Robust 3D MRI of the Mouse Lung Using ZTE Imaging with Background Correction

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Introduction Proton MRI of lung tissue is challenging due to low water content and very short transverse relaxation times T2*, typically on the order of one millisecond or below. Therefore, for pulmonary imaging, projection techniques have been employed with ultra-short¹⁻⁶ or zero echo time⁷⁻¹⁰ which enable capturing signal with very short T2 or T2*. Zero echo time (ZTE) imaging^{11,12} offers particularly high efficiency and has been shown to enable very rapid and motion-insensitive 3D MRI of the mouse lung⁹. As a downside, it has been observed that signal is also detected from hardware parts in the sensitive range of the RF coil, in particular components of the coil itself. Such signals typically have T2s of a few tens of microseconds and thus appear blurred and potentially aliased in the image (Fig. 1a). Associated changes in image intensity are especially critical in regions of low signal levels, such as the lung. Therefore, in the present work, a subtraction technique is suggested for background correction in ZTE MRI¹³ and employed to enable robust pulmonary imaging in mice.

Methods <u>ZTE imaging</u> uses 3D radial center-out encoding where RF excitation is applied with a short hard pulse while the projection gradient is already on¹². The associated initial RF dead time induces a central k-space gap which is addressed by 1D algebraic reconstruction before 3D gridding¹². For rapid 3D MRI of the mouse lung, the following protocol with isotropic geometry was chosen: matrix size = 160, FOV = 50 mm, spatial resolution = 0.31 mm, TR = 1 ms, flip angle = 3.7°, pulse duration = 1 µs, signal bandwidth = 200 kHz, readout duration = 400 µs, radial oversampling = 4, k-space gap = 1.5 nominal dwells, 80888 radial spokes, NSA = 2, respiratory triggering, and scan time ≈ 4 m 30 s.

For <u>background correction</u>, one separate data set was acquired with the subjects replaced by a glass tube filled with $D_2O + 9$ g/l NaCl, to mimic the coil load of a mouse without creating MR signal. The coil image was smoothed, and a weighting factor for complex subtraction was determined in region 1 of Fig. 1b as the ratio of data with and without subject.

<u>Measurements</u> were conducted on a 4.7 T Bruker small animal scanner equipped with a linearly polarized transmit-receive whole-body coil with inner diameter = 38 mm. Six healthy mice approved by the institutional animal care committee were used in this study. They were anesthetized with isoflurane and held at a breath rate below 50 per minute as observed via a pressure sensor. SNR calculations were performed in lung tissue on magnitude images, including bias correction for magnitude noise¹⁴.

Results Figure 1 illustrates the effectiveness of the subtraction-based background correction. The uncorrected image (Fig. 1a) exhibits signal from the RF coil housing. The empty coil data (Fig. 1b) additionally reveals signal in the centre with opposite phase, which has been aliased from outside the FOV. After appropriate subtraction, the background signal is efficiently reduced to values only slightly above noise level (Fig. 1c). Importantly, signal in lung tissue is recovered which is virtually cancelled by destructive superposition in the uncorrected image.

Figure 2 shows the ZTE images obtained for all six mice. They provide high image quality, excellent background correction, and significant signal for lung tissue. The residual background-to-noise ratio across all data sets is 1.53 ± 0.19 , achieved with individually weighted subtraction of the same coil data set. The SNR measured in lung tissue, excluding visible vessels, is 18.5 ± 2.3 . Overall, the results are very consistent and reproducible, indicating the robustness of the employed technique.

 $\ensuremath{\textbf{Discussion}}$ In this work, rapid, isotropic 3D ZTE imaging of the mouse lung was enabled with high



Figure 1 Background correction for ZTE MRI, applied in the lung. a) The original, uncorrected image exhibits background signal from the RF coil. b) The image of the empty coil also shows the coil (1) and furthermore reveals signal in the centre with opposite phase aliased from outside the FOV (2). c) By weighted complex subtraction, the background is removed and the lung signal is recovered. The residual background-to-noise ratio is ≈1.5.



Figure 2 Pulmonary proton MRI in six mice using the ZTE technique. Coronal views are displayed from 3D data sets with isotropic resolution of 313 μ m. All images are of high quality, exhibit significant signal in lung tissue, and show excellent background correction, thus demonstrating the high robustness and reproducibility of the approach.

robustness and reproducibility by employing a subtraction-based correction for background signal. Without correction, ZTE data acquired with the used setup would not be usable due to comparable signal levels of lung tissue and the obtained artefacts. The correction scheme relies on the acquisition of data with the empty setup using a coil load which is representative for the actual subject. Although this could be achieved with a suitable phantom in the current study, other coils may be more sensitive to load changes and require more advanced replacements. Nevertheless, the subtraction approach can be of interest also for other short-T2 applications, as rapid transverse relaxation frequently coincides with low proton density, making the associated low signal particularly prone to errors. The obviously ideal solution to background signal would be avoiding it in the first place. However, many already existing coils could not be used for undisturbed ZTE imaging, and designing and building proton-free hardware is not trivial¹⁵. Furthermore, out-of-band signal can also stem from non-NMR sources such as RF switching transients which may be tackled similarly¹⁶. Of course, using the demonstrated ZTE technique also for lung MRI in humans is a promising perspective, given the availability of RF hardware capable of sufficiently rapid RF switching¹⁷.

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