Published in final edited form as:

Magn Reson Med. 2017 October ; 78(4): 1458–1463. doi:10.1002/mrm.26516.

Signal-to-Noise Ratio, T_2 , and T_2^* for Hyperpolarized Helium-3 MRI of the Human Lung at Three Magnetic Field Strengths

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Abstract

Purpose—To evaluate T_2 , T_2^* and signal-to-noise ratio (SNR) for hyperpolarized helium-3 (^3He) MRI of the human lung at three magnetic field strengths ranging from 0.43T and 1.5T.

Methods—Sixteen healthy volunteers were imaged using a commercial whole-body scanner at 0.43T, 0.79T, and 1.5T. Whole-lung T_2 values were calculated from a Carr-Purcell-Meiboom-Gill spin-echo-train acquisition. T_2^* maps and SNR were determined from dual-echo and single-echo gradient-echo images, respectively. Mean whole-lung SNR values were normalized by ventilated lung volume and administered ^3He dose.

Results—As expected, T_2 and T_2^* values demonstrated a significant inverse relationship to field strength. Hyperpolarized ^3He images acquired at all three field strengths had comparable SNR values and thus appeared visually very similar. Nonetheless, the relatively small SNR differences among field strengths were statistically significant.

Conclusions—Hyperpolarized ^3He images of the human lung with similar image quality were obtained at three field strengths ranging from 0.43T and 1.5T. The decrease in susceptibility effects at lower field that are reflected in longer T_2 and T_2^* values may be advantageous for optimizing pulse sequences inherently sensitive to such effects. The three-fold increase in T_2^* at lower field strength would allow lower receiver bandwidths, providing a concomitant decrease in noise and relative increase in SNR.

Keywords

Hyperpolarized helium-3; signal-to-noise ratio; T_2 , T_2^* ; magnetic field strength

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Introduction

Most hyperpolarized-gas MRI studies have used conventional 1.5T or 3T clinical scanners due to the wide availability of such systems. With conventional proton MRI in a body-noise dominated regime, the approximately linear dependence of signal-to-noise ratio (SNR) on field strength confers significant advantages to imaging at higher fields. This is not the case for hyperpolarized-gas MRI in which the polarization of hyperpolarized gases is generated external to the static magnetic field of the MR scanner. Thus, the SNR should be largely independent of the field strength of the scanner in the body-noise dominated regime [1].

The many air-tissue interfaces within the lung induce significant susceptibility effects that cause the signal from hyperpolarized gases in the lung to have a relatively short T_2^* value [2–5]. Decreased susceptibility-related effects at lower magnetic field strengths may improve the performance of certain techniques or permit use of techniques that perform poorly at high magnetic field strengths [6]. The lower cost, easier siting, and lower RF power deposition within tissues of a low field system are important advantages for development of a system that could be easily sited in a clinic for lung imaging [7].

Parra-Robles et al. developed a theoretical model for the dependence of SNR on static magnetic field strength that accounted for effects of susceptibility differences, transverse relaxation times, and gas diffusion. They found the optimum field strength for hyperpolarized helium-3 (^3He) MRI to be 0.1–0.6T [1]. Several studies have experimentally investigated the properties of hyperpolarized-gas MRI at relatively low field strengths [6,8–14], but to our knowledge the lung-imaging characteristics at the commonly-used field strength of 1.5T have not been systematically compared to those for field strengths below 1.5T. The purpose of this study was to perform hyperpolarized ^3He MRI of the human lung at field strengths between 0.4T and 1.5T using the same MR scanner, and evaluate the associated T_2 , T_2^* and SNR values as a function of field strength [15].

Methods

All imaging was performed on a commercial 1.5T whole-body MR scanner (Avanto, Siemens Medical Solutions, Malvern, PA) that was ramped to two lower field strengths (0.43T and 0.79T), and reshimmed (Resonance Research Inc., Billerica, MA) at each field strength to achieve field homogeneity of 0.9 ppm (root mean squared) over a 30-cm diameter spherical volume. The lowest field strength was chosen so that the corresponding frequency was well within the stopband of the gradient-noise filters for the scanner. The middle field strength was chosen so that the ratio of the middle to low field strength was approximately the same as the ratio of the high to middle field strength, and that the frequency corresponded to an established operating frequency of the scanner. (The field strength 0.79T for ^3He corresponds to 1.5T for ^3P .) Appropriately tuned, flexible chest, transmit/receive ^3He RF coils of identical size and geometric configuration (Clinical MR Solutions, Brookfield, WI) were used at all three field strengths. The 0.79T RF coil was the same physical coil as the 0.43T RF coil, except retuned to operate at the higher field strength. The flexible circuit boards, which included the copper conductor paths for the coils, were of identical size and configuration for the 0.43T/0.79T and 1.5T RF coils. Each

of the three coils had its own transit/receive switch and first-stage preamplifier. However, only the 1.5T RF coil included proton-blocking circuits to permit ^1H imaging using the body RF coil with the ^3He RF coil in place. The experiments at each field strength occurred several months apart due to constraints on scheduling of the ramp down of the scanner.

Q values for the RF coils were measured using an RF network analyzer (Agilent model 8712ES, Santa Clara, CA) and the procedure outlined by Gilbert et al.[16]. Unloaded and loaded conditions were achieved by wrapping the flexible RF coil around hollow acrylic shells matched to the size of the coil. For the unloaded condition, the acrylic shell was empty, and, for the loaded condition, the acrylic shell contained a saline solution that presented the same load as a medium-sized adult chest.

Data for determining whole-lung T_2 values, T_2^* maps, and SNR (from spin-density images) were obtained at 0.43T, 0.79T and 1.5T in 16 healthy volunteers (mean age 23 years, range 20 to 30 years). Nine of these volunteers (mean age 23 years, range 20 to 29 years) were imaged at all three field strengths. (Some of the subjects imaged at 0.43T were not available several months later for the studies performed at 0.79T. Thus, these subjects were replaced.) Subjects had smoked less than 100 cigarettes in their lifetime, had no history of pulmonary disease and were not pregnant.

Results of apparent diffusion coefficient measurements performed in 12 of the 16 subjects at 0.43T and 1.5T have been previously reported [17]. All experiments were performed under a Physician's IND for imaging with hyperpolarized ^3He (IND #57,866) using a protocol approved by our Institutional Review Board. Informed written consent was obtained in all cases. The subject's heart rate and oxygen saturation level were monitored (3150 MRI Patient Monitor; Invivo Research Inc., Orlando, FL) during each MRI session.

Helium-3 gas was polarized by collisional spin exchange with an optically-pumped rubidium/potassium vapor using a custom-built system that yielded polarizations between 50 and 60% [18]. For each MR acquisition, subjects inhaled a gas mixture containing hyperpolarized ^3He and medical grade nitrogen for a total volume equal to approximately one-third of forced vital capacity. The ^3He "dose" (total magnetization) was determined for each inhalation using a commercial polarization-measurement system (Model IGS.9900.Xp, Amersham Health).

Whole-lung T_2 relaxation times were calculated from a spectroscopic (i.e., non-spatially selective RF pulses and no spatial-encoding gradients) Carr-Purcell-Meiboom-Gill spin-echo-train acquisition with an echo spacing of 30 ms. Least-squares fitting of the echo amplitudes corresponding to each subject and each field strength was performed using mono- and bi-exponential functions over echo train durations of 2.9 s for 0.43T and 0.79T, and 0.8 s at 1.5T.

For T_2^* measurements, a dual-echo gradient-echo pulse sequence was used; the first echo time (TE) was 2.1 ms, and the second TE was 22.1, 17.1, and 12.1 ms at 0.43, 0.79 and 1.5T, respectively. Data corresponding to the two echo times was acquired in an interleaved fashion. That is, the data for both TE values (acquired in separate repetitions so that diffusion-induced signal attenuation was the same for both echoes) were acquired for a given

line of k space before proceeding to the next line of k space. To minimize acquisition time, the repetition time (TR) was minimized for each echo time, yielding a TR of 5.9 ms for the first TE and TR values of 16, 21 and 26 ms for the second TE at 0.43, 0.79 and 1.5T, respectively. All acquisitions used flip angle 8° and voxel size $6.3 \times 6.3 \times 10 \text{ mm}^3$. After thresholding the coronal image data at three times the background noise variance, T_2^* maps were calculated on a pixel-by-pixel basis as the difference between the natural logarithms of the signal intensities divided by the difference in TE. For each subject at a given field strength, the median T_2^* value over the lung was calculated. For all subjects at each field strength, the whole-lung mean T_2^* was derived as the average of the corresponding median whole-lung T_2^* values at that field strength. Whole-lung histograms were also calculated from the T_2^* maps.

For determination of SNR, a gradient-echo pulse sequence was used with TR/TE 6.0/2.3 ms, flip angle 9° , and voxel size $3.3 \times 3.3 \times 10 \text{ mm}^3$. The same receiver bandwidth was used for all three field strengths. SNR was calculated from the coronal images as the mean signal of all voxels with intensities higher than three times the noise variance divided by mean background noise. Mean noise was calculated from a region of background voxels free of lung tissue/airways. To account for differences in lung volume and ^3He dose (polarizer performance) among subjects, mean whole-lung SNR values were normalized with respect to the subject's ventilated lung volume (volume of voxels with signal above three times the noise variance) and administered ^3He dose.

Whole-lung T_2 and T_2^* values for the different field strengths were compared using ANOVA on ranks. SNR values for each subject were compared using repeated measures one-way ANOVA.

Results

The unloaded Q values for the 0.43T, 0.79T and 1.5T RF coils were 157, 88 and 87, respectively, and the loaded Q values were 47, 26 and 21, respectively.

Whole-lung T_2 values determined from mono-exponential and bi-exponential fits are plotted in Fig. 1a versus field strength. As expected, T_2 values demonstrated an inverse relationship with field strength ($1.04 \pm 0.12 \text{ s}$ at 0.43T, $0.46 \pm 0.05 \text{ s}$ at 0.79T and $0.21 \pm 0.02 \text{ s}$ at 1.5T for the mono-exponential fit). A bi-exponential provided a better fit of the T_2 signal decays than a mono-exponential, particularly at 0.79T and 1.5T as illustrated in Fig. 1b. An inverse relationship with field strength was observed for both the short and long T_2 components of the bi-exponential fit. The values were pairwise significantly different ($p < 0.05$) for each set of fitting parameters based on Kruskal-Wallis one-way analysis of variance on ranks and Dunn's post-hoc test.

Whole-lung mean T_2^* values versus field strength, averaged over all subjects, are shown in Fig. 2a. The T_2^* values were significantly different ($p < 0.05$) and demonstrated an inverse relationship with field strength ($0.127 \pm 0.016 \text{ s}$ at 0.43T, $0.042 \pm 0.008 \text{ s}$ at 0.79T and $0.022 \pm 0.002 \text{ s}$ at 1.5T) as determined by Kruskal-Wallis one-way analysis of variance on ranks. Whole-lung T_2^* histograms, normalized by the respective median T_2^* value, were

comparable among the three field strengths. Fig. 2b shows 0.43T, 0.79T and 1.5T histograms from a representative subject. These histograms show a relatively small shift toward higher values with increasing field strength, but are otherwise quite similar. Coronal T_2^* maps from the same subject are shown in Fig. 2c. An increased number of focal areas with relatively high T_2^* values are seen as field strength decreases. The location and pattern of these areas are consistent with field inhomogeneity arising from the susceptibility difference between the lung and surrounding ribs. More generally, as the field strength decreased, the effects of macroscopic factors, such as the shape of the lung and the presence of ribs, appeared to play a larger role in determining T_2^* values.

Representative images from the gradient-echo acquisitions used for calculating SNR values are illustrated in Fig. 3. Aside from a slight increase in the prominence of vascular structures at 1.5T, the images obtained at three field strengths appear very similar. Prior to normalization, SNR values combined for all 16 subjects and all three field strengths were 71 ± 22 (63.0 ± 15.5 , 78.8 ± 23.1 , 75.9 ± 19.9 at 0.43T, 0.79T and 1.5T, respectively). As shown in Fig. 4 for the 9 subjects imaged at all three field strengths, there was a mild but significant ($p < 0.05$) dependence of normalized SNR on field strength (47.17 ± 9.6 , 63.49 ± 10.79 and 54.59 ± 8.63 at 0.43T, 0.79T and 1.5T, respectively) as determined by one-way repeated measures analysis of variance and Holm-Sidak method pairwise post-hoc test. The highest SNR was at 0.79T for each subject. For comparison, the RF-coil loading factors ($1 - Q_{\text{loaded}}/Q_{\text{unloaded}}$) at 0.43T, 0.79T and 1.5T were 0.70, 0.70 and 0.76, respectively.

Discussion

Hyperpolarized-gas imaging of human lungs has been performed at field strengths as low as 3mT and as high as 3T [3,10,19]; however, the optimal field strength has not been established. While the linear dependence of thermal-equilibrium magnetization on field strength provides a substantial SNR advantage for conventional proton MRI at higher fields (e.g., 3T vs. 1.5T), the non-equilibrium nature of hyperpolarized magnetization results in SNR that is expected to be largely independent of field strength when the relative contribution of coil noise is small [1]. Nonetheless, the lung contains many air-tissue interfaces that induce susceptibility effects such that the SNR of hyperpolarized-gas lung imaging may actually decrease with field strength. To investigate the optimal field strength, T_2 , T_2^* , and SNR of hyperpolarized ^3He in the human lung were measured at three different field strengths between 0.4T and 1.5T. At each field strength, a very similar experimental set-up was used that included the same MRI scanner, very similar RF coils, similar ^3He dosing, and the same healthy volunteers. As expected, we found a strong inverse relationship between field strength, and T_2 and T_2^* . With this experimental set-up, the normalized SNR from a gradient-echo spin-density (ventilation) acquisition was weakly dependent on field strength, and the maximum SNR occurred at 0.79T for all subjects.

A bi-exponential model provided a much better fit to the experimental T_2 data than a mono-exponential model, particularly at higher field strengths. As demonstrated in proton NMR relaxometry studies, multi-exponential T_2 relaxation has been suggested to represent a finite number of compartments [20]. The mechanism underlying the bi-exponential nature of transverse relaxation that was most prominent at higher field strengths in the present study is

unknown. Nonetheless, we speculate that there may be at least two discrete mechanisms for T_2 decay of inhaled ^3He : one associated with diffusion-mediated susceptibility effects at gas-tissue interfaces in the terminal airways, and another, less field-dependent effect, possibly related to ^3He interactions with molecular oxygen [21].

Prior studies with hyperpolarized-gas lung imaging demonstrated an inverse relationship between field strength and T_2^* . Similar to our findings, Salerno et al. found a 2.5-fold increase in T_2^* for ^3He in the human lung at 0.54T as compared with 1.5T [2]. Deppe et al. found that the T_2^* of ^3He was only 14 ms at 3T, about half the value at 1.5T [3], and that the increased susceptibility effects at the higher field appeared in ventilation images as increased signal attenuation adjacent to intrapulmonary blood vessels. The decrease in susceptibility effects at lower field, as reflected in longer T_2 and T_2^* values, may have advantages for imaging with pulse sequences that are inherently sensitive to these effects, such as balanced steady-state free precession methods. The three-fold increase in T_2^* at 0.43T would allow lower receiver bandwidths that provide a concomitant decrease in thermal noise and relative increase in SNR.

A theoretical analysis suggested that hyperpolarized ^3He imaging of the lungs would be optimal at a field of 0.1–0.6T, although the optimal field strength depended on RF coil design and imaging parameters [1]. In an experimental study comparing hyperpolarized ^3He MRI at 1.5T and 3T, the decreased T_2^* at 3T was thought to be the source of a 7% signal loss at 3T compared to 1.5T [22]. Furthermore, as predicted theoretically and after accounting for the difference in T_2^* , no significant differences in SNR were found between 1.5T and 3T [22]. In another experimental comparison of SNR between clinical field strengths of 1.5T and 3T that used xenon-129 (^{129}Xe), SNR was approximately 1.2 times higher at 3T [5]. This increase in SNR between 1.5T and 3T for ^{129}Xe is similar to that we observed between 0.43T and 0.79T for ^3He . Considering the difference in gyromagnetic ratios between ^{129}Xe and ^3He , the frequencies associated with the two experiments are also similar. Nonetheless, differences between the 1.5T and 3T scanners, or between the RF coils used at 1.5T or 3T, could have caused or contributed to the SNR difference observed for the ^{129}Xe study.

The use of different equipment with different technical capabilities at different field strengths is a limitation of several of the prior comparison studies. In our study, we attempted to control for the effects of equipment variation by using the same MR scanner and RF coils that were as similar as possible for the measurements at three field strengths. We measured a similar SNR at 0.43T and 1.5T, but a somewhat higher value at 0.79T. The RF-coil loading factors were all greater than 0.5, indicating that all coils operated in the body-noise dominated regime [16]. The loading factor was the same at 0.43T and 0.79T, and slightly higher at 1.5T; these values do not explain the somewhat higher SNR at 0.79T. However, it should be noted that the RF-coil loading factors were measured using phantoms, not the individual subjects. For the TE value of 2.3 ms used for SNR measurements, the decrease in mean T_2^* with field strength predicts a 4% and 8% decrease in SNR at 0.79T and 1.5T, respectively, compared to 0.43T; these values do not explain that the lowest SNR was measured at 0.43T. Perhaps differences in the performance of the front-end electronics

for the coils, or differences in coil loading among subjects, were responsible for differences in SNR that cannot be explained by phantom-based coil-loading factors or T_2^* values.

Considering the recent trend of shifting from hyperpolarized ^3He to ^{129}Xe as the agent of choice for lung imaging (largely because of diminished availability and increased price for ^3He in recent years), it would be valuable to perform studies analogous to those reported here, but using hyperpolarized ^{129}Xe in place of ^3He . Based on our results and the lower resonance frequency of ^{129}Xe , we expect that ^{129}Xe would suffer a relatively greater decrease in SNR with a field strength decrease from 1.5T to a few tenths of a Tesla.

Conclusions

Using a carefully controlled experimental set-up to compare three field strengths (0.43, 0.79, and 1.5T) for hyperpolarized ^3He MRI, we found only a weak dependence of SNR on field strength but, as expected, a marked increase in T_2 and T_2^* at lower fields. The increased T_2 and T_2^* values at lower field strengths may significantly improve performance for pulse sequences that are inherently sensitive to susceptibility effects. The advantage of lower field strength should be counterbalanced against the practicality of the now ubiquitous high-field scanners built for proton imaging.

Acknowledgments

Supported by the National Heart, Lung, and Blood Institute of the National Institutes of Health under Award Number R01 HL079077. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. Supported by Siemens Healthcare.

The authors thank Drs. Piotr Starewicz and William Punchard of Resonance Research Inc. for invaluable support in shimming the scanner magnet at 0.43T and 0.79T.

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Figure 1.

(a) Mean ($\pm$ standard deviation) over all subjects of whole-lung T_2 values as a function of field strength based on mono-exponential ("Monoexp.") or bi-exponential ("Biexp.") least-squares fits. The triangles show the short T_2 ("comp. 1") and long T_2 ("comp. 2") components of the bi-exponential fit. (b) R^2 values for the mono-exponential and bi-exponential fits, adjusted for degree of freedom.

Figure 2.

(a) Effect of field strength on mean ($\pm$ standard deviation) of T_2^* over all subjects. (b) Whole-lung T_2^* histograms at 0.43T, 0.79T and 1.5T from a representative subject. (c) Coronal T_2^* maps from the same subject at 0.43T, 0.79T and 1.5T (two maps per field strength). The colorbar is in units of T_2^* divided by the median T_2^* .

Figure 3.
Contiguous coronal gradient-echo images (TR/TE 6.0/2.3 ms, flip angle 9°) obtained at 0.43, 0.79 and 1.5T from one of the subjects.

Figure 4.

Effect of field strength on normalized SNR. Data from each of the 9 subjects imaged at all three field strengths are shown; a different plotting symbol is used for each subject. To permit easy identification of the data for each subject, the plotting symbols corresponding to each field strength are spread out slightly along the field-strength axis.