

MR Elastography of Human Lung Parenchyma: Preliminary validation with an interactive respiratory feedback system

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Introduction: Lung disease is a significant and growing health issue and is the third leading cause of death within the United States [1]. It is appreciated that several lung diseases such as emphysema and interstitial lung disease are associated with significant changes in lung mechanical properties, suggesting that knowledge of this parameter may be significant in terms of earlier diagnosis and improved patient management. Evidence is also emerging indicating that change in the mechanical properties of lung parenchyma precede clinical symptoms and may initiate disease progression [2]. Although Magnetic Resonance Elastography (MRE) is well established in solid organs such as the liver [3,4], ¹H lung MRE remains challenging due to the low tissue density, ultra-short T₂ of lung parenchyma as well as cardiac and respiratory induced motion artifacts. We have recently demonstrated with a ¹H pulmonary MRE pulse sequence that the shear stiffness of human lung parenchyma can be spatially resolved in vivo [5]. The objective of this work was to validate this technique by quantifying lung shear stiffness in healthy volunteers throughout the respiratory cycle and to compare these values to established relationships between shear stiffness and lung volume.

Methods: All experiments were performed on a 1.5-T whole-body MR scanner (Signa EXCITE, GE Healthcare, Waukesha, WI) and were conducted in accordance with our institutional review board guidelines. Five healthy male subjects were recruited and after obtaining written consent, were placed supine within the scanner as shown schematically in figure 1a. Prior to imaging, a respiratory bellow was placed below the diaphragm of the volunteer and was connected to a commercially available interactive breath hold control (IBC) system (Medspira, Minneapolis, MN) shown in figure 1b. This system provided the subject with visual feedback allowing the subject to monitor in real time the degree of their lung inflation. Breath-held MRE data were acquired at four levels of respiration that included residual volume (RV), total lung capacity (TLC) and two intermediate states. 50 Hz shear vibrations were induced within the lungs with a pressure-activated driver through a passive driver placed on the anterior chest wall above the right lung. A spin echo based pulmonary MRE pulse sequence with a short TE of 9.4 ms that included two 2-ms MEG lobes (as reported in [5]) was used for acquiring all MRE data. Shear stiffness maps of the lungs were calculated from the shear displacement data with a local frequency estimation algorithm with spatio-temporal directional filters [6]. Other imaging parameters included: imaging plane = sagittal (within the right lung), FOV = 35 cm, acquisition matrix = 128x64 frequency-encoding direction = SI, motion-sensitizing direction = RL, TR/TE = 200/9.4 ms, slice thickness = 10 mm, and 4 phase offsets. Differences in shear stiffness at the four levels of respiration were assessed with Analysis of Variance (ANOVA) using the software package JMP (JMP 8.0, Cary, NC).

Results: All volunteers were able to consistently maintain a breath-hold at the four respiratory states (within ± 2 mm accuracy). Example wave data and shear stiffness maps obtained from one of the volunteers at the four respiratory states are shown in figure 2. The top row and the bottom row show shear wave fields and stiffness maps superimposed onto the magnitude images. Note the increase in the lung area moving from RV to TLC. The increase in shear wavelength and stiffness from RV to TLC is evident and is consistent with the previously reported values of shear stiffness [2,7]. Figure 3 shows the density weighted stiffness values obtained from all five volunteers and the intra-group mean and standard deviation are listed immediately below. Intra-group stiffness values were similar and the inter-group differences were statistically highly significant with a p-value of 1.9×10^{-6} .

Conclusions: According to established physiologic principles, lung stiffness is expected to increase with increasing lung volume. The data presented in this study confirms this phenomenon and provides preliminary validation of MRE-derived estimates of lung shear stiffness. Translation of this methodology into the clinical setting has the potential to provide new insights into pathophysiology, diagnosis and management of several lung diseases.

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References: (1) Lung disease data: American Lung Association, 2008. (2) Suki et al., *Respir Physiol Neurobiol* 163 : 33-43, 2008. (3) Huwart et al., *NMR in Biomed* 19: 173-179, 2006. (4) Asbach et al., *MRM* 60 :373-379, 2008. (5) Mariappan et al., *JMRI* 33 :1351-1361, 2011. (6) Manduca A et al., *Med Imag Anal.* 5: 237-254, 2001. [7] Zhang et al., *Ultrasonics* 51(3):289-295.

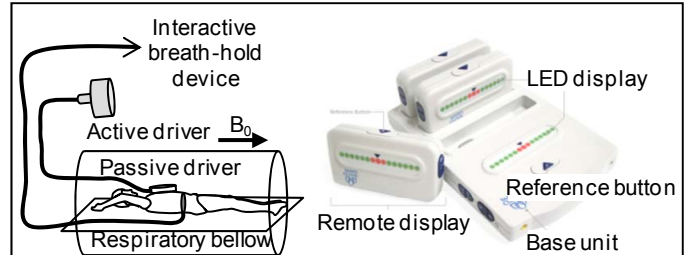


Fig 1a: Experimental setup. 1b. Interactive breath-hold device

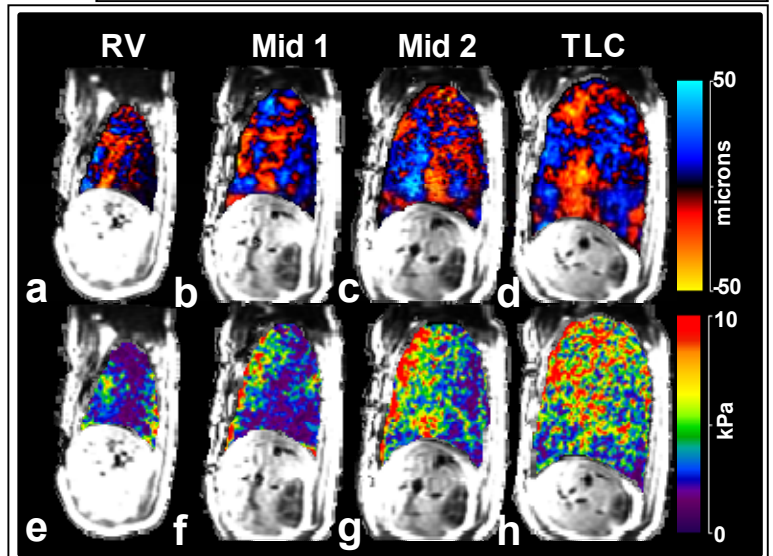


Fig 2: (a-d) Shear wave fields and (e-h) stiffness maps from a volunteer at the four states of respiration.

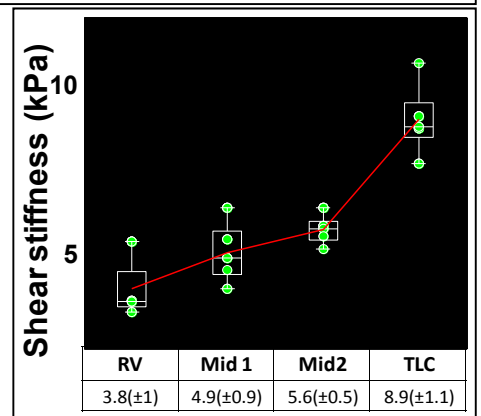


Fig 3: Shear stiffness values from the 5 volunteers at the 4 states of respiration