RF Instrumentation for Same-Breath Triple Nuclear Lung MR Imaging of $^1$H and Hyperpolarized $^3$He and $^{129}$Xe at 1.5T

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**INTRODUCTION**

Imaging the lungs with inhaled hyperpolarized gases $^3$He and $^{129}$Xe has been shown to provide functional information that cannot be accessed with proton ($^1$H) MRI or other imaging modalities (1–6). The two gases have distinct physical properties, which provide different but complementary functional information (7–9). The ability to image both nuclei in the same breath alongside the $^1$H anatomical images adds further structural and functional sensitivity to the acquisition. $^3$He is highly diffusive when compared with $^{129}$Xe (10–12), and the visualization and quantification of lung ventilation and diffusion with these two gases at the same time can help address important physiological questions such as the position of the diffusion-convection front in the lungs. The capability to measure the diffusivity of both $^3$He and $^{129}$Xe gases in the same lung inflation level also provides added information for measuring and modeling lung microstructure based on their measured apparent diffusion coefficients (ADC) (13). $^{129}$Xe is also denser and more viscous than $^3$He and as such has different fluid dynamic properties that define airflow in the airways, which can be measured with phase contrast MRI (14). $^{129}$Xe has the added feature that it is soluble in blood and has a wide range of chemical shift, which enables quantification of perfusion and gas exchange in the lungs (8,9,15–17). In recent years, MRI of perfluorinated $^{19}$F gases has also gained interest (18–20) as another MR-sensitive gaseous tracer of regional lung function.

Therefore, same-breath, multinuclear lung imaging with $^3$He-$^{129}$Xe mixtures and $^1$H MRI provides a unique combination of functional and structural information that is spatio-temporally coregistered in the same physiological time frame (21,22). Preliminary studies have used separate and spatially nested transmit-receive (T-R) coils for each nucleus (22). The reliance on the $^1$H MR system’s birdcage body coil for signal reception constrains the signal-to-noise ratio (SNR) in $^1$H images of the lung, which is already limited by the low proton density of lung parenchyma. In a recent study (23), we showed that the $^1$H lung SNR in same-breath imaging can be improved with a nested $^1$H receive array, which is compatible with operation with either a $^3$He or a $^{129}$Xe T-R coil.

The motivation of this study was the design and construction of an integrated radiofrequency (RF) coil and T-R switching system for triple nuclear lung imaging in the same breath. To achieve this, we developed a new dual-tuned flexible T-R RF coil to operate in quadrature for both $^3$He and $^{129}$Xe at 1.5T. For $^1$H imaging, we incorporated the $^1$H array developed in our previous study.
designed to nest within either $^3$He or $^{129}$Xe T-R RF coils (23). With the developed RF instrumentation, we demonstrated triple nuclear same-breath lung imaging with hyperpolarized $^3$He and $^{129}$Xe ventilation images and $^1$H anatomical images. With the same system ADC measurement of mixtures of $^3$He and $^{129}$Xe were performed in the same breath at a particular lung inflation state.

METHODS

$^3$He and $^{129}$Xe Dual-Tuned Coil Design

A dual-tuned ($^3$He-$^{129}$Xe) flexible quadrature T-R coil was constructed in-house. The conducting elements were made from self-adhesive copper tape (FE-5100–5276-7; 3M, Bracknell, UK) of 66-$\mu$m thickness and 6-mm width, which was fixed on a substrate of 0.5-mm-thick polytetrafluoroethylene (Direct Plastics, Sheffield, UK) as shown in Figure 1b. The capacitors used on the resonant circuit were of 10C package (Dalian Dalicap Technology Co., Ltd, Dalian, China). The thickness of the array with the foam was 6 mm (3 mm each side). The dual-tuned flexible T-R coil was a dual Helmholtz-like pair of quadrature design in which the Helmholtz for the in-phase resonance of the quadrature spans the anterior right lung to posterior left lung, connected over left trapezius. Similarly, the Helmholtz for the quadrature-phase resonance spans the anterior left lung to posterior right lung, via the right trapezius. The cross-over of the copper strip for each of the Helmholtz pairs (which forms a “figure eight” topology) was positioned such that it was within the other resonant element (anterior) and was balanced on either side to minimize coupling as shown in Figure 1a and 1b. The schematic of the dual-tuned T-R coil circuit is shown in Figure 1a, and a photograph is shown in Figure 1b. The assembled topology of the flexible coil constitutes a bij design wrapped around the subject longitudinally, as shown in Figure 1c. Both the elements of the dual Helmholtz were fitted with two traps; one trap at the $^1$H frequency to enable $^1$H imaging with this coil in situ and the other trap to dual-tune the coil to the $^{129}$Xe and $^3$He Larmor frequencies. The trap design was based on the formalism established in our earlier study for multituned resonators (23), the frequency of the trap for dual-tuning was 47.81 MHz. A high-pass matching circuit was used to match the coil at both resonant frequencies of $^3$He (48.62 MHz) and $^{129}$Xe (17.65 MHz) at 1.5T. The $^1$H trap was tuned with a 47-pF capacitor and a seven-turn wire wound inductor with a diameter of 6 mm. The trap for dual-tuning the coil was tuned with a 56-pF capacitor and a nine-turn wire wound inductor with a diameter of 6 mm. Wire wound inductors were constructed from 21 AWG insulated copper wire. RF measurements were performed with an Agilent 5061B Network Analyzer (Keysight Technologies, Santa Rosa, California, USA). For the RF measurement, the dual-tuned coil was wrapped longitudinally around the thorax of the subject, as shown in Figure 1c. This coil was designed to work with full functionality when the four-channel $^1$H chest receiver array from our earlier study (23) was nested inside for in situ high SNR $^1$H lung imaging.

MR Imaging Methods for $^3$He, $^{129}$Xe and $^1$H

All in vivo imaging with $^3$He and $^{129}$Xe was performed with approval from the National Research Ethics Committee. The imaging was performed on a healthy male volunteer (age, 31 years; height, 185 cm; weight, 89 kg). Lung MRI was performed on a GE whole body 1.5T Signa HDx system with $^3$He and $^{129}$Xe gas polarized with spin exchange optical pumping (24). The gas dosage and the imaging and pulse sequence parameters used for all three nuclei are shown in Table 1. The hyperpolarized
| Measurement | Lung structure and ventilation | ADC | Whole lung ventilation | Flip angle map |
|-------------|-------------------------------|-----|------------------------|----------------|
| **Physiological details** | | | | |
| RF coil | 1H array, dual-tuned coil | Dual-tuned coil | Dual-tuned coil | Dual-tuned coil |
| **Nuclei** | 1H, 3He, 129Xe | 3He, 129Xe | 3He, 129Xe | 3He, 129Xe |
| Dosage (mL) | | | | |
| 1H | — | — | — | — |
| 3He | 350 | 300 | 200 | 50 |
| 129Xe | 500 | 500 | 500 | 100 |
| **Flip angle** | | | | |
| 1H | 50° | — | — | — |
| 3He | 8° | 9° | 10° | — |
| 129Xe | 9° | 10° | 10° | — |
| **TE (ms)** | | | | |
| 1H | 0.9 | — | — | — |
| 3He | 1.1 | 4.8 | 0.6 | 1.1 |
| 129Xe | 3.6 | 12.5 | 2.1 | 3.6 |
| **TR (ms)** | | | | |
| 1H | 2.9 | — | — | — |
| 3He | 3.6 | 10 | 1.9 | 3.6 |
| 129Xe | 18.9 | 27 | 6.4 | 18.9 |
| **Matrix** | | | | |
| 1H | | | | |
| Phase | 192 | — | — | — |
| Frequency | 256 | — | — | — |
| 3He | | | | |
| Phase | 104 | 48 | 82 | 52 |
| Frequency | 80 | 64 | 80 | 44 |
| 129Xe | | | | |
| Phase | 78 | 48 | 82 | 52 |
| Frequency | 64 | 64 | 80 | 44 |
| **Slice thickness (mm)** | | | | |
| 1H | 15 | — | — | — |
| 3He | 15 | 15 | 4 | 200 |
| 129Xe | 15 | 15 | 10 | 200 |
| **Number of slices** | | | | |
| 1H | 3 | | | |
| 3He | 3 | 2 | 46 | 1 |
| 129Xe | 3 | 2 | 24 | 1 |
| **Field of view (cm)** | | | | |
| 1H | 40 | | | |
| 3He | 40 | 44 | 40 | 40 |
| 129Xe | 40 | 44 | 40 | 40 |
| **Axis** | 2D, coronal | 2D, coronal | Coronal | 2D, coronal |
| **Pulse sequence** | bSSFP, FSGRE | FSGRE | 3D bSSFP | FSGRE |
| **Imaging time (s)** | | | | |
| 1H | 1 | — | — | — |
| 3He | 2 | 6 | 7 | 0.9 |
| 129Xe | 4 | 8 | 13 | 2.4 |
| **Multiphase** | | | | |
| 1H | — | — | — | — |
| 3He | — | — | — | 6 |
| 129Xe | — | — | — | 6 |
| **b Value (s · cm⁻²)** | | | | |
| 1H | — | — | — | — |
| 3He | — | 1.6 | — | — |
| 129Xe | — | 8 | — | — |
| **Corresponding figure** | | | | |
| 1H | 3a, 3d, 3e | — | — | — |
| 3He | 3b, 3d | 2e | 4a | 2c |
| 129Xe | 3c, 3e | 2f | 4b | 2d |

Abbreviations: ADC, apparent diffusion coefficient; bSSFP, balanced steady-state free precession; FSGRE, fast spoiled gradient echo.
$^3$He and $^{129}$Xe gas was delivered in separate Tedlar bags and was mixed at the mouth piece at the time of inhalation, as illustrated in Figure 1e. $^3$He had polarization of 25% ($\approx 100\%$ of He is $^3$He), $^{129}$Xe had a polarization of 40%–50% (87% of Xe is $^{129}$Xe).

**RF Signal Routing and Calibration**

To route the transmit RF signal ($^3$He-$^{129}$Xe) from the appropriate T-R switch on the scanner to the dual-tuned coil and to route the received RF signal ($^3$He-$^{129}$Xe) from the dual-tuned coil back to the appropriate T-R switch on the scanner, a 2-kW rated coaxial antenna RF switch (CX-SW2PL; Watson, Essex, UK) was used. The RF power required for the desired flip angle for the $^3$He and $^{129}$Xe sequences was calculated based on a standard calibration procedure, whereby the rate of depletion of polarization was calculated from the decay of signal resulting from a set of hard RF pulse-acquires of equal amplitude. The period to prescribe calibration values on the spectrometer between the end of imaging a particular nucleus and initiation of the sequence for imaging the next nucleus was less than 4 s. The time required to operate the RF switch manually between acquisitions was 3 s.

**Same-Breath ADC ($^3$He and $^{129}$Xe) and Triple Nuclear ($^3$He, $^{129}$Xe, and $^1$H) Structure and Ventilation Lung Imaging Methods**

For same-breath ADC measurement, the dual-tuned $^3$He-$^{129}$Xe coil was wrapped longitudinally as shown in Figure 1c, without the $^1$H array nested inside. To demonstrate same-breath ADC maps, two sets of ADC measurements were acquired back-to-back in a single breath, with $^3$He ADC measurement followed by $^{129}$Xe measurement. The imaging parameters are shown in Table 1.

For triple-nuclear lung imaging, the dual-tuned $^3$He-$^{129}$Xe coil and the $^1$H array from our earlier study (23) were nested as shown in Figure 1d. To demonstrate imaging of all three nuclei in the same breath, three sets of images were acquired back-to-back in a single breath in the order, with $^3$He imaging followed by $^{129}$Xe imaging, in turn followed by $^1$H imaging. The imaging parameters are shown in Table 1.

The $T_1$ of hyperpolarized gases when inhaled into the lungs is sensitive to the oxygen partial pressure in the lung during the breath-hold (25). $^3$He is more sensitive to this effect because the gyromagnetic ratio of $^3$He is approximately three times larger than that of $^{129}$Xe, as
such the dipolar coupling to the electrons in the paramagnetic oxygen molecule is stronger. This rationale for the order of acquisition is $^3$He followed by $^{129}$Xe, in turn followed by $^1$H.

Flip Angle Mapping and High-Resolution Imaging Performance of the Coil as a Stand-Alone T-R Coil for $^3$He and $^{129}$Xe

Flip angle maps of the dual-tuned coil at the $^3$He and $^{129}$Xe frequencies were calculated by measuring the depletion of polarization of the hyperpolarized gas $^3$He and $^{129}$Xe at each voxel in the lungs by repeated imaging at breath-hold with a two-dimensional spoiled gradient echo sequence. The imaging parameters for this measurement are shown in Table 1, and $T_1$ relaxation was neglected when calculating the flip angle. In addition, to demonstrate the coil’s performance as a stand-alone $^3$He or $^{129}$Xe T-R coil (without the $^1$H array in situ), high-resolution, three-dimensional (3D) imaging data sets were acquired with a 3D balanced steady state sequence (26) with imaging parameters as shown in Table 1.

RESULTS
Dual-Tuned Coil RF Performance

The two traps on the coil at 47.81 MHz and 63.86 MHz ($^1$H trap) generated three resonant modes at 17.65 MHz ($^{129}$Xe Larmor frequency), 48.62 MHz ($^3$He Larmor frequency), and 79.2 MHz. The isolation between the two ports of the Helmholtz was less than $-15$ dB. The quality (Q) factor of the dual-tuned coil at the $^{129}$Xe Larmor frequency (17.65 MHz) was 61 in the unloaded condition and 17 in the loaded condition. The Q factor of the dual-tuned coil at the $^3$He Larmor frequency (48.62 MHz) was 32 in the unloaded condition and 7 in the loaded condition. Thus, the ratio of Q factor unloaded to loaded condition was 3.5 at the $^{129}$Xe Larmor frequency (17.65 MHz) and 4.5 at the $^3$He Larmor frequency (48.62 MHz). Under the loaded condition, the dual-tuned coil was matched to less than $-20$ dB at both ports at both the $^{129}$Xe (17.65 MHz) and $^3$He (48.62 MHz) Larmor frequencies, as shown in Figure 2a. The isolation between the dual-tuned coil and the $^1$H array was less than $-15$ dB, as shown in Figure 2b. Flip angle maps from the dual-tuned coil for the transmit RF power prescribed for the nominal flip angles used for triple nuclear same-breath imaging and ADC measurement (Table 1) are shown in Figure 2c for $^3$He and Figure 2d for $^{129}$Xe. The standard deviation of the flip angle map was calculated to be 0.7° (mean = 8°) for $^3$He and 0.3° (mean = 9°) for $^{129}$Xe.

Multinuclear Lung Imaging

Same-breath ADC measurement of $^3$He and $^{129}$Xe performed in the same lung-inflation state is shown in Figure 2e and 2f. The $^3$He ADC map shown in Figure 2e

FIG. 3. a: $^1$H images from lungs. b: Same-breath $^3$He images from lungs. c: Same-breath $^{129}$Xe images from lungs. d: $^3$He images superimposed over $^1$H images. e: $^{129}$Xe images superimposed over $^1$H images.
and the $^{129}$Xe ADC map shown in Figure 2f were acquired in the same breath.

Same-breath triple nuclear lung (structure and ventilation) images are shown in Figure 3. The $^1$H images shown in Figure 3a, $^3$He images shown in Figure 3b, and $^{129}$Xe images shown in Figure 3c, all of which were acquired in the same breath, are coregistered as shown in superimposed images in Figure 3d and 3e.

Volumetric ventilation images from the 3D balanced steady-state free precession sequence for the coil in operation as a stand-alone transceiver for $^3$He and $^{129}$Xe are shown in Figure 4a and Figure 4b, respectively.

**DISCUSSION**

The construction of the flexible dual-tuned coil is in the form of a bib, which enables a close fit to the subject’s
Triple Nuclear Lung Imaging of \(^1\)H, \(^3\)H, and \(^{129}\)Xe

Thorax irrespective of body type. The design was optimized to the typical subject size mentioned earlier. As the shape/form deviates from the optimal design with other body types, the distributed inductance and T-R efficiency of the dual-tuned coil changes accordingly. The B\(_2\) field homogeneity of the dual Helmholtz design is inherently inferior to that of a birdcage design (27), and the flexibility of the dual-tuned coil adds some variability in this respect. Considering the typical anatomy of a torso, the distance between the RF coil and lung air spaces generally increases from superior (upper) to inferior (lower). This means that sensitivity in the lower lung is reduced for two reasons: first, due to proximity of the conducting elements to the lungs, and second, as the parallel condition for a Helmholtz pair is disrupted. Despite these factors, the observed B\(_2\) transmit homogeneity (variation in flip angle, 3% for \(^{129}\)Xe and 9% for \(^3\)He) is comparable to (28) or better than (29) studies reported previously using single-tuned flexible T-R coils for \(^3\)He and \(^{129}\)Xe lung imaging.

Because the RF switches are currently manually operated, and the spectrometer has an inherent delay time for precalibration for each nucleus, the method is not currently compatible with repetition time resonant frequency interleaved imaging, as demonstrated in our earlier study with same-breath \(^3\)He-\(^1\)H lung imaging (22). It should be noted that this limitation is not due to the RF coil design or configuration; instead, it is due to the MR system, which supports only one spectrometer T-R switch (single-nuclear) to be actively connected at any given point in time (in addition to \(^1\)H). Both the dual-tuned RF coil and the nested \(^1\)H array from the earlier study (23) are capable of operating simultaneously. If we consider the coil’s operation as part of the system for triple nuclear imaging, 50%–60% of the time (ie, 18–20 s of the breath-hold) is consumed by switching the spectrometer between the nuclei. This can be reduced with the appropriate spectrometer software engineering and using electrically driven RF switches (eg, PIN diodes and Field Effect Transistor).

The free diffusion (in air) of \(^3\)He is 0.88 cm\(^2\) s\(^{-1}\) (30,31); in this study, we report 0.85 cm\(^2\) s\(^{-1}\) for \(^3\)He in the trachea (slightly lower than \(^3\)He free diffusion). The free diffusion of \(^{129}\)Xe is 0.14 cm\(^2\) s\(^{-1}\) (31); in this study, we report 0.22 cm\(^2\) s\(^{-1}\) for \(^{129}\)Xe in the trachea. The higher ADC value for \(^{129}\)Xe in the trachea, we presume is due to its mixture with the highly diffusive \(^3\)He (as shown in Table 1). In the ventilation images, any observed asymmetry beyond what can be attributed to the measured variation/asymmetry in the flip angle was verified to be caused by the distribution of \(^3\)He and \(^{129}\)Xe as a gas mixture in the lung (variation in the local concentration of the gases). These findings are currently being investigated in future work studying the physiology of gas mixing in the lung with the two gases.

In contrast to our previous triple nuclear same-breath lung imaging experiments demonstrated at 3T on a Philips system using the \(^1\)H body T-R coil, a \(^3\)He birdcage T-R coil, and a nested \(^{129}\)Xe T-R coil (22), the design used in this study at 1.5T has several potential benefits. First, from the coil perspective, the use of the dual-tuned \(^3\)He, \(^{129}\)Xe coil minimizes the number of individually tuned coils, and the nested \(^1\)H array (23) improves the \(^1\)H SNR by closer proximity to the lung. Applications of this triple nuclear RF system for lung MRI are manifold and allow the different physical and physiological properties of the two gases to be explored in the same time course with added provision of high-quality and coregistered \(^3\)He structural images.

In conclusion, we have demonstrated a system for triple nuclear same-breath lung imaging of \(^1\)H with hyperpolarized gases \(^3\)He and \(^{129}\)Xe at 1.5T using a custom integrated RF system. This system incorporates a new design of dual-tuned RF coil for \(^3\)He and \(^{129}\)Xe and RF switches, together with a nested receiver array for \(^1\)H imaging. With this system, we have demonstrated high-quality, same-breath \(^3\)He with \(^3\)He and \(^{129}\)Xe ventilation imaging and the capability for ADC mapping of \(^3\)He and \(^{129}\)Xe in the same lung-inflation state. In addition, the image quality on all three nuclei is comparable with those acquired with separate RF coils for the given nucleus.

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