

Effects of Posprandial State and Mesenteric Blood flow on the Repeatability of Magnetic Resonance Elastography

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Introduction: MR elastography (MRE) is a promising technique for non-invasive detection and assessment of liver fibrosis. Like any biomarker, its clinical utility will depend greatly on its repeatability (precision), which may be affected by physiological variability such as hepatic blood flow. It is well known that eating will dramatically increase splanchnic blood flow^{1,2}, and fasting status of patients has been recognized as a factor that may affect hepatic stiffness measured with MRE³.

Ongoing studies at our institution demonstrate that the largest source of variability in the repeatability of MRE occurs for individuals imaged on two different days, likely reflecting the effects of diurnal variation⁴. In this past work, the effects of meals were not controlled, and may explain this source of this variability.

Thus, the effects of increased blood flow on hepatic shear stiffness after a meal have not been fully explored with regards to repeatability. Preliminary work by Yin *et al* has shown that hepatic stiffness may increase in cirrhotic patients after a meal. The purpose of this work is to quantify and determine the impact of blood flow and fasting status on the repeatability of MRE stiffness measurements of the liver.

Methods: Twelve healthy volunteers (9 men, 3 women) with no known liver disease were imaged with MRE after 4 hours of fasting from food and liquid. Mean age was 30.3 years (range, 23-39). Imaging was performed at 1.5T (TwinSpeed HDx, GE Healthcare, Waukesha, WI) using an eight-channel phased array coil. An axial MRE sequence was performed according to Yin *et al*⁵, followed by a breath-held 2D bSSFP sequence to locate the superior mesenteric vein (SMV). An axial 2D cine-PC sequence with respiratory compensation and cardiac gating was used to measure the blood flow through the SMV in the S/I direction using VENC = 40 cm/s. Flow imaging parameters included the following: TE/TR = 7/33ms, BW = ±15.63kHz, 256x192 matrix, FOV=28x28, slice thickness = 5mm, 1 repetition, and flip = 30°.

Following the exam, volunteers ate a standardized meal consisting of 20 ounces of non-diet soda and a high fat, high protein meal (one piece of pepperoni pizza (931 cal, 22.2g fat, 164.5g carb, 30g protein)). After approximately 60 minutes, the entire imaging exam was repeated using a VENC of 80cm/s for the flow sequence to avoid velocity wrap from anticipated increased flow in the SMV. Five weeks after the initial scans, the entire process was repeated again such that four exams over two days were obtained.

Flow was determined through segmentation of the SMV using CVFlow (Medis, Raleigh, NC). MRE stiffness measurements were performed according to Hines *et al*⁶. A linear mixed effects (LME) model⁷ was used to estimate the sources of variability in the data, which included day (exams on different days), and subject. In addition, these sources were combined to calculate the standard deviation of a single MRE measurement.

Results: Figure 1 displays the MRE stiffness maps of a healthy volunteer before and after eating on both days of the study. No differences between stiffness values are seen on after the meal, even though flow in the SMV more than tripled after eating; average flow before eating was 3.5±2.0mL/cycle and after eating was 12.0±6.4mL/cycle. Figure 2 displays all measured stiffness values versus measured flow for all volunteers in this study. Shear stiffness remains constant for all volunteers as measured flow increases as a result of eating. Results from one volunteer were excluded due to abnormally elevated liver stiffness that could not be explained by volunteer's medical history or from possible technical failure.

No statistically significant differences were observed between stiffness values before and after eating ($p = 0.65$), where average fasting values are 2.41 kPa (standard error (se)=0.06) and average fed values are 2.38 kPa (se=0.06). The calculated standard deviation (i.e. coefficient of variation, expressed as a percent of the mean measured stiffness) among subjects was 7.1%. The calculated standard deviation due to day was 3.1%, not separated by fed or fasted state. The standard deviation due to subject for the fasting state was 8.5%, and fed state was 6.9% ($p = 0.97$, ie: subject variability in states are not different), and the standard deviation due to day of imaging for the fasted state was 4.5% and fed state was 5.1% ($p = 0.28$, ie: variability due to day of exam in fed and fasted states are not different). The residual standard deviation, which includes all sources of variability not explicitly accounted for in the LME model, was 3.8%. Thus, the overall standard deviation of one MRE measurement, which is calculated by summing the individual variabilities above, is 8.5% in the fasted state, and 9.0% in the fed state, although they are not statistically different from one another ($P = 0.66$).

Discussion and Conclusion: No significant differences are seen in stiffness values measured using MRE in fasted and fed states were observed in healthy volunteers, where increased blood flow after a meal was theorized to increase stiffness values. Increased blood flow and fasting status had no effect on stiffness values in these individual healthy volunteers. These observations suggest that the normal auto-regulatory mechanisms of the healthy liver, in response to a meal, maintain constant liver stiffness. Additional work in patients with liver disease, correlating increases in splanchnic blood flow after meal with changes in liver stiffness remains to be performed. These studies are needed in order to determine whether patients should be scanned with MRE in the fed or fasting state.

References: [1] Burkart, et al. Radiology 1995 [2] Dautaz M, et al. Eur J Appl Phys Occup Physiol 1994 [3] Yin M, et al. ISMRM 2009 (#110) [4] Hines et al, JMRI in revision [5] Yin M, et al. Clin Gastro Hepatol 2007 [6] Hines et al, ISMRM 2008 (#2621) [7] Pinheiro and Bates, Springer 2000.

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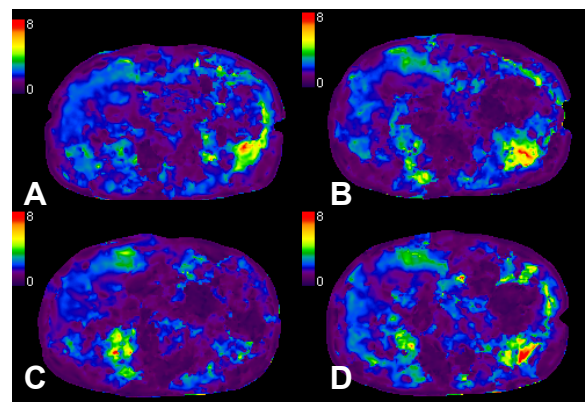


Figure 1: MRE images from a 39-year-old healthy male volunteer. A) Day 1 fasting state. Stiffness and SMV flow values: 2.32 ± 0.32 kPa, -7.67 mL/cycle. B) Day 1 fed state: 2.31 ± 0.40 kPa, -16.0 mL/cycle. C) Day 2 fasting state: 2.34 ± 0.34 , -4.81 mL/cycle. D) Day 2 fed state: 2.42 ± 0.40 , -20.5 mL/cycle.

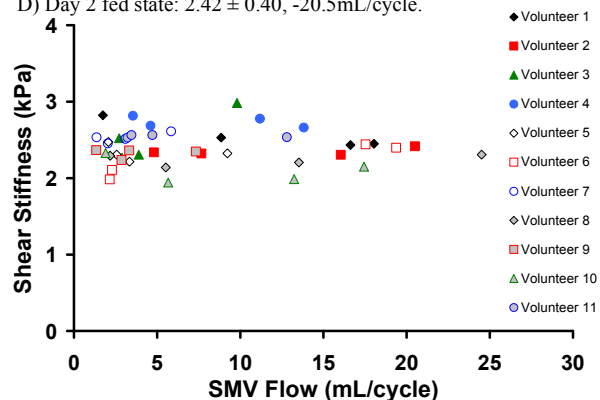


Figure 2: Plot of shear stiffness vs. flow through the SMV for each volunteer displays no correlation between measured stiffness and blood flow (slope = -0.0011 ± 0.005 , intercept = 2.41 ± 0.05 , $R^2 = 0.0009$). Both fed and fasted state data are shown for all volunteers on both days of imaging.