PROGRESS IN MR ELASTOGRAPHY OF HUMAN LUNG PARENCHYMA: EVALUATION OF REGIONAL DENSITY MEASUREMENTS AND FASTER IMAGING SEQUENCES

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Introduction. Respiratory diseases are the third leading cause of death within the US and account for 17.4% of all deaths in the world[1]. Because the mechanical properties of the lung play a major role in pulmonary pathophysiology their quantification is an active area of research. MR Elastography (MRE), a noninvasive MR-based method of quantifying tissue stiffness has the potential to provide new insights into those processes that initiate and promote lung disease. However, because the primary function of the lung is gas exchange, it possesses inherently poor ^{1}H MR signal properties due to low density and significantly reduced T_2* rendering the implementation of pulmonary MRE slow and challenging. We have recently demonstrated with a spin echo (SE) technique that the effective shear stiffness of human lung parenchyma can be spatially resolved in vivo[2]. We hypothesized that pulmonary MRE can be made both faster and capable of obtaining the "true" density-independent shear stiffness with appropriate pulse sequence development. The goal of this work was to develop and evaluate a SE EPI-MRE and a GRE density estimation sequence for spatially resolving the absolute shear stiffness of lung parenchyma.

Methods. All experiments were performed on a 1.5-T whole-body MR (GE, Signa Excite, Waukesha, WI) scanner and were conducted in accordance with institutional review board guidelines. We have previously reported on the feasibility of an SE EPI-MRE sequence with a short TE and sufficient motion sensitivity using modifications similar to an earlier described SE-MRE sequence[2]. MR imaging parameters (including EPI-specific parameters, number of shots and effective TE) were further optimized to provide a TE of 11.7 ms and a total acquisition time of ~30s (two breath holds of 15s each). The SE EPI-MRE sequence included two, 2-ms unipolar MEG lobes and used chemical presaturation pulses for fat suppression. **Density Estimation:** The working equation for MRE inversion is $\mu=\rho V_s^2$ where μ is the shear stiffness, ρ is the physical density and V_s is the wave speed. Typically MRE algorithms assume ρ to be 1 g/cm^3 for soft tissues. However, since lung density is approximately 1/3rd of solid organs, spatially heterogeneous and varies significantly through the respiration cycle, this value must be measured in order to calculate "true" shear stiffness (shear stiffness reported before density correction = effective stiffness in this work). To spatially resolve lung density, a fast GRE approach for lung density estimation (FGRE-LDE) as described by Thielmann in [4] was implemented and involves acquisition of 12 images with two distinct TE values (1 ms and 1.8 ms). Physical density is calculated by fitting a single exponential equation. A gadolinium doped water phantom was simultaneously imaged with the sample to provide a reference density of 1.0 g/cm^3.

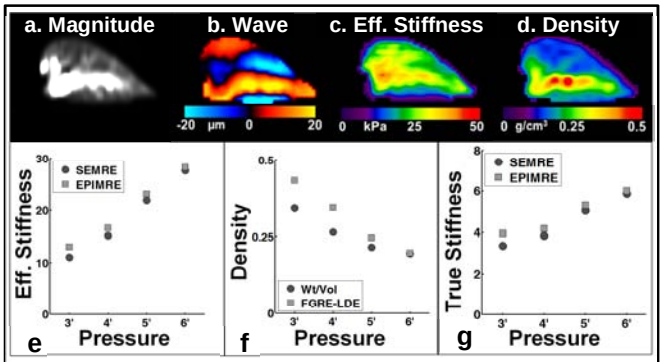

Figure 1: MRE data of an ex vivo pig lung lobe with 6' of water pressure. The effective stiffness (e) and true stiffness (g) obtained from both SE-MRE and EPI-MRE increased and the density (f) decreased with increasing pressure.

EPI-MRE and density estimation sequences were evaluated on a preserved swine lung lobe connected to an in-room air source. The lung was pressurized to 4 transpulmonary pressures (3', 4', 5' and 6' of water), shear vibrations of 100 Hz were introduced into the lungs with a pressure activated shear driver placed under the lungs, and the resulting shear waves were imaged with both the SE-MRE and EPI-MRE sequences and compared. A local frequency estimation algorithm was used to calculate effective tissue stiffness. Regional density values were measured with the FGRE-LDE sequence at these pressures and were compared to volumetric weight-to-volume ratios (Wt/Vol) calculated from degassed lung weight measurements and volume measurements obtained from separate multislice MR acquisitions. True stiffness values were obtained as a product of effective stiffness and regional density measurements. The EPI-MRE and the FGRE-LDE sequences were also tested on 2 healthy volunteers using 50-Hz vibrations at two states of suspended respiration: end expiration (Exp) and end inspiration (Ins).

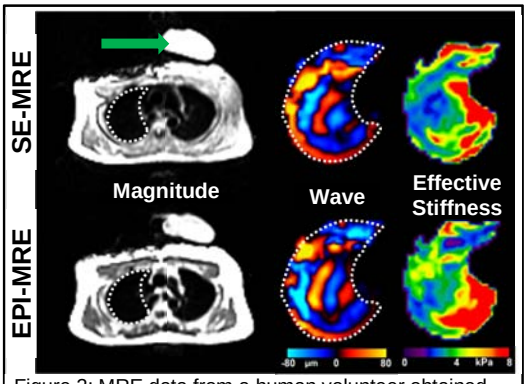

Figure 2: MRE data from a human volunteer obtained using the SE-MRE and EPI-MRE pulse sequences provide comparable measurements

Results. MRE data of the lung with 6' of water pressure obtained with the SE EPI sequence are shown in the top row of Fig. 1. The effective stiffness increased with the increasing pressures (Fig. 1e). It can also be seen that EPI-MRE provided values similar to SE-MRE. A typical density map is shown in Fig. 1d and the density values for the 4 different pressures are shown in Fig. 1f. The density values obtained as Wt/Vol are also plotted in Fig. 1f, and agree with the FGRE-LDE data. The true stiffness also increased with pressure (Fig. 1g). MRE data using 50 Hz vibrations obtained on a human volunteer at end expiration are shown in Fig. 2. The arrow in the magnitude image indicates the doped water phantom. The results shown in Figs. 2 and 3 demonstrate that the two sequences provide comparable data, even though the EPI sequence was twice as fast (30s for EPI vs. 62s for SE). Density maps obtained at end expiration and end inspiration from the FGRE-LDE technique are shown in Fig. 3b. Mean density values obtained at these states are indicated on the figure and were within the expected range[4]. True stiffness values are plotted in Fig. 3c, indicating that even after density correction, lung stiffness at end inspiration was higher than at end expiration, as expected.

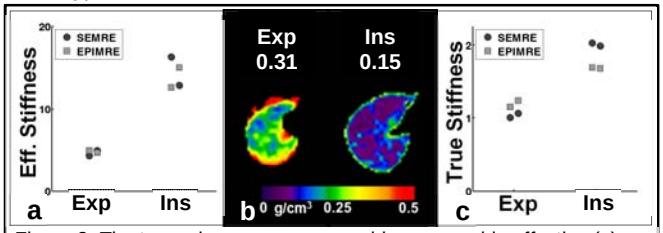

Figure 3: The two pulse sequences provide comparable effective (a) and true stiffness values (c) both at end expiration and end inspiration. Lung density values (b) obtained at end inspiration were less than those obtained at end inspiration.

Conclusions. The data obtained from the ex vivo lung specimen and human volunteers suggest that pulmonary MRE can be improved by application of a SE EPI and GRE density estimation sequences. Ongoing work involves the evaluation of these approaches in a larger group of normal volunteers and interstitial lung disease patients.

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References. (1) Word Health Organization, *WHO/MNC/CRA/02.1,*2002. (2) Mariappan et al., JMRI 33 :1351-1361, 2011. (3) Mariappan et al.,ISMRM 20th annual meeting, 3970, 2012. (4) Thielmann et al.,JMRI 30:527-534, 2009.