Quantitative MRI measurement of lung density must account for the change in T2* with lung inflation

R. J. Theilmann[1], T. J. Arai[2], A. Samiee[2], S. R. Hopkins[1,2], R. B. Buxton[1], D. J. Dubowitz[1], and G. K. Prisk[1,2]

[1]Radiology, UCSD, La Jolla, CA, United States, [2]School of Medicine, UCSD, La Jolla, CA, United States

Introduction

Quantitative determination of lung water content is important in the monitoring and study of pulmonary interstitial edema, and also for evaluating lung physiology under a variety of conditions. However, the lung is an unique organ in that the density varies approximately 3-4 fold as the lung is inflated from residual volume (air volume ~1000 ml, tissue + blood volume ~1000ml, with a specific gravity ~1, density ~0.5 g/ml) to total lung capacity (air volume ~6000 ml, tissue + blood volume ~1000ml, density ~0.14 g/ml). MRI, with its intrinsic sensitivity to water proton density, provides a promising approach for measuring lung water. However, because of high magnetic susceptibility effects in the lung, T_2^* is extremely short and as a result standard gradient echo imaging of the lung suffers from significant signal loss. Consequently, for an accurate determination of lung water content (M_0) one must back-extrapolate the signal from lung to an echo time of 0. In addition, because the lung expands and contracts one would expect T_2* to change based on the breath-hold volume, and T_2* itself may provide additional information on lung pathology, where the lung air content may vary secondarily to a disease process. Our goal was to implement a fast gradient echo sequence specifically for rapid lung water imaging and evaluate M_0 and T_2* at different levels of lung inflation in healthy subjects.

Methods

To obtain T_2* and lung density measurements a gradient echo (GRE) sequence was developed that rapidly acquires multiple single echo acquisitions within a breath-hold. While keeping TR fixed, the GRE sequence collects a single line of k-space after each excitation. The sequence repeated for the first echo time until k-space is filled. The sequence then repeated at the second echo time. The acquisition was adapted to allow acquisitions with 2 closely space echoes alternating between a short and a long echo time (4 images at TE_1 = 1.0ms and 4 images at TE_2 = 1.8ms). The first echo is the shortest time permitted by sequence parameters, and the second echo time was selected such that at total lung capacity (where density is minimum) mean signal intensity in the lung was at least twice that in the background, and thus discernable from noise.

We measured T_2* and M_0 in 10 healthy volunteers (6 males / 4 females). The right lung was imaged with our fast gradient echo sequence on a 1.5T GE HDx EXCITE twinspeed clinical scanner. Sequence parameters were repetition time (TR) = 10 msec, flip angle = 10 deg, slice thickness = 15 mm, receiver bandwidth = 125 kHz, and matrix size 64 × 64. Single coronal slices were acquired during breath-holds at total lung capacity, functional residual capacity, and residual volume. Each scan included simultaneous imaging of a gadolinium-doped water phantom for absolute calibration, allowing each measurement to be expressed as a percentage of water. All measurements were repeated in three independent breath-hold GRE scans of 9 secs each.

Regions of interest (ROIs) were drawn for the lung and phantom in each scan using AMIRA (TGS systems). The mean signal intensity within the ROI was determined for each echo. M_0 and T_2* were calculated for each breath-hold by fitting a set of data point to $I_i = M_0 \exp(-t_i / T_2^*)$, where I_i is the mean signal intensity within the ROI at each echo time, t_i (t_1 = 1.0 ms, t_2 = 1.8 ms, t_3 = 1.0 ms, …, t_8 = 1.8 ms). Average T_2* and M_0 were reported for each lung volume.

Results

One-way repeated measures ANOVA compared ROI volume, T_2*, and M_0 values between lung volumes. As expected, lung ROI changed significantly with lung volume ($P < 0.0001$). There was also a significant difference in T_2* and M_0 between each lung volume ($P < 0.0001$ and $P < 0.0001$, respectively). Average ROI volumes, T_2*, and M_0 at each lung volume are reported in **Table 1**.

Conclusions

As expected, M_0 (and thus lung density) decreased with increasing lung volume. At residual volume, the measured fractional density of 0.48 is consistent with previous studies [1]. T_2*decreased significantly as lung volume increased, but remained within the previously reported range (0.89 ms $< T_2^* <$ 2.18 ms) [2]. The large change in T_2* with lung volume shows that if quantitative lung density is to be measured, then imaging at a single echo time and assuming a fixed value for T_2* is not accurate, and images with multiple TEs must be collected within a single breath-hold to account for the effect of differing T_2^*. Together with other non-invasive techniques in physiology, this imaging approach for assessing lung water content will allow basic mechanisms in pulmonary physiology to be elucidated by allowing quantitative determination of regional lung density. (Supported by NIH grants HL81171-01, HL80203-01 and AHA 054002N)

Lung Volume	ROI Volume (ml)*	T_2^* (ms)*	M_o (% of water)*
residual volume	142 ± 31	2.01 ± 0.22	0.48 ± 0.06
functional residual volume	153 ± 30	1.71 ± 0.16	0.42 ± 0.06
total lung capacity	259± 48	1.23 ± 0.13	0.18 ± 0.03

Table 1. ROI Volume, T_2^*, M_0 results from imaging acquired at residual volume, functional residual capacity, and total lung capacity at 1.5T. * Main effect for lung volume significant at $P < 0.0001$

References

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