Optimized 3D Ultrashort Echo Time Pulmonary MRI

Kevin M. Johnson,1* Sean B. Fain,1–3 Mark L. Schiebler,1 and Scott Nagle1,2

Purpose: To optimize 3D radial ultrashort echo time MRI for high resolution whole-lung imaging.

Methods: 3D radial ultrashort echo time was implemented on a 3T scanner to investigate the effects of: (1) limited field-of-view excitation, (2) variable density readouts, and (3) radial oversampling. Improvements in noise performance and spatial resolution were assessed through simulation and phantom studies. Their effects on lung and airway visualization in five healthy male human subjects (mean age 32 years) were compared qualitatively through blinded ordinal scoring by two cardiothoracic radiologists using a nonparametric Friedman test (P < 0.05). Relative signal difference between endobronchial air and adjacent lung tissue, normalized to nearby vessel, was used as a surrogate for lung tissue signal. Quantitative measures were compared using the paired Student’s t-test (P < 0.05). Finally, clinical feasibility was investigated in a patient with interstitial fibrosis.

Results: Simulation and phantom studies showed up to 67% improvement in SNR and reduced blurring for short T2* species using all three optimizations. In vivo images showed decreased artifacts and improved lung tissue and airway visualization both qualitatively and quantitatively.


Key words: MRI; lung; ultrashort echo time; radial imaging

Magnetic resonance imaging (MRI) holds potential to provide safe and comprehensive assessment of lung disease. MRI techniques now exist to measure ventilation and parenchyma microstructure with hyperpolarized He1 (1,2) and Xe129 gas (3,4), gadolinium contrast enhanced (5) and noncontrast(6) perfusion, pulmonary angiography, and pulmonary flow (7). Additionally, emerging techniques hold promise for the assessment of pulmonary cellular metabolism with hyperpolarized C13-labeled tracers (8) and inflammation with F19 (9) or super paramagnetic iron oxide particles (SPIOs) (10). Despite this array of promising techniques for assessing lung function, structural lung imaging with MRI has proven to be challenging. Traditional MR techniques for anatomical assessment are largely hindered by short transverse relaxation times [T2* ≈ 0.5–3 ms (11–15)], low proton density, and the presence of respiratory and cardiac motion. Subsequently, structural proton-based lung MRI has seen limited success.

Short echo time (TE) has been shown to be crucial to maintaining image quality in the lungs (16,17). With short echo times, fast spin echo sequences show clinical utility for the assessment of nonsmall cell lung cancer (18), diffuse lung disease (19), and pulmonary edema (20). However, due to T2 blurring and low acquisition efficiency, fine-scale structures of the lung are not generally well-visualized. This has sparked substantial interest in sequences that provide near zero echo times, such as ultrashort TE (UTE), swept Fourier (SWEPT) (21) imaging, zero TE techniques [e.g. ZTE (22) and WASPI (23)], single point imaging techniques [e.g. SPRITE (24)], and hybrid techniques [e.g. PETRA (25) and AWSOS (26)]. However, despite attempts dating back to the early 90’s (17), lung imaging with these techniques has only recently seen significant progress. In small animal studies, UTE sequences have now demonstrated high resolution morphologic lung imaging (27–29), inflammation (10), oxygen-enhanced ventilation, contrast-enhanced perfusion (30), and T2* mapping (31).

Clinical translation of UTE and other short T2* imaging techniques to humans remains highly challenging. Conventionally, these sequences utilize short repetition time (TR) free induction decay sampling that limits signal recovery for species with long longitudinal relaxation times (T1), such as the lung parenchyma [T1 ≈ 1200 ms (32)]. Furthermore, low proton density and limited breath-hold times further reduce signal levels for parenchymal and airway structures. Thus, previous human studies have used relatively thick slice 2D breath-hold UTE sequences (12,17,33) that provide limited spatial coverage and are highly susceptible to inflow related artifacts (33). 3D UTE has several potential advantages over 2D UTE approaches and has seen substantial success in animal models (10,27–31). These include a more efficient radiofrequency (RF) excitation, isotropic spatial resolution with full chest coverage similar to computed tomography (CT), and reduced sensitivity to structured motion artifacts (34). Unfortunately, 3D radial UTE is impractical to perform in a single breath-hold and provides lower SNR efficiency than 2D radial sampling (35). Free breathing motion compensation methods are not easily adapted to 3D lung imaging and respiratory gating or triggering is necessary, typically either with an

1Department of Medical Physics, University of Wisconsin, Madison, Wisconsin, USA.
2Department of Radiology, University of Wisconsin, Madison, Wisconsin, USA.
3Department of Biomedical Engineering, University of Wisconsin, Madison, Wisconsin, USA.

Grant sponsor: NIH; Grant numbers: R01NS066982, R01HL072260-05; Grant sponsor: National Center for Research Resources; Grant number: 1ULTRRO290111; Grant sponsor: National Center for Advancing Translational Sciences; Grant number: 5U54TR000021; Grant sponsor: UWM School of Medicine and Public Health.

*Correspondence to: Kevin M. Johnson, Ph.D., Department of MR/CT Research, University of Wisconsin-Madison, 11221 Wisconsin Institutes Medical Research, 1111 Highland Ave., Madison, WI 53705-2275. E-mail: kmjohnson3@wisc.edu

Received 15 March 2012; revised 9 October 2012; accepted 27 October 2012.

DOI: 10.1002/mrm.24570
Published online 4 December 2012 in Wiley Online Library (wileyonlinelibrary.com).

© 2012 Wiley Periodicals, Inc.
external respiratory bellows (36,37) or using a navigator pulse (38).

3D imaging of short $T_2$ is further limited by challenges with short $T_2$ excitation. Excitation schemes for short $T_2$, 3D imaging must provide high bandwidth excitation and minimize $T_2$ decay between excitation and acquisition. Suitable schemes include hard RF pulses, frequency swept RF pulses (21), and half pulses (39). Of these techniques, only half pulses provide spatial selectivity but at the cost of (1) increased susceptibility to eddy currents and $T_2$ decay and (2) increased scan time due to the necessity of two excitations per k-space trajectory (40). As an alternative, quadratic phase outer volume suppression can be performed before excitation (41); however, this substantially increases RF power requirements and specific absorption rate (SAR). Subsequently, 3D short $T_2$ imaging is most often performed with hard RF excitation. This forces the imaging FOV to be much larger than the area of interest and/or excites spins well outside the FOV where the gradient non-linearity and $B_0$ inhomogeneity cause artifacts.

The purpose of this study was to optimize the 3D radial UTE technique for lung imaging to improve the SNR and image quality. This will allow future translational studies exploring the utility of combined structural and functional MRI in specific patient populations, potentially avoiding the need for CT and its associated radiation burden. Specifically, we hypothesized that the following techniques would improve the SNR and image quality of 3D radial UTE MRI of the lungs: (1) limited field-of-view (FOV) excitation, (2) variable readout gradients with eddy-current corrections, and (3) radial oversampling. These techniques were first evaluated through simulation and phantom studies. A small pilot study in five healthy human subjects was also performed to illustrate the technical feasibility of using these methods along with a novel adaptive respiratory respiratory gating method in vivo to perform high-resolution anatomical imaging of human lungs.

**METHODS**

**Pulse Sequence**

Figure 1 shows an overview of the 3D radial UTE pulse sequence with an oversampled, variable density readout.

**Readout Trajectory and Corrections**

Traditionally, center-out radial sampling with trapezoidal gradients has been utilized for UTE acquisitions. This trajectory collects a half line in k-space in a time-efficient fashion, but can be sensitive to gradient errors and provides low signal-to-noise (SNR) efficiency. SNR inefficiency arises from non-uniform sampling density (35). The efficiency relative to uniform sampling, $\eta$, can be computed:

$$\eta = \frac{\sum d_i}{\sqrt{N \sum d_i^2}}.$$  \[1\]

where $d_i$ is density compensation function for each k-space sample and $N$ is the number of samples. This is minimized when $d_i$ is uniform. For a 3D radial trajectory with $k^2$ sampling density compensation, this inefficiency results in a 25.5% reduction in SNR (42). This loss can be compensated through the use of variable density gradients (43,44). In the context of $^{23}$Na imaging, these techniques have been shown to provide images with higher SNR and reduced blurring (42,45,46) compared to standard ramp sampled trapezoid gradients. However, these techniques have not been applied to proton MRI techniques.

To facilitate improved design of SNR-optimized gradients in a flexible framework, we design gradients with a discrete arc length formulation (47). This modified algorithm allows (1) incorporation of arbitrary density compensation functions and sampling patterns, (2) automatically chooses optimal parameters for a given readout length, and (3) provides more optimal waveforms in slew limited cases. In this formulation, trajectories are first parameterized from k-space into arc length, $s$. Subsequently the optimal trajectory is determined based upon a position-dependent slew limitation (47) and variable density gradient strength limitations:

$$g(s) < \min \left(\frac{A}{COV(s,I)}, G_{\text{max}}\right).$$  \[2\]

where $g$ is the gradient strength, $s$ is the position along the arc, $A$ is an arbitrary scaling factor, $COV$ is the covariance, $G_{\text{max}}$ is the maximum gradient strength, and $I$ is the final image. For gridding reconstructions, $COV(s,I)$ is equivalent to the sampling density correction utilized during reconstruction and is equal to $s^2$ in the case of center-out radial imaging with analytical sampling density compensation:

$$g(s) < \min \left(\frac{|A|}{s^2}, G_{\text{max}}\right).$$  \[3\]

$A$ scales the noise covariance to a desired gradient strength and subsequently controls the total duration of the readout. $A$ is initially set to $G_{\text{max}} \cdot \max(COV(s,I))$. In this case, the desired gradient is always greater than $G_{\text{max}}$ and the algorithm will produce the time-optimal gradient (i.e. a trapezoid). Subsequent iterations reduce $A$ until the readout time is greater than or equal to the desired time. To allow rapid computation, this is
performed with a simple multi-resolution search. For realistic readout lengths, this operation takes less than a second to obtain 4 μs accuracy using a desktop computer (Intel i7 860). Figure 1 shows an example with out-and-back sampling to collect ultrashort (0.08 ms) and conventional (2.1 ms) echo time images.

The increased slewing of variable density readouts has the potential to increase eddy currents and sensitivity to timing errors. Similar errors are also seen with trapezoid gradients and can dramatically lower the spatial resolution and SNR for short T2 or T2* structures in the lung (48). To compensate for these eddy currents and timing errors, we utilize per-subject thin slice calibrations (49,50) to estimate gradient and $B_0$ eddy current terms. This calibration is performed immediately following the acquisition and used to retrospectively correct $k$-space positions and to perform global $B_0$ demodulation.

**Limiting the Field of View**

The effective flip angle experienced by a short T2 species can be derived from Bloch equations and is well developed for constant amplitude RF pulses (51–54). The excitation performance of selective excitations can be derived utilizing a similar framework. For species with long T1, assuming full recovery, the flip angle is approximately equal to the frequency domain overlap of the Lorentzian distribution and that of the Fourier transform of the RF pulse:

$$M_z(T2) \approx M_0 \int_{-\infty}^{\infty} \cos(\alpha(s))\Omega(f)df,$$

where $\alpha$ is the flip angle as a function of frequency is derived from Bloch equations, $M_0$ is the initial magnetization, $\gamma$ is the gyromagnetic ratio, $\Omega$ is the normalized spin distribution function (Lorentzian), and $f$ is the frequency. From this, it is immediately recognized that the RF pulse bandwidth must be greater than the line width of the species of interest in order to provide efficient excitation. This describes the effect on longitudinal magnetization, which is independent of phase imparted to spins with different off resonant frequencies. The detectable signal, $S$ at the end of the RF pulse is approximately:

$$S \approx M_0 \int_{-\infty}^{\infty} \sin(\alpha(s))e^{i\phi(s)}\Omega(f)df,$$

where $\phi$ is the imparted phase of the RF pulse as a function of frequency. Thus, RF pulses must impart minimal phase within the pass band to allow signal detection. For large excitation slabs, both high bandwidth and minimum imparted phase can be achieved with short, minimum-phase Shinnar-LeRoux (SLR) RF-pulses.

Minimum phase RF pulses were compared to hard and windowed Sinc excitations in Bloch simulations. Minimum phase RF pulses were designed for a 300 μs excitation, nominal bandwidth of 30 kHz, and 4% ripple in stop and pass bands. A symmetric, Hann windowed sinc was subsequently designed to achieve identical peak B1 and pulse width. Bloch simulations were performed for a 6° nominal flip angle to compare the excitation and signal efficiency with pulse width ranging from 10 μs to 5 ms. Simulations assumed no T1 decay and a T2 of 0.5 ms, a conservative estimate of T2* in the lungs. For sinc and SLR pulse, slice profiles were computed for a 28 cm selective excitation and measurements of fractional transition width were made.

Even with slab selection, spins may still be excited outside the FOV (e.g. patient arms, excitation side lobes). Since each radial readout is low pass filtered to the prescribed FOV, signal from these spins will lead to artifacts similar to computed tomography (CT) truncation artifacts. To prevent these artifacts, the readout sampling rate was doubled to effectively double the imaging FOV. This comes at the expense of increased data storage requirements, but since all data are used for reconstruction, there is no noise penalty.

**Respiratory Gating**

For 3D UTE, the long scan time makes it impractical to use breath-hold acquisitions. Therefore, an adaptive respiratory gating method using a respiratory bellows signal was used (Fig. 2). This method has been shown to be robust to respiratory drift and irregular breathing patterns in the setting of renal angiography (36,37). Every TR, the bellows signal is analyzed to continuously adapt the gating based on the last 10 s of data. This is achieved by sorting the bellows signal in a histogram and setting an acceptance window. In this work, we utilize a simple 50% threshold to accept end expiratory data and reject inspiratory data. If the bellows position is beyond the threshold, data is not stored and the same inspiratory gating method using a respiratory bellows signal is repeated until the bellows position is below the threshold. To mitigate the possibility of structured artifacts from cardiac and residual respiratory motion, we acquire projections with pseudo-random view ordering determined by a 2D bit-reverse algorithm.

**Simulations and Phantoms**

All experiments assumed the performance or utilized a clinical 3T scanner (MR750, GE Healthcare, Waukesha, WI, Max slew = 200 T/m/s, Max gradient = 50 mT/m). Digital phantom simulations were first performed to evaluate the effect of variable density gradients with...
respect to T2* blurring and SNR performance. Images were simulated using the analytical k-space values for a cylinder with 12 mm diameter. Both variable density and conventional trapezoid gradients were designed with a 1 ms readout and 0.7 mm isotropic resolution images. For variable density gradient design the max gradient strength \( G_{\text{max}} \) was set to 18.4 mT/m corresponding to a required sampling rate of ±125 Hz for a 32 cm FOV. For trapezoid gradients, the 1 ms duration required a gradient strength of 9.7 mT/m, approximately 7.5µs/sample, with an 88 µs ramp time. Simulated T2* values ranged from 0 to 10,000 s⁻¹ \( (T2^* = 0.1 \text{ to } \infty \text{ ms}) \). From these images, the spatial resolution was estimated from the edge width that was calculated:

\[
\text{SNR} = \frac{\text{Peak Signal}}{\text{Standard Deviation of Noise}}
\]

Phantoms were created consisting of 5 mL glass vials filled with varying concentrations of gadopentetate dimeglumine (Magnevist, Bayer, Wayne, NJ) : 250, 166, 100, 55, and 12 mM. The nominal dimensions of these vials were 12.7 mm (O.D) x 11.3 mm (I.D) x 40 mm (length). Vials were placed in a water bath of deionized water and ten consecutive images were acquired with variable density and trapezoid gradients identical to those utilized for digital simulations. Relevant scan parameters included: 0.7 mm isotropic resolution, TE = 5.4 ms, flip angle = 5°, scan-time = 2:46 min, eight-channel head coil (HD Brain, GE Healthcare, Waukesha, WI) and 39,816 radial projections. Immediately following acquisition, thin slice gradient calibrations were performed for both trapezoid and variable density gradients requiring 10 s of additional time. Images were reconstructed at 0.17 mm isotropic resolution with an optimized gridding routine and analytical density compensation (55). T2* maps were estimated utilizing a two-point complex least squares fitting of the short and long echo time images. Subsequently, regions of interest (ROI) were drawn in the short and long echo time maps from a slice at the midpoint of the vial. SNR was estimated from the standard deviation from 10 repeated scans using an ROI placed in the vial and normalized to the SNR in the long T2* phantom (~11.6 ms) acquired with variable density sampling. To assess spatial resolution, the edge width was measured using 25% and 75% maximum thresholds for each vial as was the case for the digital simulations.

**Human Comparison Study**

Using a HIPAA-compliant, IRB-approved protocol, five subjects were recruited and scanned on a 3T clinical scanner (GE MR750, GE Healthcare, Waukesha, WI) without hardware modification. Subjects were recruited from an healthy subject database and had no known disease at time of recruitment. Informed written consent was obtained from all subjects. Three acquisitions were performed on each subject: (1) 40µs non-selective hard RF pulse, no radial oversampling, and ramp-sampled trapezoid readouts, (2) axially-selective RF pulse, radial oversampling, and ramp-sampled trapezoid readouts, and (3) axially-selective RF pulse, radial oversampling, and variable density readouts. For all acquisitions, a 1 ms readout duration was utilized. This readout duration is slightly greater than the expect T2* of lung tissue at 3T. Some blurring of fine lung structures is subsequently expected; however, SNR will be improved in larger structures. For variable density gradient design the max gradient strength \( G_{\text{max}} \) was set to 18.4 mT/m corresponding to a required sampling rate of ±125 Hz for a 32 cm FOV. For trapezoid gradients, the 1 ms duration required a gradient strength of 9.7 mT/m, ~7.5µs/sample, with an 88 µs ramp time. All images were collected with adaptive respiratory gating using a 50% acceptance window. Other relevant parameters included: 1.25 mm isotropic resolution, 32 x 32 x 32 cm³ FOV, TE/TE/TR = 0.080/2.1/4.1 ms, flip angle = 6°, twenty channel phased array coil (Torso Array, Neocoi, Pewaukee, WI, USA), nominal scan time = 9:18 min. No intravenous contrast was administered. Images were reconstructed at 0.83 mm isotropic resolution using iterative non-Cartesian SENSE (56) with coil sensitivities estimated from the central over-sampled center of k-space for the first echo (57).

**Image Analysis**

Regions of interest (ROI) were manually drawn in the right main bronchus and nearby lung tissue and large vessels for each dataset. Subsequently, the difference between air and lung tissue signal normalized to vessel signal was used as a normalized contrast ratio, \( C_R \), and was calculated:

\[
C_R = \frac{\text{Lung} - \text{Airway}}{\text{Vessel}}.
\]

Additionally, the same ROI’s were utilized to estimate the “apparent signal to noise” ratio:

\[
S_R = \sqrt{\frac{2}{\pi} \text{Lung}}.
\]

Due to the nonuniform noise distribution and undersampling, this is a mixed metric of both stochastic noise and image artifacts. A paired Student’s t-test was used to assess differences between the three acquisitions for both \( C_R \) and \( S_R \). For qualitative evaluations, axial and coronal reformatted volumes of the first echo were presented in a randomized order and evaluated using consensus methodology by two cardiothoracic radiologists. The Likert scale used for grading these images is shown in Table 1. Individual scores were assigned for artifacts from blurring, cardiac motion, streaks and noise, and image quality of lung tissue and airways. Large (segmental and larger) and small (subsegmental and smaller) airways received separate scores. Readers were blinded to the acquisition type. Statistical differences in image quality between the three acquisitions were assessed for each patient with a nonparametric Friedman test. Statistical significance was set at the \( P < 0.05 \) level for all comparisons.

**Feasibility in Interstitial Fibrosis**

To provide initial clinical feasibility, a single, 74-year-old, female subject with a history of mixed connective
with a was strongly correlated with concentration \((R^2 = 0.11, 3.1)\) containing long tissue disease undergoing a clinical cardiac MRI was recruited for imaging using a HIPAA-compliant, IRB-approved protocol. Due to scan time and setup limitations, 3D UTE images were only collected using selective excitation, radial oversampling, and variable density readouts, a shorter 5:30 scan time with a higher degree of radial undersampling, and an eight channel phased array coil (HD Cardiac, GE Healthcare, Waukesha, WI, USA). All other parameters, including scanner model were identical to those in healthy volunteers. High resolution CT (HRCT) images were acquired 11 weeks after the MRI examination for clinical purposes. HRCT images were acquired on a 64-slice scanner (Lightspeed VCT, GE Healthcare, Waukesha, WI, USA) utilizing a 1.25 mm slice thickness, 120 kVp, 65.78 dose length product \((~1.1 \text{ mSv dose})\), and reconstructed with an edge-preserving kernel at a 0.7 mm nominal in-plane spatial resolution.

### RESULTS

Simulation and Phantom Studies

Figure 3 shows phantom images and simulations resulting from variable density and trapezoidal gradients. \(T2^*\) was measured to be \(0.53 \pm 0.07, 0.99 \pm 0.08, 1.65 \pm 0.11, 3.1 \pm 0.21,\) and \(11.6 \pm 0.69\) ms for the five vials. \(R2^*\) was homogenous across the fluid-filled vials and was strongly correlated with concentration \((r = 0.98)\) with a \(R2^*\) relativity of 7.5 mM\(^{-1}\) s\(^{-1}\). In UTE images reconstructed using the first echo, short \(T2^*\) vials were well visualized with both sampling techniques. For vials containing long \(T2^*\) fluid, limited differences between the two sampling patterns were seen. However, short \(T2^*\) vials exhibited higher SNR and less blurring with variable density sampling, matching the results of numerical simulation. The edge width was found to be relatively constant until \(T2^*\) became shorter than the readout length. Measured edge widths of the phantoms were larger than predicted by the simulations. This was likely due to off-resonance blurring that was neither accounted for in simulations nor corrected for in reconstructions. Digital simulations and experiment were in agreement for SNR, which was found to be higher with variable density sampling for all \(T2^*\) values. The largest improvement was found for the shorter \(T2^*\) values, with a 67% gain for the shortest \(T2^*\) phantom \((0.53\) ms). For the long \(T2^*\) phantom, (not shown in plots) the variable density gradients still improved SNR by 31%.

#### Selective RF Pulses

The minimum phase RF pulses required a maximum B1 of 10.3 \(\mu\)T for a 6° flip angle and 300 \(\mu\)s pulse width. For the same max B1 and flip angle, 36 \(\mu\)s were required for the same excitation with a hard pulse. Figure 4a shows the effective flip angle as a function of pulse width for minimum phase SLR, sinc, and hard pulses. With a 300 \(\mu\)s pulse duration, excitation flip angles were 5.85°, 5.96°, and 5.48° for SLR, sinc, and hard pulses respectively. Figure 4b shows corresponding signal at the end of the RF pulse as function of pulse width. Signal levels with a 300 \(\mu\)s pulse duration were 92.5%.

<table>
<thead>
<tr>
<th>Categories</th>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Airways (large, small)</td>
<td>Poor – Indistinguishable from nearby lung tissue</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Fair – Lower signal than nearby lung tissue</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Good – Lower signal than nearby lung tissue and bronchial wall visible</td>
<td>3</td>
</tr>
<tr>
<td>Lung tissue signal</td>
<td>None – Indistinguishable from air</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Minimal – Barely distinguishable from air</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Good – Clearly distinguishable from air, but fissions not visible</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Excellent – Clearly distinguishable from air, with lung fissions visible</td>
<td>4</td>
</tr>
<tr>
<td>Artifacts (blurring, cardiac motion, streaks and noise)</td>
<td>Severe – Renders images non-diagnostic</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Moderate – Obscures lung anatomy</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Mild – Present but does not obscure lung anatomy</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Minimal/none</td>
<td>4</td>
</tr>
</tbody>
</table>

**Table 1**

Likert Scales for Qualitative Scoring for the Three Acquisitions in Each Healthy Subject

**Trapezoid**

**Variable**

**FIG. 3.** Phantom images acquired with trapezoidal gradients (a) and variable density gradients (b) with vials arranged left to right from short to long \(T2^*\) \((0.53–3.1\) ms). Note the longest \(T2^*\) phantom \((11.6\) ms) is not shown for brevity. Note the increase in noise and decrease in edge sharpness in the short \(T2^*\) vials. Similar trends are observed in experimental and theoretical measures for edge width (c), and SNR (d). For the shortest \(T2^*\) species \((T2^* = 0.53\) ms) there is a 67% gain in SNR with variable density sampling compared with ramp sampled trapezoidal gradients. Disagreement in edge width likely arises from off-resonance effects that were not included in the theoretical model.
73.5%, and 75.3% for SLR, sinc, and hard pulses respectively. Despite achieving the highest flip angle, sinc pulses consistently resulted in the lower signal. For a given pulse width, minimum phase RF pulses consistently resulted in higher signal and hard pulses resulted in lower signal. However, for the same max B1, hard pulses were more efficient. The 38μs hard pulse with the same max B1 as the 300 μs SLR had a higher signal at the end of the RF, 97.1% vs. 92.5%.

Figure 4c,d shows the flip angle and signal profile for the minimum phase SLR pulse. Outer volume excitation and profile broadening is observed as the RF pulse length increases. Despite outer volume excitation, limited signal is detectable from outside the selected volume as shown in Figure 4d. This is due to the incoherent phase of the excited spins. The signal fractional transition width increased with pulse length and was measured to be 0.09, 0.12, 0.27, and 0.62 for 10 μs, 300 μs, 1 ms, and 5 ms pulses respectively. For the same pulse widths, sinc signal profiles were substantially wider with fractional transition widths of 0.25, 0.25, 0.27, and not measurable for 5 ms pulse due to limited signal.
these highly averaged acquisitions, with no statistical difference between the three methods tested.

**Feasibility in Interstitial Fibrosis**

Figure 8 shows 3D reformations of HRCT, 3D UTE, and the second echo from the 3D UTE sequence. HRCT images do have higher apparent spatial resolution than the MRI images, allowing improved visualization of airways and fissures. However, both CT (Fig. 8a) and 3D UTE (Fig. 8b) show advanced interstitial fibrosis with honeycombing, consistent with usual interstitial pneumonia (UIP). The same findings are much less visible on the later echo time images, which grossly underestimates the extent of fibrosis.

**DISCUSSION**

In this work, we demonstrate the feasibility of free-breathing 3D radial UTE whole lung imaging with a 1.25 mm isotropic resolution comparable with CT. The proposed technique utilized a variable density readout gradient which increased SNR levels of short $T_2^*$ species by as much as 67% in phantom studies and provided significantly improved image quality in human volunteers. Techniques to limit the FOV were found to be essential to mitigate artifacts. The appearance of these artifacts was pronounced on superior lung segments and often present but not obvious on inferior sections. With an adaptive respiratory gating scheme, we were able to perform free-breathing scans without interrupting the steady state acquisition. This increased SNR through signal averaging without causing significant artifacts or incurring detectable blurring. With this optimized 3D UTE pulse sequence many lung features were well visualized, including fissures and airway walls.

UTE MR lung imaging has had a long history of development, but its clinical impact to date has been low. The proposed technique mitigates many of the image quality...
issues that have heretofore limited UTE imaging and may enable the development of clinically useful structural lung imaging with MRI. Compared to previous 2D techniques (11,12), 3D UTE approach is less sensitive to blood inflow, requires a single excitation, and provides whole chest coverage. In addition, the 3D UTE technique proposed here requires no hardware modifications and allows for simple large volume prescription on a commercially available MR scanner. This is in contrast to SWIFT and ZTE based techniques, which require hardware modifications to enable rapid RF switching critical to maintain SNR levels (58). Furthermore, selective excitation, which was shown to substantially improve image quality, is not currently feasible with ZTE and SWIFT based techniques. Compared to 3D UTE sequences shown in small animal studies, the proposed sequence provides higher SNR efficiency, selective excitation, and has now been shown to be feasible in normal human volunteers with physiologic conscious breathing patterns. Additionally, we utilized gradient calibrations to correct for k-space trajectory deviations, a well-known cause of errors in non-Cartesian acquisitions; this correction has been ignored in many previous 2D and 3D UTE techniques.

Substantial development is still needed to verify the efficacy and robustness of the proposed 3D UTE sequence in patients with lung disease. In this study, we have imaged a limited number of healthy human subjects and a single patient with interstitial fibrosis, which may not be representative of clinical patients. Patients, for example, are expected to have a substantially wider range of breathing patterns than observed. Additionally, respiratory gating currently relies on input from a respiratory bellows, which can exhibit poor coupling with lung volume in obese patients. Data-driven respiratory metrics using the center of k-space (59,60) may provide improved fidelity, but these techniques are designed for retrospective gating and will require more extensive changes for prospective sequences that sample k-space more uniformly. Despite respiratory gating, the acquisition remains sensitive to bulk motion during the scan. With the current axial selective RF excitation, the sequence is particularly sensitive to motion of the patient’s arms, which may create artifacts in the images. Future studies will determine the efficacy of respiratory gating in a larger clinical population and compare the bellows to data driven self-gating approaches.

The performance of UTE MRI in pathological conditions of the lung is still relatively unexplored. In our exams, we were able to visualize lobar lung fissures and demonstrated similar findings to CT in a single patient with interstitial fibrosis. However, it is unknown whether the UTE sampling will be sufficient to visualize structures typically seen with CT such as pulmonary edema, lung nodules, air trapping, or early stage interstitial fibrosis. The MR tissue properties, including $T_2^*$, of diseased human lungs are relatively unstudied. Studies in animals suggest that $T_2^*$, specifically, will be reduced in diseases such as emphysema (31,61). Many lung diseases replace air with soft tissue or fluid, which should prove to be beneficial for $T_2^*$ weighted MR imaging with this new UTE method. However, with reduced $T_2^*$
values, the 1ms readout utilized may be suboptimal. With shorter readout windows, the SNR gains from variable density sampling will be reduced. The different relaxation times of blood, pulmonary edema, malignancy and purulent material may also offer a multiparametric imaging data set for clinical analysis to further help characterize lung diseases that now are simply seen as a high attenuation areas on CT. All of our scans were performed on a 3T system where the T2* is substantial shorter than 1.5 T. Subsequently, the use of lower field scanners may allow for improved characterization of lung tissue with pathologically shortened T2*.

CONCLUSION

In this work, we demonstrated the feasibility of free-breathing 3D radial UTE whole lung imaging. We demonstrate improved image quality after incorporating a variable density readout gradient, respiratory gating, and techniques to limit the FOV. These improvements improve the apparent SNR, reduce obscuring artifacts, and allowed visualization of lung parenchyma, airways, and fissures.

ACKNOWLEDGMENTS

The authors acknowledge research support from GE Healthcare and The Hartwell Foundation. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

REFERENCES


