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Dynamic MRI of Grid-Tagged Hyperpolarized Helium-3 for the Assessment of Lung Motion during Breathing

Jing Cai, Ph.D.¹, Ke Sheng, Ph.D.¹, Stanley H. Benedict, Ph.D.¹, Paul W. Read, M.D., Ph.D.¹, James M. Lerner, M.D.¹, John P. Mugler III, Ph.D.², Eduard E. de Lange, M.D.¹, Gordon D. Cates Jr., Ph.D.², and G. Wilson Miller, Ph.D.²

¹ Department of Radiation Oncology, University of Virginia, Charlottesville, VA

² Department of Radiology, University of Virginia, Charlottesville, VA

Abstract

Purpose—To develop a dynamic magnetic resonance imaging (MRI) tagging technique using hyperpolarized helium-3 (HP He-3) to track lung motion.

Methods and Materials—An accelerated non-Cartesian k -space trajectory was used to gain acquisition speed, at the cost of introducing image artifacts, providing a viable strategy for obtaining whole-lung coverage with adequate temporal resolution. Multiple-slice 2D dynamic image of the lung were obtained in three healthy subjects after inhaling He-3 gas polarized to 35–40%. Displacement, strain and ventilation maps were computed from the observed motion of the grid peaks.

Results—Both temporal and spatial variations of pulmonary mechanics were observed in normal subjects, including shear motion between different lobes of the same lung.

Conclusion—These initial results suggest that dynamic imaging of grid-tagged hyperpolarized magnetization may be potentially a powerful tool for observing and quantifying pulmonary biomechanics on a regional basis, and for assessing, validating, and improving lung deformable image registration algorithms.

Keywords

deformable image registration; dynamic MRI; hyperpolarized gas; lung motion

INTRODUCTION

Radiation therapy (RT) for lung cancer has been greatly hampered by respiration-induced lung motion and deformation. The recent advent of new technologies, such as 4-dimensional computed tomography (4D-CT) and deformable image registration, have significantly improved the management of lung cancer, by allowing more precise targeting of the administered radiation (1–4). The registration affects the overall accuracy of 4D-RT and therefore needs to be as accurate as possible. However, validation of deformable image

Please send all correspondence to: G. Wilson Miller, Ph.D., Department of Radiology, University of Virginia, PO Box 801339, 480 Ray C Hunt Drive, Charlottesville, VA 22908, Wilson.Miller@virginia.edu, Phone: 434-243-9216, Fax: 434-924-9435.

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registration and quantitative assessment of the deformable image registration accuracy are difficult, especially in humans as there is no known reference that can be used for comparison. To tackle this problem, various deformable phantoms which can move with known motion patterns have been designed (5,6). Whereas these phantoms allow verification of non-rigid displacements to some extent, their motion differs greatly from real lung motion in many aspects. For instance, the shear motion between different lung lobes has never been simulated in any of these phantoms. To fully validate deformable image registration, a 4D *in vivo* imaging technique capable of measuring regional lung motion and deformation during breathing is highly desired.

We previously demonstrated a Magnetic Resonance Imaging (MRI) tagging technique, using hyperpolarized helium-3 (HP He-3) as a gaseous contrast agent, to image the human lungs at end-inhalation and end-exhalation in a single acquisition and subsequently use these images to generate a deformation map (7,8). In this technique a 2D tagging grid is created at breath-hold following inhalation of HP He-3 gas, by using sinc-modulated radio frequency (RF) pulse trains in combination with magnetic field gradients applied consecutively along any two of the principal axes. This tagging preparation destroys the hyperpolarized magnetization along orthogonal sets of parallel planes. MR images of the resulting magnetization distribution reveal a 2D grid pattern of signal peaks.

Following creation of the tagging grid, MR images were immediately acquired first at end-inhalation and then a few seconds later at end-exhalation, using a partial *k*-space short echo-time (TE) fast low-flip-angle shot (FLASH)-based MR imaging sequence. This technique provides a direct, *in vivo*, and non-invasive method to measure lung deformation during breathing. Application of this original implementation, however, is restricted by its limited temporal resolution (only two respiratory phases are acquired). Since lung deformation during breathing is intrinsically nonlinear both spatially and temporally, this two-point implementation is not capable of resolving the full dynamics of lung motion.

The objective of the current study is to develop a dynamic MR imaging strategy using HP He-3 for tracking the evolution of 2D tagging grids at intermediate time points during breathing, and to demonstrate the potential of this advanced technique for providing time-resolved, regional measurements of lung motion and deformation. Multiphase imaging with HP He-3 is feasible due to the very large initial magnetization of the hyperpolarized gas, which permits multiple images with high signal-to-noise ratio (SNR) to be obtained from a single inhaled dose, and the relatively long T1 relaxation time that allows the tag contrast to persist for many seconds. However, there are several challenges in developing a dynamic MR tagging pulse sequence. For one, unlike conventional MRI the HP He-3 magnetization does not spontaneously recover once it has been used up by an excitation RF pulse. This characteristic necessitates efficient use of the initially available magnetization to generate multiple images of adequate quality per inhaled dose, especially since the signal will be declining throughout the scan not only by the application of RF pulse but also by the exhalation of the hyperpolarized gas. Second, the acquisition time per image must be kept short enough to “freeze” the lung motion, so that the tag pattern does not appear blurred in the resulting images used for quantitative analysis.

MATERIAL AND METHODS

MR pulse sequence

The basic MR pulse-sequence strategy we used to address the challenges outlined above was to sacrifice image quality in favor of temporal resolution, since the goal in this particular application was not to make attractive images of the tag pattern, but to make images that are good enough to track tag motion over a reasonable length of time. Our dynamic MR pulse sequence was therefore designed to combine the lowest acceptable image spatial resolution

(the fundamental pixel width is approximately equal to 1/4 of the tag spacing) with an aggressive, radially symmetric k -space trajectory with angular under-sampling (9).

Although image artifacts associated with the under-sampled radial k -space trajectory may diminish overall image quality, they should not interfere with the ability to resolve the location of individual grid elements. For an equivalent Cartesian matrix of size $N \times N$, a fully sampled radial trajectory requires $\pi N/2$ symmetric k -space lines to meet the Nyquist requirement (10). Using fewer lines (under-sampling) can lead to streak artifacts in the reconstructed image. Figure 1 shows a radially acquired image of tagged magnetization in a cylindrical water phantom. The image quality is best at full sampling density. At half sampling density, there are minor streak artifacts in the background but one can barely notice any difference in the definition of the grid elements. Tagging grids were observed to start breaking down at one third of the full sampling density. Based on these observations, an angular sampling density of at least 35% was maintained.

A representative sampling grid for our radial k -space acquisition is shown in Fig. 1f. The composite k -space trajectory consists of multiple interleaves of equally spaced radial lines, and during execution of the pulse sequence all k -space lines from a given interleaf were acquired for each 2D slice before proceeding to the next interleaf. Real-time dynamic imaging was achieved by continuously repeating the entire acquisition (11,12). The use of multiple interleaves evenly spaced in time allows one to use sliding-window reconstruction to update the image of each slice more frequently (13), which yields finer temporal pseudo-resolution (analogous to the “frame rate” of an ordinary movie) but results in a slower “shutter speed” since the time required to acquire a complete set of data for a single slice is nearly equal to the time required to acquire a complete set of data for all slices.

MR imaging

Three healthy subjects (female, ages 23–32) participated in this feasibility study. HP He-3 MRI was performed under a protocol approved by our institutional review board, and each subject gave written informed consent. The HP He-3 was administered under a physician's Investigational New Drug application (IND 57,866). Subjects were positioned supine in a 1.5T MR scanner (Sonata, Siemens Medical Solutions, Malvern, PA), and a flexible transmit/receive RF coil (IGC Medical Advances, Milwaukee, WI) tuned to the He-3 resonance frequency was used for image acquisition. He-3 gas was polarized to 35–40% using a commercial system (Magnetic Imaging Technologies, Durham, NC). For each scan, approximately 450 ml of polarized He-3 was dispensed into a Tedlar bag, diluted with medical grade nitrogen to a total volume of 1 L, and then transported to the scanner. Immediately before imaging, the subject quickly inhaled the gas and then held her breath, at which point the grid-tagging preparation was applied. The subject was then instructed to begin exhaling, and the dynamic MR image acquisition was applied.

Radially symmetric lines of k -space were acquired using a low-flip-angle, gradient-echo pulse sequence. Subject #1 was imaged in the coronal orientation with the following parameters: FOV: 320×320 mm, equivalent Cartesian matrix: 64×64, flip angle: 4°, number of slices: 5, slice thickness/gap: 25/5 mm, TR/TE: 3.4/1.2 ms, bandwidth: 50 kHz, tag spacing: 22 mm. Crusher gradients were applied in the slice-select direction. The radial trajectory consisted of 51 symmetric lines (50% sampling density) grouped into 17 interleaves of 3 lines each. Thus the total acquisition time to obtain a complete image set was 867 ms, and the temporal pseudo-resolution (frame rate) attainable using sliding window reconstruction was 51 ms. Subject #2 was imaged in the sagittal orientation with the following parameters: FOV: 320×320 mm, equivalent Cartesian matrix: 64×64, number of slices: 8, slice thickness/gap: 20/5 mm, flip angle: 3°, TR/TE: 2.5/1.4 ms, bandwidth: 50 kHz, tag spacing: 18 mm. Shorter TR was achieved for this scan by using RF spoiling instead of crusher gradients. The radial trajectory consisted

of 35 symmetric lines (35% sampling density), all grouped into a single interleaved. Thus the total acquisition time per slice (shutter speed) was 87.5 ms, and a new image of the same slice was obtained every 700 ms (frame rate). Subject #3 was imaged in the sagittal orientation with the following parameters: FOV: 288×288 mm, equivalent Cartesian matrix: 64×64, number of slices: 5, slice thickness/gap: 25/18 mm, flip angle: 4.5°, TR/TE: 3.8/1.9 ms, bandwidth: 25 kHz, tag spacing: 18 mm. RF spoiling was used. The radial trajectory consisted of 35 symmetric lines (35% sampling density) grouped into 7 interleaves of 5 lines each. Thus the total acquisition time to obtain a complete image set was 665 ms, and the temporal pseudo-resolution attainable using sliding window reconstruction was 95 ms.

Data analysis

The radially acquired imaging data were reconstructed onto a 64×64 Cartesian image matrix using standard gridding techniques. Each raw image was then interpolated by a factor of 3 onto a finer matrix (192×192), to reduce pixilation and improve tag definition, and intensity-filtered using a disk-shaped kernel of diameter slightly larger than the tag spacing, to achieve balanced signal intensity throughout the image.

We define a tissue grid element in the grid-tagged image as a high signal region bordered by tagged lines or by the surface of the lung (7). The position of each grid element was defined as the center of mass of the local intensity distribution. These positions were located and analyzed using an automated image processing procedure implemented in MATLAB (The MathWorks, Natick MA), with occasional manual intervention. In cases where a grid element disappeared or became unrecognizable due to out-of-plane motion or reduced SNR (which mostly happened at the borders of the lung lobes), the position of the corrupted grid element was interpolated spatially using the surrounding grid elements. A column number and a row number were assigned to each grid element, representing its relative coordinates. The motion of the grid elements was tracked by matching these coordinates in temporally consecutive images.

Displacement vector maps were computed from the observed motion of the grid elements. Regional Lagrangian strain E was computed by means of an isoparametric formulation with triangular elements (14). Fractional ventilation maps were also calculated, using the formula $(V_1 - V_2)/V_1$ where V_1 and V_2 are the volumes of corresponding triangular elements at two different time points. Each imaged slice generally encompassed two lung lobes, which were easily distinguishable in the tagged images obtained later in the exhalation, and grid elements were assigned to upper or lower lobes by manual assessment. Based on these assignments, mean values of *ventilation*, E_1 and E_2 were calculated separately for the upper and lower lung lobes, and plotted as a function of time to evaluate the evolution of these parameters during exhalation.

RESULTS

Figures 2 and 3 show coronal and sagittal, respectively, multi-slice 2D grid-tagged lung images obtained from subjects #1 and #2 at several time points during exhalation. The grid pattern is preserved very well in all slices during the acquisition. SNR decreases and the grid elements become somewhat blurred toward the end of the acquisition, but the grid elements are still readily resolvable. Streak artifacts are observed in some of the images, but are typically in the peripheral image areas outside the lung, and do not significantly affect the conspicuity of the grid elements. Some grid elements, especially at the edges of the lung, tend to fade away at later times. This phenomenon is presumably caused by motion of the grid elements out of the imaging plane, which is more significant in the coronal orientation than in the sagittal orientation since lung motion in the AP direction is generally greater than that in the ML direction (15). These images clearly show the motion and deformation of the lung during

exhalation. The sliding motion between the upper and lower lung lobes was observed in both cases, although it is more obvious in the sagittal planes where the lobar fissure is longer.

Figure 4 shows grid-tagged images of a representative slice obtained from subject #3. It is apparent from these images that the subject did not begin exhaling until several seconds after the acquisition was started. Unfortunately, the tag definition had degraded significantly by this time, and the majority of the lung motion was not captured. In contrast, Figure 5 shows a color-coded example of the motion trajectories of the grid elements from one of the coronal slices from subject #1, in which the temporal and spatial nonlinearity of lung motion is quite evident. It was observed in this example that the lung motion is more linear and rapid at earlier times than at later times during exhalation.

Figure 6 shows an example of the dynamic functional lung images, including displacement vector maps, strain maps (E_1 and E_2), and ventilation maps, that were generated from the dynamic grid-tagged MR images of subject #2. The motion of each grid element during the exhalation is clearly revealed in the displacement vector maps. We can also see distinct spatial differences in the motion pattern. During the exhalation, the lower lobe moved superior-posteriorly and the upper lobe moved mostly posteriorly. Quantitative analysis of the displacement throughout the exhalation, as shown in Figs. 7a and 7b, revealed that both lung lobes moved approximately the same distance in the AP direction at any time point, but the lower lobe moved significantly greater distance in the SI direction than the upper lobe at any time point.

Strains and ventilation are generally uniform throughout each lobe, while the values are slightly higher in the lower lobe than those in the upper lobe, especially in the later images, as illustrated in Figs. 6 and 7. On average, E_1 , E_2 , and ventilation at the end of exhalation are -0.15 ± 0.03 , -0.07 ± 0.03 , and 0.39 ± 0.08 respectively in the upper lobe, and are -0.18 ± 0.03 , -0.11 ± 0.03 , and 0.50 ± 0.08 respectively in the lower lobe. Distortion of the tagging grid at the fissure between the upper and lower lobes is evident in the later strain and ventilation maps. The anomalous values at the fissure likely arise from the relative motion of the lobes, rather than truly abnormal strains and ventilation within the lung tissue. The strain and ventilation maps are more uniform than the displacement vector map throughout the interior of each lobe, which illustrates that although some parts of the lung move much farther than others during respiration, the local expansion is fairly uniform in normal pulmonary mechanics.

Temporal variations in the lung motion are also revealed by these dynamic images. For example as shown in Fig. 6, there is pronounced motion between the second and third images, but the motion is much less pronounced between the third and fourth images. This difference is more obvious in the differential displacement maps (Fig. 8), where the two lung lobes have been color-coded to highlight the regional difference. Between the second and third images (Fig. 8a), the lower lobe contracted much more (16.8 ± 6.3 mm superiorly, 4.6 ± 3.0 mm posteriorly) than the upper lobe (0.3 ± 3.0 mm superiorly, 4.1 ± 3.0 mm posteriorly), and in a different direction. Between the third and fourth images (Fig. 8b), the upper lobe contracted much more (2.3 ± 2.8 mm superiorly, 7.3 ± 3.3 mm posteriorly) during this time interval than during the previous one, while the lower lobe contracted less (7.7 ± 2.8 mm superiorly, 4.7 ± 2.9 mm posteriorly). Although the frame rate was relatively modest for this scan (~ 1.4 frames per second, due to the use of a single interleaved), it was still fast enough to resolve spatial and temporal variations of the pulmonary mechanics, and the relatively fast shutter speed (less than 100 ms per image) was very effective at freezing the tag motion for quantitative analysis.

DISCUSSION

The ability to obtain lung displacement maps at multiple phases during respiration makes our technique a promising tool for the assessment, validation, and improvement of lung deformable image registration algorithms. Current image registration treats the whole image as an entity and does not consider motion discontinuities between different organs or sub-organs. Displacement vector fields of the lung generated in such a manner are typically smooth and continuous, incorrectly indicating that the lungs are equally and homogeneously elastic. The present study showed large discrepancies in both motion amplitude and direction between different lung lobes. The discontinuity between the upper lobe and lower lobe during the breathing was observed to be as large as 2 cm, which if not taken into account in deformable image registration can reduce greatly the accuracy of registration. Recently much effort has been devoted to investigating this problem. For example, Brock *et al.* developed a multi-organ deformation registration method (MORFEUS) whereby the registration and alignment of different organs are achieved by explicitly defining the deformation of a subset of organs and assigning surface interfaces between organs (16). Wu *et al.* developed a subanatomical segmentation deformable image registration with a boundary-matching penalty strategy to account for the discontinuity at the pleural interface, which is caused by the sliding motion of lung against the chest wall (17). Their preliminary results showed inclusion of lobar segmentation in lung deformable image registration significantly improved the accuracy of the FEA modeling.

Functional heterogeneity within the lung is present in many patients with lung cancer. Pixel-wise functional maps provide information regarding the distribution of pulmonary bio-pathological functions, which can be incorporated in the RT treatment planning to avoid radiation to the functional lung regions (18,19). Lung functions such as ventilation and strain have been measured with varieties of techniques, which were thoroughly reviewed in recent publications by van Beek *et al.* and Reinhardt *et al.* (20,21). To name a few, Guerrero *et al.* developed a registration-based technique to calculate the regional lung ventilation, in which the optical flow image registration was used for voxel mapping between image pairs and changes in CT values in Hounsfield units (HU) were used to calculate the local air change (18). Chon *et al.* measured local lung ventilation in animal models by observing the xenon gas wash-in and wash-out rates on serial CT images (22). These methods are able to generate quantitative maps of regional ventilation, but not without shortcomings. The accuracy of registration-based ventilation calculation relies greatly upon the accuracy of the deformable image registration algorithm, and the xenon-CT technique is currently limited to animal studies since it requires sophisticated ventilation devices to achieve the same lung volume for each breath (to avoid having to use image registration techniques). Our HP He-3 MR tagging technique, despite its limitations in its current format, provides a direct approach in humans to determine regional lung deformation and ventilation, and is potentially advantageous because fewer sources of error are introduced in the process.

Only healthy volunteers were included in this initial study. Implementation of the dynamic tagging MR technique in patients with lung cancer may encounter extra difficulties. First of all, subject cooperation is very important to acquire high quality images during MR scan using hyperpolarized gas. Thus patients who have severe breathing difficulties may not be suitable for such a procedure. Furthermore, our failure to obtain dynamic information from subject #3 demonstrates that even if the subject *should* be able to carry out the required breathing maneuver, successful execution is necessary to produce useful results. Secondly, patients with lung cancer tend to also have lung diseases such as emphysema that impede ventilation. If the inhaled HP gas cannot reach some parts of the lung, then it is impossible to track the motion in these regions using our tagging technique. A general limitation of the technique is that diffusion of the HP gas within the lung airspaces tends to smear the tag contrast over the time

of the image acquisition. Although this phenomenon was not a problem in the present study, the gas will diffuse much faster in emphysematous lungs (23), potentially making it difficult to resolve grid elements at later times. It is worth noting that using hyperpolarized xenon-129 instead of He-3 may help in this regard, since the diffusion of xenon gas is much slower than helium.

The current MR tagging technique is limited to 2D. However, with breathing the lung movements are in 3 directions and hence implementation of dynamic tagging MR technique in full 3D is necessary for the comprehensive evaluation of lung motion. In our previous study we showed the feasibility of acquiring two-phase 3D MR tagging images of lung using HP He-3 (8). A full 3D application of the technique is more difficult, since competing factors such as temporal resolution, spatial resolution, SNR, and limited dose have to be precisely coordinated and optimized. However, it is possible that since the lung motion in the ML direction is relatively small, typically less than 5 mm (15), 2D sagittal dynamic images may be sufficient for many applications.

CONCLUSIONS

We have developed a dynamic MR tagging technique using HP He-3 to monitor lung motion and deformation during breathing. Our results demonstrate that the use of simple k -space trajectories consisting of under-sampled radial acquisitions is a viable strategy for real-time imaging of tagged lung motion. Using this technique, we were able to observe both temporal and spatial variations of lung motion in normal subjects. We also demonstrated the use of displacement vector fields to generate dynamic functional maps of strain and ventilation. These preliminary results suggest that dynamic imaging of grid-tagged hyperpolarized magnetization may be potentially a powerful tool for observing and quantifying pulmonary biomechanics on a regional basis.

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References

1. Keall PJ, Starkschall G, Shukla H, et al. Acquiring 4D thoracic CT scans using a multislice helical method. *Phys Med Biol* 2004;49:2053–2067. [PubMed: 15214541]
2. Low DA, Nystrom M, Kalinin E, et al. A method for the reconstruction of four-dimensional synchronized CT scans acquired during free breathing. *Med Phys* 2003;30:1254–1263. [PubMed: 12852551]
3. Schreiber E, Xing L. Image registration with auto-mapped control volumes. *Med Phys* 2006;33:1165–1179. [PubMed: 16696494]
4. Yan D, Jaffray DA, Wong JW. A model to accumulate fractionated dose in a deforming organ. *Int J Radiat Oncol Biol Phys* 1999;44:665–675. [PubMed: 10348298]
5. Kashani R, Lam K, Litzenberg D, et al. Technical note: a deformable phantom for dynamic modeling in radiation therapy. *Med Phys* 2007;34:199–201. [PubMed: 17278505]
6. Serban M, Heath E, Stroian G, et al. A deformable phantom for 4D radiotherapy verification: design and image registration evaluation. *Med Phys* 2008;35:1094–1102. [PubMed: 18404944]
7. Cai J, Altes TA, Miller GW, et al. MR grid-tagging using hyperpolarized helium-3 for regional quantitative assessment of pulmonary biomechanics and ventilation. *Magn Reson Med* 2007;58:373–380. [PubMed: 17654579]
8. Cai J, Miller GW, Altes TA, et al. Direct measurement of lung motion using hyperpolarized helium-3 MR tagging. *Int J Radiat Oncol Biol Phys* 2007;68:650–653. [PubMed: 17445997]

9. Peters DC, Korosec FR, Grist TM, et al. Undersampled projection reconstruction applied to MR angiography. *Magn Reson Med* 2000;43:91–101. [PubMed: 10642735]
10. Bernstein, MA.; King, KF.; Zhou, XJ. *Handbook of MRI Pulse Sequences*. Burlington, Massachusetts: Elsevier Academic Press; 2004. p. 906
11. Rasche V, de Boer RW, Holz D, et al. Continuous radial data acquisition for dynamic MRI. *Magn Reson Med* 1995;34:754–761. [PubMed: 8544697]
12. Wild JM, Paley MN, Kasuboski L, et al. Dynamic radial projection MRI of inhaled hyperpolarized ^3He gas. *Magn Reson Med* 2003;49:991–997. [PubMed: 12768575]
13. Riederer SJ, Tasciyan T, Farzaneh F, et al. MR fluoroscopy: technical feasibility. *Magn Reson Med* 1988;8:1–15. [PubMed: 3173063]
14. Moaveni, S. *Finite element analysis: theory and application with ANSYS*. NJ: Prentice Hall; 1999.
15. Keall PJ, Mageras GS, Balter JM, et al. The management of respiratory motion in radiation oncology report of AAPM Task Group 76. *Med Phys* 2006;33:3874–3900. [PubMed: 17089851]
16. Brock KK, Sharpe MB, Dawson LA, et al. Accuracy of finite element model-based multi-organ deformable image registration. *Med Phys* 2005;32:1647–1659. [PubMed: 16013724]
17. Wu Z, Rietzel E, Boldea V, et al. Evaluation of deformable registration of patient lung 4DCT with subanatomical region segmentations. *Med Phys* 2008;35:775–781. [PubMed: 18383700]
18. Guerrero T, Sanders K, Noyola-Martinez J, et al. Quantification of regional ventilation from treatment planning CT. *Int J Radiat Oncol Biol Phys* 2005;62:630–634. [PubMed: 15936537]
19. Miften MM, Das SK, Su M, et al. Incorporation of functional imaging data in the evaluation of dose distributions using the generalized concept of equivalent uniform dose. *Phys Med Biol* 2004;49:1711–1721. [PubMed: 15152926]
20. Reinhardt JM, Ding K, Cao K, et al. Registration-based estimates of local lung tissue expansion compared to xenon CT measures of specific ventilation. *Med Image Anal.* 2008
21. van Beek EJ, McLenna G, Hoffman EA. Ventilation imaging using computed tomography. *Imaging Decision* 2004;4:15–23.
22. Chon D, Beck KC, Simon BA, et al. Effect of low-xenon and krypton supplementation on signal/noise of regional CT-based ventilation measurement. *J Appl Physiol* 2007;102:1535–1544. [PubMed: 17122371]
23. Wang C, Miller GW, Altes TA, et al. Time dependence of ^3He diffusion in the human lung: measurement in the long-time regime using stimulated echoes. *Magn Reson Med* 2006;56:296–309. [PubMed: 16791861]

Figure 1.

(a–e) Conventional grid-tagged MR images of a water phantom, reconstructed from radially acquired k -space data at angular sampling densities of 100%, 50%, 45%, 35%, and 17%, respectively. (f) Radial k -space trajectory with 35% angular sampling density. In this example, the 35 total lines are grouped into 7 color-coded interleaves, each composed of 5 evenly-spaced radial lines.

Figure 2.

Multi-slice dynamic HP He-3 coronal grid-tagged MR images of the lung acquired from subject #1 during exhalation. Total acquisition time for a full image set is 867 ms, but the use of sliding-window reconstruction allows us to update the image of each slice more frequently. The mean time between consecutive images shown here is 500 ms. Slices are arranged anterior to posterior from the top to the bottom of the figure.

Figure 3.

Multi-slice dynamic HP He-3 sagittal grid-tagged MR images of the lung acquired from subject #2 during exhalation. The four slices from the right lung are shown here. Total acquisition time for a full image set is 700 ms (88 ms per slice). Slices are arranged lateral to middle from the top to the bottom of the figure.

Figure 4. Multi-slice dynamic HP He-3 sagittal grid-tagged MR lung images acquired from subject #3 during exhalation. The lateral-most slice from the left lung is shown here, updated every 1.14s.

Figure 5.

Representative map of grid-element motion paths during exhalation. This map corresponds to Slice #4 in Fig. 2, with extra dynamic tagging images interpolated using the sliding window technique for generating the trajectories (temporal pseudo-resolution is 50 ms). Dark color corresponds to the earlier positions and lighter color corresponds to later positions of the tag elements. Lung motion is more linear and rapid at earlier times than at later times during exhalation.

Figure 6.

Representative results from a sagittal dynamic MR tagging study from Subject #2 (Slice #2 in Fig. 3 was used in this example). From top to bottom: displacement vector maps, E_1 strain maps, E_2 strain maps, and ventilation maps. In the displacement vector maps, the tail of each displacement vector indicates the initial position of the associated tissue grid element (at end-inhalation), and the head indicates the position at the current time point during the exhalation. In the strain maps, the lines within each pixel indicate the principal direction of lung motion. These images showed distinct spatial differences in the motion pattern between two lung lobes. During the exhalation, the lower lobe moved superior-posteriorly and the upper lobe moved mostly posteriorly.

Figure 7.

Mean displacements in AP direction (a) and in SI direction (b), principle strains of E_1 (c) and E_2 (d), and ventilation (e) as a function of time during the exhalation for each lung lobe, calculated from the sagittal-slice images shown in Fig. 6. It can be seen that both lung lobes moved approximately the same distance in the AP direction at any time point, but the lower lobe moved significantly greater distance in the SI direction than the upper lobe at any time point. Strains and ventilation are generally uniform throughout each lobe, while the values are slightly higher in the lower lobe than those in the upper lobe, especially in the later images.

Figure 8.

Differential displacement vector maps, generated (a) between the second and the third tagging images; and (b) between the third and fourth tagging images in Fig. 5. The tail of each displacement vector indicates the position of the associated tissue grid element at the previous time point, and the head indicates the position at the current time point during the exhalation. There is pronounced motion between the second and third images, but the motion is much less pronounced between the third and fourth images.