹, Venkata Sita Priyanka Illapani^{1,2}, Joshua Dowell, M.D.³, Xiaokui Mo, Ph.D, M.A.S.⁴, Richard D. White, M.D.^{1,2,3}, and Arunark Kolipaka, Ph.D^{1,2,3}

¹Department of Radiology, Wexner Medical Center, The Ohio State University, Columbus, Ohio, USA

²Department of Biomedical Engineering, The Ohio State University, Columbus, Ohio, USA

³Department of Internal Medicine, Division of Cardiovascular Medicine, Wexner Medical Center, The Ohio State University, Columbus, Ohio, USA

⁴Center for Biostatistics, The Ohio State University, Columbus, Ohio, USA

Abstract

Purpose—To assess MRE-derived aortic shear stiffness (μ_{MRE}) measurements for: 1. Reproducibility 2. changes over the cardiac cycle; and 3. relationship with age.

Methods—Cardiac-gated aortic MRE was performed on 20 healthy volunteers (ages 20–73yrs). For assessing reproducibility of stiffness measurements, scans were repeated per volunteer. MRE wave images were analyzed to obtain stiffness of the abdominal aorta across the cardiac cycle, and comparisons were made with subject age.

Results—Analysis of concordance correlation coefficient between scans 1 and 2 showed that $r_c=0.86$ (95% confidence interval (CI):0.77,0.94) with $P<0.0001$. Significantly higher μ_{MRE} was observed for all volunteers during end-systole when compared to end-diastole ($P<0.0001$). μ_{MRE} increased with age; end-systolic stiffness demonstrated a relatively stronger correlation with age ($r=0.62, P=0.003$) when compared to end-diastolic stiffness ($r=0.51, P=0.023$); the slopes of end-systole and end-diastole were found to be significantly different ($P=0.011$). $\sqrt{\mu_{\text{MRE}}}$ at end-systole and end-diastole correlated linearly with PWV with an $r=0.54 (P=0.013)$ and $r=0.58 (P=0.008)$, respectively.

Conclusion—The results of this study indicate that MRE-derived aortic shear stiffness measurements are robust (reproducible and comparable to similar techniques). Mean μ_{MRE} was higher during end-systole when compared to end-diastole. μ_{MRE} was found to increase with age and showed a stronger correlation with end-systolic stiffness than with end-diastolic stiffness.

Keywords

Aortic stiffness; Aortic MRE; MRE; MR Elastography

Introduction

Arterial stiffness is an important indicator of cardio-/cerebro-vascular co-morbidities (e.g. hypertension, diabetes, and atherosclerosis) (1–4) and risks (e.g. stroke) (5). It also aids in tracking the progression of other common cardiovascular diseases, such as Marfan syndrome and abdominal aortic aneurysm (6,7). Thus, the early assessment of arterial stiffness could help in diagnosis and prognostication of such conditions, impacting patient treatments and outcomes.

It is important to estimate the stiffness of the aorta from both temporal and spatial perspectives. While changes in aortic stiffness can affect the onset or progression of hypertension (8), it varies dependently (1,9) as well as independently (10) of blood pressure at different temporal points of the cardiac cycle. During systole the blood pressure is higher causing aorta to be stiffer compared to diastole. On the other hand, in the case of AAA, the local tissue composition characteristically differs, and hence stiffness varies spatially depending on the area of aneurysm (11).

There are currently both invasive (12,13) and noninvasive (14–16) clinical methods for measuring arterial stiffness. Invasive methods include arterial catheterization, which requires greater involvement of medical personnel and technical precision, lengthy procedure and recovery times, and procedural risk from complications; in addition, they only provide a global measure of aortic stiffness (17). Of the noninvasive methods, pulse wave velocity (PWV) has been considered to be the gold standard for clinical use (4). However, PWV measurements have many limitations in quantifying aortic stiffness; PWV techniques that rely on peripheral pulse pressure do not adequately represent the true aortic pulse pressure (4,18) and cannot provide true path length of the pulse wave. While magnetic resonance imaging (MRI)-based PWV techniques provide accurate path length, they lack temporal resolution (19). Additionally, PWV analysis provides only global and indirect estimates, which do not account for the temporal and spatial variation inherent in arterial stiffness.

Magnetic resonance elastography (MRE) is a novel, noninvasive MRI-based technique used to determine the shear stiffness (μ) of soft tissue by examining propagating mechanical waves (20–24). MRE is a three-stage process: 1. Mechanical waves are induced in a region of interest; 2. A phase-contrast MRI sequence is synchronized with the mechanical waves to image propagating waves in the tissue of interest; and 3. The wave images are processed to yield spatial stiffness maps known as elastograms (25,26). Recently, MRE has been demonstrated to successfully determine aortic stiffness (27–29). However, none of the earlier studies have estimated the stiffness of the aorta temporally over the cardiac cycle.

The aims of this study are to: 1. Determine the reproducibility of shear stiffness estimates within subjects between two separate scans and compare data with MRI PWV; 2. Evaluate

MRE-derived aortic shear stiffness (μ_{MRE}) over the cardiac cycle; and 3. Assess the relationship of MRE-derived aortic stiffness to age.

Methods

Abdominal aortic MRE was performed on 20 healthy volunteers (aged 20–73 years old) after obtaining written informed consent with the approval of the Institutional Review Board.

Experimental Setup

All imaging was performed on a 3T MRI scanner (Tim Trio, Siemens Healthcare, Germany). The volunteers were positioned supine and headfirst in the scanner. For MRE, 70Hz mechanical waves were induced into the abdomen using a pneumatic driver system (Resoundant Inc., Rochester, MN) as shown in Figure 1 (27). The passive driver was strapped to the abdomen just inferior to the xiphoid process of the sternum; it was connected to the active driver (i.e. acoustic speaker) located outside the scan room via a plastic tube to induce vibrations. Upon completion of the first MRE scan, each volunteer was asked to step out of the scan room and then return for passive driver repositioning for the second scan, allowing for roughly five minutes between first and second scans. This common approach was previously adopted for staging liver fibrosis using MRE (30,31).

It was determined after the scanning of three volunteers that peripheral blood pressure (BP) measurements are needed to determine its correlation to MRE-derived shear stiffness. Therefore, the BP measurements were taken before the first scan and after the second scan for the subsequent seventeen volunteers.

Image Acquisition

Cine MRE (20,32–34) and phase contrast (PC)-MRI (35,36) sequences were performed to obtain wave and velocity data in the aorta. A 2D multi-slice segmented, retrospective cardiac-gated (pulse gating), gradient recalled echo-MRE cine sequence (20,32–34) was performed to acquire wave data in sagittal views of the abdominal aorta. The imaging parameters included: echo time (TE)= 9.52 ms; repetition time (TR) = 14.28 ms; number of slices (non-contiguous) = 3; slice thickness = 6 mm with a 3 mm overlap with adjacent slices; acquisition matrix = 128×64 ; $\alpha = 25^\circ$; field of view (FOV) = 40 cm^2 ; number of segments = 6–8 (+/- motion encoding); heart rate = 44–90 beats per minute; 8 cardiac phases; 4 MRE phase offsets (to allow tracking of wave propagation over time); and a motion-encoding gradient of 120 Hz was applied separately in the x, y, and z directions to encode the displacements. Standard bSSFP cine cardiac imaging (32) of the left ventricular outflow tract was performed to determine trigger times for end-diastolic (ED) and end-systolic (ES) phases based on aortic valve closure and opening. All images were acquired within a 16–20 sec breath-hold under end-expiration depending on the heart rate. The imaging parameters for the PC-MRI included: TE/TR = 2.1/9.1 ms, $v_{\text{enc}} = 150 \text{ cm/s}$, acquisition matrix = 192×144 , FOV = $30 \times 40 \text{ cm}^2$, slice thickness = 5 mm, flip angle = 15° , number of cardiac phases = 128, GRAPPA acceleration factor = 2 with 24 reference lines

collected in the same scan, number of averages = 2 and lines per segment = 15. PC-MRI images were acquired using retrospective gating under free breathing.

Image Analysis

The sagittal images were masked to delineate the abdominal aorta. MRE wave images were processed using MRE-lab (Mayo Clinic, Rochester, MN). The images were filtered using 2D Butterworth bandpass filter with cutoff values of 0.4m (1 Wave/FOV) to 0.01m (40 Waves/FOV) to remove the longitudinal component of motion and directionally filtered to remove the reflected waves (25). The first harmonic component of displacement field was then processed to obtain effective 3D shear stiffness (μ_{MRE}) maps of the abdominal aorta using a local-frequency estimation (LFE) inversion algorithm (25,26), which was used earlier to estimate aortic shear stiffness (27). The term shear stiffness is referred to as 'stiffness' in this manuscript. Wave images were processed separately in the x, y, and z directions to determine the phase-difference signal-to-noise ratio (SNR). A manual region of interest (ROI) was drawn to exclude any areas of the aorta with phase-difference SNR values < 3 , for areas below this threshold have been found to be unreliable (37). Finally, the center-slice data from the resultant stiffness maps was eroded by two pixels to account for edge effect stemming from the lognormal filters used in the LFE algorithm and processed to calculate mean and standard deviation (SD) values using Matlab (Mathworks, Natic, MA). Trigger times for ES and ED obtained from the bSSFP sequence were matched with MRE data and simultaneously mapped to the rest of the cardiac cycle to report the stiffness values across the cardiac cycle. PWV was measured using PC-MRI phase images using a custom-built Matlab software as detailed elsewhere (27).

Statistical Analysis

For assessment of reproducibility, the agreement between scans 1 and 2 was evaluated by concordance correlation coefficient (38); data were analyzed using STATA13 (StataCorp LP, College station, Texas). A linear regression was performed between ED μ_{MRE} and both PWV and age, and also between ES μ_{MRE} and both PWV and age to determine the correlations; data were analyzed using SAS 9.3 (SAS, Inc. Cary, NC). Additionally, linear regression was performed to determine correlation between blood pressure and μ_{MRE} . Wilcoxon signed rank test was performed to test the difference between ED and ES μ_{MRE} . Volunteers were separated into two age groups (20–54 and 55–73 years of age) as determined by previous studies (27,39). We also assessed the correlation between μ_{MRE} vs age and age vs BP using Pearson method.

Results

Higher μ_{MRE} was observed for all volunteers during ES when compared to ED. Figure 2 demonstrates this trend in both younger (22 years) and older (73 years) healthy volunteers. Figure 3 provides the values of μ_{MRE} during ED and ES for all volunteers, demonstrating significantly higher aortic stiffness at ES ($P < 0.0001$).

Good agreement in stiffness measurements was found between repeated scans within the same volunteer. Figure 4a shows inter-scan differences in mean stiffness values across

cardiac cycle in three volunteers. The concordance plot between two scans for all volunteers is shown in Figure 4b demonstrating a significant strong correlation of $r_c = 0.86$ (narrow 95% CI: 0.77, 0.94, $P < 0.0001$) for inter-scan differences in mean stiffness values.

MRE-derived stiffness of the aortic wall showed moderate correlation with PWV in each volunteer. Figure 5 demonstrates the linear association between PWV and square root of MRE-derived stiffness at both ED and ES. As the PWV increased by 1 unit, ED $\sqrt{\mu_{\text{MRE}}}$ increased by 0.0012 ($P=0.008$; 95% CI: 0.00017, 0.002). As the PWV increased by 1 unit, ES $\sqrt{\mu_{\text{MRE}}}$ increased by 0.0016 ($P=0.01$; 95% CI: 0.00053, 0.0026). ES and ED $\sqrt{\mu_{\text{MRE}}}$ demonstrated comparable ($P=0.61$) correlations to PWV with $r = 0.54$ (residual mean square error = 0.0706) and $r = 0.58$ (residual mean square error = 0.0349), respectively. However, when we exclude PWV > 700 cm/s (possibly an outlier) from our analysis, non-significant correlations between PWV and $\sqrt{\mu_{\text{MRE}}}$ were determined with $r = 0.44$ ($P=0.06$) at ED with a residual mean square error of 0.036 and $r = 0.37$ ($P=0.1$) at ES with a residual mean square error of 0.0709.

Additionally, aortic stiffness varied cyclically across the cardiac cycle differently between age groups. Figure 6 demonstrates the average stiffness across the cardiac cycle for all volunteers between the two age groups (<55 years and ≥55 years). While both age groups demonstrated a consistent cyclic pattern of μ_{MRE} across the cardiac cycle with higher stiffness values during ES when compared to ED, mean μ_{MRE} for the 20–54 age group was considerably lower than for the 55–73 age group.

Aortic stiffness increased with increase in age. Figure 7 demonstrates the linear association of both ED μ_{MRE} and ES μ_{MRE} as a function of age. Results from linear regression model indicated that as the age increased by 1 year, the ED μ_{MRE} increased by 0.03 kPa ($P=0.058$; 95% CI: 0, 0.062), while the ES μ_{MRE} increased by 0.06 kPa ($P=0.001$; 95% CI: 0.03, 0.09). The two slopes are significantly different ($P=0.02$). Consistent with the regression findings, ES μ_{MRE} showed relatively good correlation to age ($r = 0.62$) when compared to ED μ_{MRE} ($r = 0.51$).

Moderate linear correlation was observed between aortic stiffness and blood pressure. Figure 8 demonstrates the correlation between μ_{MRE} (ES, ED) and BP (ES, ED). Linear regression model indicated a moderate correlation of BP to μ_{MRE} with $r = 0.41$ and as the BP increased by 1 mmHg, the stiffness increased by 0.02 kPa ($P=0.001$; 95% CI: 0.009, 0.03). Furthermore, non-significant correlation was observed between BP measurements at ES, ED and age with $r=0.36$ ($P=0.15$) and $r=0.39$ ($P=0.12$), respectively. However, mean pressure vs age demonstrated a moderate correlation of $r=0.6$ with significant P-value of 0.006.

Discussion

This study demonstrated that aortic MRE to estimate wall stiffness is 1) robust; 2) changes across cardiac cycle with significantly higher ES stiffness compared to ED; and 3) varies differently with age, which agrees with previous reports (1,10,27,40).

The MRE method used in this study is based on the waveguide approach of propagating shear waves in the lumen of the aorta, which has previously been validated (27,28,41). We acknowledge that shear waves do not propagate in fluid. However, the vibration of the aortic wall causes the blood to vibrate at the same frequency, allowing for an accurate measurement of stiffness of the aorta that incorporates both blood within the lumen as well as the aortic wall (27), and thus both are justifiably incorporated into the measurement of aortic wall stiffness.

Our results demonstrated very good reproducibility in stiffness estimates between two independent aortic MRE scans. The subtle variation in stiffness estimates between these two scans can be attributed to lack of temporal resolution in our MRE technique. The current MRE sequence is a segmented GRE retrospectively gated cine MRE sequence with a TR of 14.28ms. The same sequence was applied in earlier cardiac MRE studies (20,32–34), where the k-space data was continuously acquired and binned together based on the R-wave to reconstruct systolic and diastolic phases. Based on the above temporal resolution the peak systole will include data from early systole and late systole. So, with current resolution it is difficult to capture peak systole, however there is sufficient resolution to capture diastolic phases. Slight variation in heart rate from one scan to the other repeat scan can cause subtle variation in the ES stiffness estimates due to lack of enough temporal resolution. Additionally, the ES and ED phases were determined based on the trigger times obtained from a separate sequence using aortic valve opening and closing, which were then matched to the trigger times in cine aortic MRE sequence. So, slight variation in heart rates between scans can cause slight variation in trigger times leading to subtle mismatch of ES phase. However, based on the concordance plot between scan 1 and scan 2 an $r_c=0.86$ demonstrated very good agreement.

A good correlation between blood pressure and arterial stiffness has been previously demonstrated in a longitudinal study obtaining serial measurements over 25 years in 777 subjects to study the effects of aging (40). A commonly accepted explanation suggests that the pressure wave distributed to stiffer arteries during systole is returned to the heart faster than in compliant arteries, therefore increasing systolic BP (1,3,4). As a result of these findings, it is reasonable to assume that as BP varies across the cardiac cycle, arterial stiffness can also vary, as we have demonstrated with this study. Specifically, Xu et al (29) found a strong correlation between hydrostatic pressure and aortic stiffness in an ex-vivo porcine heart; and also achieved in-vivo μ_{MRE} values within the range of those from our study for the ED phase, though they were not able to achieve values for the ES phase. In this study, we showed moderate correlation between aortic stiffness to BP. We believe that stiffness measurements obtained in our study are combination of intrinsic stiffness of the aorta (i.e. active and passive properties) and the influence of pressure across the cardiac cycle. In order to observe a strong correlation between stiffness and pressure in an in-vivo aorta, the aorta has to be under constant pressurized condition i.e. similar to that in hypertensive patients (constant chronic high pressures). Temporary fluctuation in BP in volunteers as noticed between repeat scans in our study can be due to anxiety or stress experienced, which may not alter the stiffness estimates. Also, it is known that peripheral pressure do not reflect the true aortic pressure. Therefore, we believe that the correlation of stiffness to pressure in our study is moderate.

Interestingly, our data showed a significant correlation between ES stiffness and age, which agrees with a previous report that found a greater correlation between systolic PWV and age when compared to diastole (10). This observation also corroborates a number of other studies that have found a correlation between systolic BP and arterial stiffness, though these studies did not consider diastolic BP in their analysis (40).

There are a few differences between previous studies and this study in estimating aortic stiffness (27–29,41). Earlier studies have used an MRE sequence involving only single-slice 2D data with 2D inversion (27–29,41) but this study implemented multi-slice 3D processing to account for the nature of waves as they propagate in all directions throughout the aorta. Additionally, the current aortic MRE sequence used in this study was able to report stiffness values during systolic phases, which has resulted in problems for other studies (29). However, the μ_{MRE} values obtained in this study are well within the range of previously reported abdominal aortic in-vivo stiffness measurements (27,28).

This study also demonstrated moderate correlation between MRE-derived ES and ED stiffness and PWV. To our knowledge, this is the first study that could correlate different phases of stiffness estimates to PWV. However, the moderate correlation is because of the fact that MRE stiffness measurements and PWV measurements are obtained based on different physics principle i.e. MRE measurements are obtained due to external vibrations at 70Hz, whereas PWV is obtained at ~1Hz (i.e. heart cycle) due to pulse pressure. At varying frequencies, the aorta would demonstrate a different frequency response because of the viscoelastic behavior (27). Additionally, aortic wall thickness (h) and vessel radius (r) were not considered in correlating PWV to $\sqrt{\mu_{\text{MRE}}}$, since PWV is proportional to $\sqrt{\mu_{\text{MRE}} * (h/r)}$ (from Moens-Korteweg equation) which might have led to moderate correlation. Also, the different temporal resolution of PWV and MRE-derived stiffness estimates might also play a role in moderate correlation between both the techniques.

There are some limitations in this study. MRE-derived stiffness measurements provided in this study are not absolute, as it does not consider geometry of the aorta. A previous study (27) has demonstrated a strong correlation between inversions that incorporate measurements with and without the geometry of aorta. Therefore, our study adopted the same technique in estimating the 3D stiffness. It also bears mentioning that blood pressure measurements were not obtained for all individuals, as we realized after a few scans that BP can provide additional information to study the effect of pressure on stiffness estimates. As explained earlier cine MRE technique lacks temporal resolution to estimate peak systolic estimate accurately. Finally, trigger times obtained from a separate scan using aortic valve closure and opening was used to match the ES and ED phases in MRE. This is because cine MRE sequence uses peripheral gating (which has delay in R-R interval) instead of ECG due to disturbance in ECG signal caused by external vibrations used in MRE scans. However, our results demonstrated good reproducible MRE-derived aortic stiffness estimates.

In conclusion, we have demonstrated reproducible cyclic variation of aortic stiffness across the cardiac cycle in human volunteers with higher ES stiffness compared to ED stiffness. Additionally, we found a stronger linear correlation between ES stiffness and age than ED

stiffness. These findings warrant further studies incorporating a larger population to validate this new technique, leading to the development of a better diagnostic tool.

Acknowledgments

Grant Support: This work has been supported by American Heart Association, Grant #13SDG14690027, Center for Clinical & Translational Sciences, Grant # UL1TR000090, and Society of Interventional Radiology Foundation Pilot Research Grant and NIH-R01HL24096.

References

1. Agabiti-Rosei E, Porteri E, Rizzoni D. Arterial stiffness, hypertension, and rational use of nebivolol. *Vasc Health Risk Manag.* 2009; 5(1):353–360. [PubMed: 19475771]
2. Liao D. Arterial stiffness and the development of hypertension. *Ann Med.* 2000; 32(6):383–385. [PubMed: 11028684]
3. Boutouyrie P, Laurent S, Briet M. Importance of arterial stiffness as cardiovascular risk factor for future development of new type of drugs. *Fundam Clin Pharmacol.* 2008; 22(3):241–246. [PubMed: 18485143]
4. Laurent S, Cockcroft J, Van Bortel L, Boutouyrie P, Giannattasio C, Hayoz D, Pannier B, Vlachopoulos C, Wilkinson I, Struijker-Boudier H. Expert consensus document on arterial stiffness: methodological issues and clinical applications. *Eur Heart J.* 2006; 27(21):2588–2605. [PubMed: 17000623]
5. Pereira T, Maldonado J, Pereira L, Conde J. Aortic stiffness is an independent predictor of stroke in hypertensive patients. *Arq Bras Cardiol.* 2013; 100(5):437–443. [PubMed: 23579623]
6. Kiotsekoglou A, Moggridge JC, Saha SK, Kapetanakis V, Govindan M, Alpendurada F, Mullen MJ, Camm J, Sutherland GR, Bijnsens BH, Child AH. Assessment of aortic stiffness in marfan syndrome using two-dimensional and Doppler echocardiography. *Echocardiography (Mount Kisco, NY).* 2011; 28(1):29–37.
7. Kadoglou NP, Papadakis I, Moulakakis KG, Ikonomidis I, Alepaki M, Moustardas P, Lampropoulos S, Karakitsos P, Lekakis J, Liapis CD. Arterial stiffness and novel biomarkers in patients with abdominal aortic aneurysms. *Regul Pept.* 2012; 179(1–3):50–54. [PubMed: 22982141]
8. Reymond P, Westerhof N, Stergiopoulos N. Systolic hypertension mechanisms: effect of global and local proximal aorta stiffening on pulse pressure. *Ann Biomed Eng.* 2012; 40(3):742–749. [PubMed: 22016326]
9. Boutouyrie P, Fliser D, Goldsmith D, Covic A, Wiecek A, Ortiz A, Martinez-Castelao A, Lindholm B, Massy ZA, Suleymanlar G, Sicari R, Gargani L, Parati G, Mallamaci F, Zoccali C, London GM. Assessment of arterial stiffness for clinical and epidemiological studies: methodological considerations for validation and entry into the European Renal and Cardiovascular Medicine registry. *Nephrol Dial Transplant.* 2014; 29(2):232–239. [PubMed: 24084326]
10. Hermeling E, Hoeks AP, Winkens MH, Waltenberger JL, Reneman RS, Kroon AA, Reesink KD. Noninvasive assessment of arterial stiffness should discriminate between systolic and diastolic pressure ranges. *Hypertension.* 2010; 55(1):124–130. [PubMed: 19933922]
11. Vorp DA, Vande Geest JP. Biomechanical determinants of abdominal aortic aneurysm rupture. *Arterioscler Thromb Vasc Biol.* 2005; 25(8):1558–1566. [PubMed: 16055757]
12. Xu J, Shiota T, Omoto R, Zhou X, Kyo S, Ishii M, Rice MJ, Sahn DJ. Intravascular ultrasound assessment of regional aortic wall stiffness, distensibility, and compliance in patients with coarctation of the aorta. *Am Heart J.* 1997; 134(1):93–98. [PubMed: 9266788]
13. Kilic H, Yelgec S, Salih O, Akdemir R, Karakurt O, Cagirci G, Yeter E, Acikel S, Dogan M, Arslantas U, Baha RM. An invasive but simple and accurate method for ascending aorta-femoral artery pulse wave velocity measurement. *Blood Press.* 2013; 22(1):45–50. [PubMed: 22747433]
14. Yli-Ollila H, Laitinen T, Weckstrom M, Laitinen TM. Axial and radial waveforms in common carotid artery: an advanced method for studying arterial elastic properties in ultrasound imaging. *Ultrasound Med Biol.* 2013; 39(7):1168–1177. [PubMed: 23582774]

15. Butlin M, Qasem A, Battista F, Bozec E, McEniery CM, Millet-Amaury E, Pucci G, Wilkinson IB, Schillaci G, Boutouyrie P, Avolio AP. Carotid-femoral pulse wave velocity assessment using novel cuff-based techniques: comparison with tonometric measurement. *J Hypertens*. 2013; 31(11): 2237–2243. discussion 2243. [PubMed: 24077246]
16. Frimodt-Moller M, Nielsen AH, Kamper AL, Strandgaard S. Reproducibility of pulse-wave analysis and pulse-wave velocity determination in chronic kidney disease. *Nephrol Dial Transplant*. 2008; 23(2):594–600. [PubMed: 17989106]
17. Lourenco C, Antonio N, Santos L, Teixeira R, Costa S, Matos V, Calisto J, Faria H, Goncalves L, Providencia LA. Results of the routine use of 4F catheters for diagnostic catheterization in a cath lab. *Rev Port Cardiol*. 2009; 28(12):1377–1392. [PubMed: 20301984]
18. Karamanoglu M, O'Rourke MF, Avolio AP, Kelly RP. An Analysis of the Relationship between Central Aortic and Peripheral Upper Limb Pressure Waves in Man. *European Heart Journal*. 1993; 14(2):160–167. [PubMed: 8449191]
19. Adji A, O'Rourke MF, Namasivayam M. Arterial stiffness, its assessment, prognostic value, and implications for treatment. *American journal of hypertension*. 2011; 24(1):5–17. [PubMed: 20940710]
20. Kolipaka A, Aggarwal SR, McGee KP, Anavekar N, Manduca A, Ehman RL, Araoz PA. Magnetic resonance elastography as a method to estimate myocardial contractility. *J Magn Reson Imaging*. 2012; 36(1):120–127. [PubMed: 22334349]
21. Muthupillai R, Lomas DJ, Rossman PJ, Greenleaf JF, Manduca A, Ehman RL. Magnetic resonance elastography by direct visualization of propagating acoustic strain waves. *Science (New York, NY)*. 1995; 269(5232):1854–1857.
22. Sack I, Beierbach B, Wuerfel J, Klatt D, Hamhaber U, Papazoglou S, Martus P, Braun J. The impact of aging and gender on brain viscoelasticity. *Neuroimage*. 2009; 46(3):652–657. [PubMed: 19281851]
23. Sinkus R, Siegmann K, Xydeas T, Tanter M, Claussen C, Fink M. MR elastography of breast lesions: understanding the solid/liquid duality can improve the specificity of contrast-enhanced MR mammography. *Magn Reson Med*. 2007; 58:1135–1144. [PubMed: 17969009]
24. Venkatesh SK, Yin M, Ehman RL. Magnetic resonance elastography of liver: clinical applications. *J Comput Assist Tomogr*. 2013; 37(6):887–896. [PubMed: 24270110]
25. Manduca A, Lake DS, Kruse SA, Ehman RL. Spatio-temporal directional filtering for improved inversion of MR elastography images. *Med Image Anal*. 2003; 7(4):465–473. [PubMed: 14561551]
26. Manduca A, Oliphant TE, Dresner MA, Mahowald JL, Kruse SA, Amromin E, Felmlee JP, Greenleaf JF, Ehman RL. Magnetic resonance elastography: non-invasive mapping of tissue elasticity. *Med Image Anal*. 2001; 5(4):237–254. [PubMed: 11731304]
27. Damughatla AR, Raterman B, Sharkey-Toppen T, Jin N, Simonetti OP, White RD, Kolipaka A. Quantification of Aortic Stiffness Using MR Elastography and its Comparison to MRI-Based Pulse Wave Velocity. *J Magn Reson Imaging*. 2015; 4(1):44–51. [PubMed: 24243654]
28. Kolipaka A, Woodrum D, Araoz PA, Ehman RL. MR elastography of the in vivo abdominal aorta: a feasibility study for comparing aortic stiffness between hypertensives and normotensives. *J Magn Reson Imaging*. 2012; 35(3):582–586. [PubMed: 22045617]
29. Xu L, Chen J, Glaser KJ, Yin M, Rossman PJ, Ehman RL. MR elastography of the human abdominal aorta: A preliminary study. *J Magn Reson Imaging*. 2013; 38(6):1549–1553. [PubMed: 23371244]
30. Lee YJ, Lee JM, Lee JE, Lee KB, Lee ES, Yoon JH, Yu MH, Baek JH, Shin CI, Han JK, Choi BI. MR elastography for noninvasive assessment of hepatic fibrosis: reproducibility of the examination and reproducibility and repeatability of the liver stiffness value measurement. *J Magn Reson Imaging*. 2014; 39(2):326–331. [PubMed: 23589232]
31. Jajamovich GH, Dyvorne H, Donnerhack C, Taouli B. Quantitative liver MRI combining phase contrast imaging, elastography, and DWI: assessment of reproducibility and postprandial effect at 3.0 T. *PLoS One*. 2014; 9(5):e97355. [PubMed: 24840288]

32. Kolipaka A, Araoz PA, McGee KP, Manduca A, Ehman RL. Magnetic resonance elastography as a method for the assessment of effective myocardial stiffness throughout the cardiac cycle. *Magn Reson Med*. 2010; 64:862–870. [PubMed: 20578052]
33. Kolipaka A, McGee KP, Araoz PA, Glaser KJ, Manduca A, Ehman RL. Evaluation of a rapid, multiphase MRE sequence in a heart-simulating phantom. *Magn Reson Med*. 2009; 62(3):691–698. [PubMed: 19572388]
34. Kolipaka A, McGee KP, Manduca A, Anavekar N, Ehman RL, Araoz PA. In vivo assessment of MR elastography-derived effective end-diastolic myocardial stiffness under different loading conditions. *J Magn Reson Imaging*. 2011; 33(5):1224–1228. [PubMed: 21509882]
35. Giri SS, Ding Y, Nishijima Y, Pedraza-Toseano A, Burns PM, Hamlin RL, Simonetti OP. Automated and Accurate Measurement of Aortic Pulse Wave Velocity Using Magnetic Resonance Imaging. *Comput Cardiol*. 2007:661–664.
36. Lotz J, Meier C, Leppert A, Galanski M. Cardiovascular flow measurement with phase-contrast MR imaging: basic facts and implementation. *Radiographics*. 2002; 22(3):651–671. [PubMed: 12006694]
37. Yin M, Talwalkar JA, Glaser KJ, Venkatesh SK, Chen J, Manduca A, Ehman RL. Dynamic postprandial hepatic stiffness augmentation assessed with MR elastography in patients with chronic liver disease. *Ajr*. 2011; 197(1):64–70. [PubMed: 21701012]
38. Lin LI. A concordance correlation coefficient to evaluate reproducibility. *Biometrics*. 1989; 45(1): 255–268. [PubMed: 2720055]
39. Bia D, Zocalo Y, Farro I, Torrado J, Farro F, Florio L, Olascoaga A, Brum J, Alallon W, Negreira C, Lluberas R, Armentano RL. Integrated Evaluation of Age-Related Changes in Structural and Functional Vascular Parameters Used to Assess Arterial Aging, Subclinical Atherosclerosis, and Cardiovascular Risk in Uruguayan Adults: CUiiDARTE Project. *Int J Hypertens*. 2011; 2011:587303. [PubMed: 22187622]
40. AlGhatrif M, Strait JB, Morrell CH, Canepa M, Wright J, Elango P, Scuteri A, Najjar SS, Ferrucci L, Lakatta EG. Longitudinal trajectories of arterial stiffness and the role of blood pressure: the Baltimore Longitudinal Study of Aging. *Hypertension*. 2013; 62(5):934–941. [PubMed: 24001897]
41. Woodrum DA, Romano AJ, Lerman A, Pandya UH, Brosh D, Rossman PJ, Lerman LO, Ehman RL. Vascular wall elasticity measurement by magnetic resonance imaging. *Magn Reson Med*. 2006; 56(3):593–600. [PubMed: 16902974]

Figure 1. Schematic of passive driver placed on the abdomen. Sound waves are non-invasively transmitted to the passive driver via active driver and into the volunteer. These waves are imaged by MRE and used to calculate stiffness.

Figure 2.

a,h) Sagittal magnitude image with contour (red) delineating abdominal aorta in a young (22 years) and an older (73 years) volunteer, respectively. Young volunteer: **b–e)** Wave propagation at four points in time. **f,g)** Weighted stiffness maps from x, y, and z encoding directions with a mean μ_{MRE} of 3.9 ± 0.7 kPa and 4.8 ± 0.7 kPa for end-diastole and end-systole, respectively. Old volunteer: **i–l)** Wave propagation at four points in time. **m,n)** Weighted stiffness maps from x, y, and z encoding directions with a mean μ_{MRE} of 5.8 ± 1.3 kPa and 8.6 ± 2.2 kPa for end-diastole and end-systole, respectively.

Figure 3. Stiffness values at end-diastole and end-systole for all volunteers with lines connecting specific volunteers' values between scans.

Figure 4.

a) Plot of μ_{MRE} throughout the cardiac cycle with bars representing the range of stiffness values between both scans for three volunteers of different ages. For all volunteers, end-diastole occurred around phase 5 and end-systole occurred around phase 8. **b)** Concordance plot demonstrating strong agreement between scans with $r_c = 0.86$ (95% confidence interval: 0.77, 0.94) with $P < 0.0001$.

Figure 5.

Comparison of end-systolic and end-diastolic $\sqrt{\mu_{MRE}}$ as a function of PWV, demonstrating r values of 0.54 for end-systolic $\sqrt{\mu_{MRE}}$ and 0.58 for end-diastolic $\sqrt{\mu_{MRE}}$.

Figure 6.

Plot of age-grouped μ_{MRE} values across the cardiac cycle with 8 cardiac phases for all volunteers. The 20–54 age group contained 15 volunteers and the 55–73 age group contained 5 volunteers. Bars represent the range of stiffness values within each age group. For all volunteers, end-diastole occurred around phase 5 and end-systole occurred around phase 8.

Figure 7. Comparison of end-systolic and end-diastolic μ_{MRE} values as a function of age, demonstrating r values of 0.62 and 0.51 for end-systole and end-diastole, respectively.

Figure 8. Plot demonstrating linear correlation between μ_{MRE} values and BP measurements with $r = 0.41$ and a significant P-value of 0.001.