Gravimetric validation of lung density measured by multi-image gradient echo quantitative MRI

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Introduction

Quantitative determination of lung water content is important in the study of pulmonary edema, and also for evaluating lung physiology under a variety of conditions. Our implementation of a multi-image gradient echo sequence that collects data at two echo times was shown to produce highly reproducible values of lung density *in vivo* [1]. This work demonstrated that not only is T_2* very short in the lung and varies with lung volume, but T_2* must be determined to obtain an accurate measure of quantitative lung density. Although our values of lung density were found to be consistent with previous studies, it is unknown how accurately these values represent absolute water content. The goal of this work was to validate our imaging technique against absolute water content measured gravimetrically using excised pig lungs as a model.

Methods

Five white farm or Yucatan pigs were heparinized and then sacrificed by overdose of pentobarbital. The heart and lungs were harvested as a block and then the right and left lung were dissected free of extraneous tissue and cannulated via the mainstem bronchus. A total of 7 lungs were studied. These were kept under normal saline soaked gauze and at 40˚F until imaging. Each lung was inflated and scanned in the coronal plane at 5 and 15 cm H_2O positive end-expiratory pressure (PEEP). These inflation pressures were selected to mimic functional residual capacity and total lung capacity lung volumes. To avoid drying of the lung during scanning, each lung was placed on plastic crates above saline impregnated gauze in a closed plastic container. The lungs were weighed before and after scanning to ensure that the water content was constant during the scan session. After scanning, the lungs were inflated and dried until the weight remained constant. The gravimetric water content was then calculated as the wet weight minus the dry weight.

Whole lung imaging was conducted on a 1.5T GE HDx EXCITE twinspeed clinical scanner duplicating sequence parameters used in our human study [1]. Our fast gradient echo pulse sequence collected 12 images per slice alternating between 12 closely-spaced echoes using the BODY coil (6 images per slice at TE_1 = 1.0ms and 6 images per slice at TE_2 = 1.4ms). Sequence parameters were repetition time (TR) = 10 msec, flip angle = 10 deg, slice thickness = 15 mm, receiver bandwidth = 125 kHz, 6 to 10 coronal slices encompassing the lung, and a matrix size of 64×64. For the current study, scan time increased to approximately 30 seconds to allow whole lung imaging using multiple slices (the *in vivo* study acquired a single slice in a 9 second breath-hold). Each scan included simultaneous imaging of a gadolinium-doped water phantom for absolute calibration, allowing each measurement to be expressed as a water fraction. All measurements were repeated in triplicate.

Regions of interest (ROIs) were drawn for the lung and phantom in each scan using MATLAB. The mean signal intensity within the ROI was determined for each echo. M_0 and T_2* were calculated 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 = 1.4 ms, t_3 = 1.0 ms, …, t_8 = 1.4 ms). The first four images of each imaging sequence were discarded to ensure signal in the lung reached steady-state. Water content in one slice was calculated as the number of voxels within the ROI x volume of the voxel x M_0. The sum of all slices yields total water content of the lung. The results of the triplicate measures were averaged.

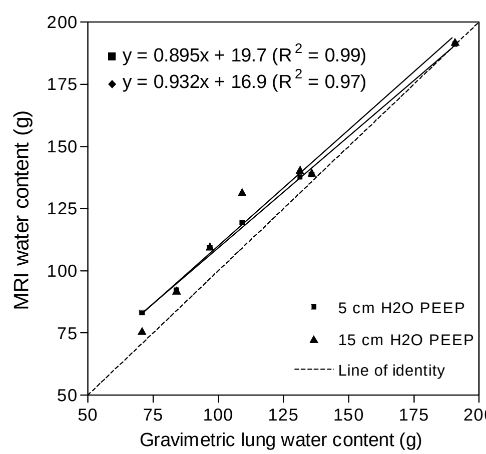
Gravimetric water content and water content of the lung measured with our imaging sequence were reported for each lung (Figure 1).

Results

Overall, as lung volume increased from 5 to 15 cm H_20 PEEP, the fractional density of the whole lung was significantly reduced from 0.19±0.03 g/cm^3 to 0.15±0.03 g/cm^3 (p=0.018) giving values that are within the range previously identified by our human study. Figure 1 shows the correlation between the water content measured gravimetrically and measured with MRI at both lung volumes. The regression curves for both pressures show a highly significant linear relationship between MRI and gravimetric measures of lung water. In addition there was no significant difference in slope (p=0.64) and y-intercept (p=0.61) between the two curves for 5 and 15 cm H_2O PEEP. The average y-intercept for 5 and 15 cm H_20 were 19.8±2.9 and 16.9±9.0 respectively. On average the water content assessed by MRI was higher than the gravimetric water content (7±5% and 9±7% for 5 and 15 cm H_20 PEEP respectively).

Conclusion

Results show that lung water content measured by our imaging approach show a linear correlation with gravimetric values at both lung volumes. In addition there were no significant differences between total lung water estimations at the two levels of lung inflation suggesting that T_2* effects were accounted for appropriately. Our imaging approach appears to overestimate absolute water content, but the errors are systematic and are within 7% of the actual gravimetric values for smaller lung volumes.



As expected, the bias in absolute water content increased for larger lung volumes where the SNR is less. In this study, portions of the voxels in the lung will have a very low signal since harvested lungs contain markedly less blood than lungs *in vivo*. For low SNR conditions the image intensity will be overestimated due to the contribution of noise an effect which will be augmented by multiple slices contributing to the error observed. In the future, we plan to estimate this bias due to noise, and thus improve the accuracy of our method.

Results show that our multi-image gradient echo imaging sequence is a reliable technique to assess absolute water content in the lung. Other studies have examined the response of MR relaxation times (T_2, CPMG T_2, and Hahn T_2) to estimate lung water in animal models [2,3]. However, our technique is capable of acquiring data within a breath-hold which is advantageous in human studies.

References

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