2D Ultrashort Echo-Time Functional Lung Imaging

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Background: Imaging of the lung by MRI is challenging due to the intrinsic low proton density and rapid T2* relaxation. MRI methods providing lung parenchyma and function are in demand.

Purpose: To investigate the feasibility of two-dimensional ultrashort echo-time (2D UTE) imaging for lung function assessment.

Study Type: Prospective.

Population: Eleven healthy volunteers.

Field Strength/Sequence: 3T, 2D tiny golden angle UTE (2D-tyUTE).

Assessment: The applicability of breath-hold (BH) and self-gated (SG) 2D-tyUTE for quantification of the lung parenchyma signal-to-noise ratio (SNR), proton fraction (fP), fractional ventilation (FV), and perfusion (f) was investigated. Dependencies on repetition time (BH/SG) and respiratory phase (expiration [EX], inspiration [IN]) were investigated and compared between smokers and nonsmokers.

Statistical Tests: Analysis of variance (ANOVA), Kendall’s W.

Results: Significant differences of SNR (EX: 10.98 ± 3.19(BH), 14.58 ± 3.89(BH), 17.59 ± 4.92(SG), IN: 7.17 ± 2.07(BH), 9.51 ± 2.37(BH), 10.49 ± 2.33(SG), 10.00 ± 4.14(SG)) (P < 0.05 for all cases) were observed between the different approaches. Where fP in expiration (0.41 ± 0.13) was independent of the BH imaging technique, it was slightly higher in SG (0.44 ± 0.06). FV was reproducible among the BH techniques (0.41 ± 0.10), but significantly lower in SG (0.21 ± 0.06) (P < 0.05). A moderate correlation (R2 = 0.47, P < 0.01) was observed between the breathing amplitude and FV. No significant differences between BH and SG were observed for the perfusion analysis (EX: 3.50 ± 1.29 mL/min/mL [BH]; IN: 2.36 ± 1.05 mL/min/mL [BH]). Significant differences in fP were found between smokers (0.48 ± 0.11 BH) and nonsmokers (0.37 ± 0.12 BH) in expiration.

Data Conclusion: This study demonstrates the feasibility of 2D-tyUTE for successful quantification of relevant lung function parameters at 3T within clinically attractive acquisition times. The low spatial resolution into the slice selection direction may limit the final sensitivity and needs further clinical evaluation.

Level of Evidence: 2

Technical Efficacy Stage: 1

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Since many lung diseases present with a highly heterogeneous pattern, methods providing regional information are needed. Where computed tomography (CT) mainly provides data on lung density and may be limited, especially in pediatric applications, magnetic resonance imaging (MRI) provides morphologic and function information with nonionizing radiation. This may especially become important for early detection of disease and for continuous therapy monitoring of novel highly specific drugs (eg, immunomodulation).

Lung MRI is challenging due to both respiratory and cardiac motion, and the intrinsic low MR signal of the lung parenchyma caused by the low proton concentration and the multiple air–tissue interfaces resulting in a short T2*.1–3 Even though fast 3D gradient echo sequences have been successfully applied to lung imaging, ultrashort (UTE) and zero-
echo-time (ZTE) techniques have recently gained attention due to their excellent properties for imaging ultrashort \( T_2^* \) compounds.\textsuperscript{1,2,4-15} UTE techniques use radial center-out \( k \)-space sampling, thus enabling echo times only limited by the time required for switching between transmit and receive mode (front-end switching time),\textsuperscript{16} while simultaneously showing beneficial motion artifact properties.\textsuperscript{17}

Where cardiac motion is negligible for anatomic lung imaging, respiratory motion has to be carefully considered to avoid impairment of the resulting image quality.\textsuperscript{2} In cases of rapid data acquisition, single breath-holds have been used.\textsuperscript{1,4,14} However, in the case of high spatial resolution and full 3D coverage of the lungs, data acquisition within a single breath-hold is not feasible and alternative approaches have been reported. They mainly rely on continuous data acquisition during free breathing with retrospective extraction of a respiratory motion surrogate marker from the MR data (self-gating). Most commonly used is the signal modulation of the \( k \)-space center (DC).\textsuperscript{18,19} Since the \( k \)-space center represents the total energy of the imaged volume it is modulated according to changes in the anatomy introduced by cardiac or respiratory motion. With center-out techniques, the extraction of this DC signal is straightforward, since the \( k \)-space center is intrinsically sampled during each acquisition.\textsuperscript{11,12,20}

Alternatively, modified spin-warped techniques frequently sampling the \( k \)-space center have been successfully applied to lung imaging.\textsuperscript{21,22} Further self-gating techniques exploit low-resolution images continuously reconstructed during free-breathing with high temporal resolution and follow, eg, the lung–liver or lung–heart interface for deriving respective gating signals.\textsuperscript{9,11,18} With either technique, images representing different respiratory and, if required, cardiac phases can be reconstructed. However, the application of non-UTE techniques is limited by the intrinsic low signal-to-noise ratio (SNR) and motion sensitivity in case of residual respiratory or cardiac motion. Pure 3D UTE techniques suffer from long scan durations and do not allow nonisotropic data acquisition and noncubic field of views. Hybrid methods like stack of stars still use Fourier-encoding along the slice selection direction, thus still being sensitive to residual motion and the application of spirals and cones appears limited by the rapid signal decay and susceptibility properties. Two-dimensional UTE appears to be an efficient candidate for providing images of the lung parenchyma in different respiratory and cardiac phases as the basis for subsequent function quantification.

The analysis of the intensity changes of the lung parenchyma over the respiratory and cardiac cycle have been reported to provide diagnostically relevant information\textsuperscript{14,23,24} for lung ventilation and perfusion without the need for any contrast agent or breathing of hyperpolarized gases\textsuperscript{25,26} or pure oxygen.\textsuperscript{27,28} Bauman et al\textsuperscript{24} reported the use of real-time MRI with subsequent Fourier-decomposition (FD) analysis for quantifying fractional ventilation and perfusion. The principle was further developed by Fischer et al\textsuperscript{29} by combining respiratory and cardiac self-gated imaging with subsequent Fourier analysis for ventilation and perfusion assessment. The approach has been translated to 3D UTE for lung function assessment.\textsuperscript{10}

The aim of this work was to investigate the applicability of self-gated 2D UTE imaging as an efficient strategy for deriving quantitative functional data of the human lung at 3T field strength. Functional data are derived from signal intensity changes between different respiratory and cardiac phases.

**Materials and Methods**

Radial 2D spoiled center-out tiny golden angle ultrashort echo time (2D- rUTE) acquisitions were performed with a clinical 3T MR scanner (Achieva 3T, Philips Healthcare, Best, The Netherlands). All data were acquired with a dedicated 32-channel cardiac receive coil. Images were reconstructed from multiple breath-hold (BH) and free-breathing (FB) data. Total data acquisition time was about 6.5 minutes. Between subsequent BH and FB acquisitions, the volunteers were asked to breathe normally for about 2 minutes, yielding an approximate protocol time of 30 minutes.

**2D UTE Breath-Hold Acquisition**

Subsequent (BH\(_i\)) and interleaved multislice imaging (BH\(_i\)) were compared for single 15-sec BH acquisitions. Acquisition parameters were: field of view (FOV) = 450 \( \times \) 450 mm, resolution \( s_v = 2 \times 2 \) mm, slice thickness \( s_D = 20 \) mm, echo time (TE) = 0.38 msec, coronal slice orientation, number of slices \( n_s = 3 \) (anterior, middle, posterior), tiny golden angle (\( \phi_B = 23.62814^\circ \)), 6-fold oversampling yielding \( T_{ACQ} = 5 \) sec per slice. For BH\(_i\), the repetition time (TR) resulted as 1.83 msec, whereas for the interleaved acquisition, TR was 5.6 msec. For further investigation of the impact of the TR, a protocol with a TR of 10 msec and prolonged breath-hold duration of 24 sec was acquired. The excitation angle, FA, was adjusted according to the actual TR to FA = 3.5\(^\circ\) (BH\(_i\)), FA = 6\(^\circ\) (BH\(_I\)), and FA = 8\(^\circ\) (BH\(_{II}\)).\textsuperscript{30}

**2D UTE Free-Breathing Acquisition**

Free-breathing data were acquired continuously with the same geometrical settings, angular increment, FA, and TE as for the breath-hold protocols. Due to specific absorption rate (SAR) constraints, TR was increased to 2.3 msec. To ensure sufficient data in the inspiration and expiration phase after gating, 20-fold oversampling was used yielding an acquisition time of \( T_{ACQ} = 1.4 \) min per slice.

**Data Reconstruction**

All data were reconstructed with an in-house developed reconstruction framework, implemented in MatLab (MathWorks, Natick, MA). Radial data were resampled onto a Cartesian grid by convolution interpolation and images reconstructed by subsequent Fourier-transform. No regularization, filtering, or iterative reconstruction were performed. During resampling, eddy-current-induced distortions of the gradient waveforms were considered by a mono-exponential decay model.
Self-gating (SG) data for respiratory and cardiac motion were derived from the modulation of the center of k-space \( (k_0) \) amplitude (DC) and additionally from an image-based technique for the respiratory motion.\(^{11,18,19}\) Coils contributing considerably to the DC signal modulation were identified according the amplitude of the respiratory and cardiac spectral component.

In the image-based approach the respiratory phase was derived from low-resolution images, reconstructed applying a sliding window technique with a temporal resolution of 460 msec with about 50% temporal overlap between subsequent frames. From the time-series a navigator-like signal was derived from the lung–liver interface.\(^{11,18}\)

For both approaches, the SG signal was filtered with a bandpass filter between 0.1 and 0.5 Hz to derive the respiratory motion navigator\(^{12,18}\) and the DC signal was filtered between 0.6 and 1.4 Hz for the cardiac motion navigator.\(^{24,29}\) The respiratory gating signals were used to identify inspiration (20% bottom values) and expiration (20% top values) imaging data.

Images from all independent receive coils were combined by calculation of the sum-of-squares to avoid any impact of erroneous coil sensitivity pattern resulting from the very low SNR in the lungs.

**Data Analysis**

All data were analyzed blind by three independent reviewers (M.B.: radiologist >25 years clinical practice, V.R.: MR scientist >25 years MR experience, and S.M.B.: radiology resident >3 years clinical practice).

All data analyses were performed on magnitude data. To avoid the substantial impact of the noise floor to the low-SNR data analysis, the mean noise level \( SL_{\text{noise}} \) was derived from a background ROI located in a low-artifact region (identified by A.B.) and subtracted from the magnitude data before further analysis.

Qualitative analysis of the images was performed on a five-point Likert scale (1: poor, 5: very good) for general image quality (IQ), visibility of the lung parenchyma (PV), sharpness of the lung–liver interface (LLI) as a marker for the quality of respiratory motion,\(^{11,18,19}\) Coils contributing considerably to the DC signal were used to identify inspiration (20% bottom values) and expiration (20% top values) imaging data.

Lung perfusion was calculated as suggested by Kjorstad et al,\(^{35}\) Fischer et al,\(^{36}\) and Pracht et al\(^{37}\) as:

\[
f = \frac{SI_{\text{lung}}}{SI_{\text{blood}}} \cdot \frac{1}{2 \cdot T_{\text{exp}}}
\]

where \( SI_{\text{lung}} \) is the intensity of a complete blood-filled voxel, which was preferably taken from one of the big vessels like the aorta. \( T_{\text{exp}} \) results as the acquisition time \( T_{\text{ACQ}} \) divided by the number of heartbeats. The required actual heart rate was derived from the respective peak in the spectra of the DC signal.

**Results**

Eleven healthy volunteers (three female, eight male, five smokers) were enrolled. Informed written consent was obtained from each volunteer before imaging. The study was approved by the local Ethics Board of Ulm University, Germany. The MR protocol was completed in all volunteers. Both self-gating approaches yielded respiratory signals, which could be applied for reconstruction of images in expiration and inspiration (Fig. 1). Please note the observed difference in the respiratory amplitude \( \Delta r \) between the breath-hold...
(Δr = 5.6 cm) and self-gated approach (Δr = 1.8 cm) in the same volunteer.

**Qualitative Analysis**

Image quality, parenchyma visibility, and delineation of the lung–liver interface showed significantly higher values for the breath-hold approaches, with superior performance of the image-based self-gating in direct comparison to the DC approach. No severe signal intensity modulations were observed over the region of the lung.

For all approaches, the visibility of the parenchyma resulted in superior in expiration, and an increase of visibility from anterior to posterior was observed by all readers. Improved visibility of the parenchyma was observed for longer repetition times.

With the exception of IQ for BH11 and image homogeneity for BH11/2, highly significant (P < 0.01) interrater agreements between 50% and 82% were observed.

For details, please refer to Table 1.

**Quantitative Analysis**

Based on the qualitative analysis outcome, the DC self-gating approach for respiratory motion was excluded from the quantitative analysis.

Differences in the lung parenchyma normalized signal intensities between expiration and inspiration were observed with all tested sequences (Supplemental Table S1). Ventilation, proton fraction, and perfusion values could be derived from all volunteers.

**Signal-to-Noise Ratio (SNR)**

Quantitative assessment of the SNR confirmed the qualitative assessment of the lung parenchyma visibility. Prolongation of the repetition time (Fig. 2a) by interleaved multislice imaging significantly (P < 0.001) improved the SNR during expiration (EX) as well as inspiration (IN) of up to 37% (TR = 1.89 msec [BH1] vs. TR = 5.6 msec [BH11], same breath-hold length) and 60% (TR = 1.89 msec [BH1] vs. TR = 10 msec [BH12], prolonged breath-hold). Self-gating (SG) resulted in lower SNR than the interleaved multislice approaches (BH11/2), but superior SNR compared with sequential breath-hold acquisitions (BH3) (Table S2). In all cases a significant (P < 0.05) reduction of the SNR in inspiration and an increase of the SNR from anterior to posterior were observed (Fig. 2b, Table S2).

Comparison between the smoker and nonsmoker groups revealed a slight, but not yet significant (P = 0.2 [EX], P = 0.13 [IN]) increase of SNR in the smoker group.

**Proton Fraction**

A significant difference (P < 0.001) between expiration and inspiration was observed for the derived proton density values, fp, for all investigated techniques (Fig. 3). fp in expiration resulted in significantly higher than in inspiration and increased from anterior to posterior (Fig. 4). Even though still significant (P < 0.001), SG revealed less pronounced differences between inspiration and expiration. In expiration, no significant differences between the BH and SG approaches (P = 0.38 BH3/SG, P = 0.40 BH11/SG, and P = 0.33 BH12/SG) were observed (Fig. 3). Furthermore, no significant difference (P = 0.57 BH3/BH11, P = 0.40 BH3/BH11, and P = 0.15 BH11/BH12) differences were observed between the BH acquisitions performed with different TRs.

A significant (P < 0.05 in all cases) increase of fp was observed for smokers (Fig. 3).
Fractional Ventilation

FV maps could successfully be obtained from the analysis of the signal intensity changes between inspiration and expiration. A strong impact of the respiratory amplitude on the FV with only moderate ($R^2 = 0.47$, $P < 0.01$) correlation was observed (Fig. 5b). On average, the respiratory amplitude during the breath-hold was more than twice as large as during free-breathing, causing significantly reduced FVs with the free-breathing approach (Fig. 5a). The huge variability of the respiratory amplitude yielded a high standard deviation in the resulting FV values.

No significant differences ($P = 0.32$ BH$_S$, $P = 0.92$ BH$_{11}$, $P = 0.61$ BH$_{12}$, and $P = 0.86$ SG) were observed for the FV between the smoker and nonsmoker groups (Table S4), both of which contained volunteers with deep and shallow breathing.

Lung Perfusion

Analysis of the calculated perfusion values showed a correlation with the respiratory phase and the location in the lung ($R^2 = 0.45$; Table 2). During expiration a significantly ($P < 0.001$ in all cases) higher perfusion than in inspiration was observed, as well as a continuous increase from anterior to posterior. No significant differences were observed between

### Table 1. Perfusion Values (Mean ± SD mL/min/mL) for All Volunteers$^a$

|       | BH$_S$     | BH$_{11}$  | BH$_{12}$  | SG         | $P$-value |
|-------|------------|------------|------------|------------|-----------|
| Anterior EX | 2.54 ± 0.62 | 2.48 ± 0.82 | 2.49 ± 0.58 | 2.23 ± 0.40 | >0.05**   |
| Middle EX  | 2.70 ± 0.54 | 3.03 ± 0.84 | 2.68 ± 0.43 | 2.81 ± 1.17 | >0.05**   |
| Posterior EX| 4.39 ± 1.37 | 5.21 ± 1.32 | 4.89 ± 1.07 | 4.28 ± 1.45 | >0.05**   |
| Anterior IN | 1.75 ± 0.69 | 1.58 ± 0.64 | 1.67 ± 0.75 | 1.93 ± 0.30 | ***       |
| Middle IN  | 1.73 ± 0.48 | 1.78 ± 0.45 | 1.67 ± 0.39 | 2.42 ± 0.56 | ***       |
| Posterior IN| 3.01 ± 1.18 | 3.33 ± 1.32 | 3.25 ± 1.33 | 3.89 ± 1.49 | ***       |

$^a$Comparison were done between expiration/inspiration, the different sequences.

**Comparison between BH$_S$/BH$_{11}$, BH$_S$/BH$_{12}$, BH$_S$/SG, BH$_{11}$/BH$_{12}$, BH$_{11}$/SG, and BH$_{12}$/SG. In all cases there was no significance detectable.

***Comparison between BHs and SG in IN is significant. Not really comparable, caused by the different breathing amplitudes.
the smoker and nonsmoker groups ($P = 0.74$ BH$_5$, $P = 0.56$ BH$_{11}$, $P = 0.23$ BH$_{12}$, and $P = 0.06$ SG). Between the different approaches (BH and free-breathing) no significant difference was observed ($P = 0.16$ BH$_5$/SG, $P = 0.06$ BH$_{12}$/SG, $P = 0.15$ BH$_{12}$/SG, $P = 0.06$ BH$_5$/BH$_{11}$, $P = 0.38$ BH$_5$/BH$_{11}$, and $P = 0.18$ BH$_{11}$/BH$_{12}$; Table S5).

**Discussion**

This study has shown the feasibility of 2D UTE for lung imaging at 3T field strength. With single-breath-hold capabilities, the technique represents an efficient approach for the initial assessment of the lung parenchyma. In combination with self-gating, high-quality low-noise data of the parenchyma could be derived for multiple respiratory phases. In combination with tiny golden angle angular increments, low spatial resolution images could be reconstructed at high temporal resolution, thus providing the basis for image-based self-gating.

It has to be mentioned that there is no consensus yet regarding the optimal field strength for lung imaging.\(^1\,\text{4,38,39}\)

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**TABLE 2. Qualitative Analysis on a 5-Point Likert-Scale (1: Poor; 5: Very Good)**

|        | IQ          | W [%] | PV          | W [%] | LLI         | W [%] | HOM         | W [%] |
|--------|-------------|-------|-------------|-------|-------------|-------|-------------|-------|
| BH$_5$ | 3.26 ± 0.68 | 61*** | 2.44 ± 0.82 | 67*** | 3.43 ± 0.66 | 68*** | 3.65 ± 0.48 | 50**  |
| BH$_{11}$ | 3.71 ± 0.58 | 38    | 2.58 ± 0.87 | 71*** | 3.78 ± 0.76 | 71*** | 3.71 ± 0.51 | 42    |
| BH$_{12}$ | 3.42 ± 0.62 | 71*** | 2.71 ± 0.91 | 64*** | 3.63 ± 0.79 | 70*** | 3.90 ± 0.30 | 16    |
| SG DC  | 2.28 ± 0.80 | 80*** | 1.85 ± 0.76 | 68*** | 3.01 ± 0.84 | 82*** | 3.55 ± 0.57 | 63*** |
| SG SW  | 2.67 ± 0.76 | 73*** | 2.03 ± 0.72 | 64*** | 3.18 ± 0.83 | 66*** | 3.45 ± 0.55 | 66*** |

IQ = image quality; PV = visibility of parenchyma; LLI = sharpness of lung–liver interface; HOM = homogeneity, W = level of agreement.

***$P < 0.001$. 
**$P < 0.01$. 

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**FIGURE 4:** Dependency of the proton fraction on the slice location. A clear increase in proton fraction can be appreciated from anterior to posterior located slices.

**FIGURE 5:** (a) Comparison of the fractional ventilation for breath-hold (BH) and free-breathing (SG) for the investigated slices. (b) Correlation between the breathing amplitude and the fractional ventilation for the free-breathing approach ($R^2 = 0.47$).
Even though 3T in general yields more signal, it also generates more susceptibility artifacts within the lung and shorter $T_2^*$. For this reason, many groups prefer 1.5T over 3T. However, with the rapid high-bandwidth acquisition of UTE there are strong indications that 3T may be advantageous.2

DC self-gating experienced some limitations in the cases of huge respiratory amplitudes and an irregular breathing pattern, which could be solved with the image-based SG approach. The still remaining inferior image quality of the SG techniques is likely caused by the rather broad acceptance window required to ensure sufficient SNR. Prolonged data acquisition may be considered for further reduction of the acceptance windows and improvement in SNR. Further, the respiratory amplitude in the self-gating data was significantly lower by about 50% for self-gating. This causes a significant reduction of fractional ventilation values, which may indicate a lower sensitivity for ventilation impairments.

For data analysis (proton fraction, fractional ventilation, perfusion), reliable segmentation of the lung and registration between the different respiratory stages is required to avoid falsified results by partial volume effects or blood vessels and comparison of nonmatching lung parenchyma.24,29

Data quality was sufficient for deriving fractional ventilation and proton fraction from the breath-hold as well as the free-breathing approach. Lung perfusion could also be derived from all acquisitions based on the DC self-gating. The rather short breath-hold times are feasible for clinical evaluation with cooperating patients.14 For severely impaired patients the free-breathing approach might provide an alternative.

Increasing proton density values from anterior to posterior are most likely introduced by water redistribution in the lungs and have been reported earlier.14

The different breathing amplitudes in the breath-hold images and free-breathing caused large differences in the fractional ventilation maps. As each volunteer breathed differently, a large standard deviation was observed in the fractional ventilation and standardization, and patient training may be required to provide more homogeneous results. The reproducibility of the technique is documented by the expiration values, which did not reveal significant differences among the investigated breath-hold and self-gating techniques, and differences in the derived function parameters can be explained by the different respiratory amplitudes yielding a rather large variation in the inspiration data.

The resulting value range of the perfusion was comparable to literature values.36,37 The correlation between the respiratory phase and perfusion had already been described in the literature and explained by a reduced blood volume per voxel and the relationship between pressure and flow of the pulmonary vasculature.37 Further, a similar increase of the perfusion values from anterior to posterior was reported. Where in general the quantification of the perfusion appeared feasible, the required reference blood signal may limit its applicability in the posterior section due to the lack of large vessels.

On average, the smoker group revealed higher $f_P$ during expiration, indicating initial diffuse lung infiltrates. The results are in agreement with recently reported CT data30 and indicate the potential of MRI for sensitive assessment of initial lung parenchymal changes without ionizing radiation. The lack of changes for the ventilation and perfusion may be explained by the still initial impact on the lung function not yet causing impaired gas exchange and the still large standard deviation of the inspiration data due to the varying respiratory amplitudes.

**Limitations**
The presented data only show the feasibility of the proposed technique. Final sensitivities need to be investigated in larger patient cohorts and self-gating data with longer data acquisition needs to be considered. Further, the 2D technique may suffer from intrinsic low spatial resolution into slice selection directions and further comparison with 3D techniques is required.

**Conclusion**
The 2D-tyUTE approach appears to be a promising technique for the evaluation of lung parenchyma changes. The possible combination with short breath-hold acquisitions renders it a potential tool for efficient quantification of lung parenchyma density and functional changes. In patients not able to perform breath-holding, self-gating can be easily realized due to the intrinsic properties of the acquisition trajectory. Compared to time-consuming 3D techniques, the limited spatial resolution into the slice selection direction may limit sensitivity and needs further clinical evaluation.

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**References**
1. Wild JM, Marshall H, Bock M, et al. MRI of the lung (1/3): Methods. Insights Imaging 2012;3:345-353.
2. Yu J, Xue Y, Song HK. Comparison of lung $T_2^*$ during free-breathing at 1.5 T and 3.0 T with ultrashort echo time imaging. Magn Reson Med 2017;66:248-254.
3. Thelmann RJ, Arai TJ, Samiee A, et al. Quantitative MRI measurement of lung density must account for the change in $T$ with lung inflation. J Magn Reson Imaging 2009;30:527-534.
4. Biederer J, Beer M, Hirsch W, et al. MRI of the lung (2/3). Why... when... how? Insights Imaging 2012;3:355-371.
5. Puderbach M, Hintze C, Ley S, Eichinger M, Kauczor H-U, Biederer J. MR imaging of the chest: A practical approach at 1.5 T. Eur J Radiol 2007;64:345-355.
6. Hatabu H, Alsop DC, Listerud J, Bonnet M, Gefter WB. $T_2^*$ and proton density measurement of normal human lung parenchyma using
submillisecond echo time gradient echo magnetic resonance imaging. Eur J Radiol 1999;29:245-252.

7. Bae K, Jeon KN, Hwang MJ, et al. Comparison of lung imaging using three-dimensional ultrashort echo time and zero echo time sequences: Preliminary study. Eur J Radiol 2019;29:2253-2262.

8. Johnson KM, Fain SB, Schiebler ML, Nagle S. Optimized 3D ultrashort echo time pulmonary MRI. Magn Reson Med 2013;70:1241-1250.

9. Zhu X, Chan M, Lustig M, Johnson KM, Larson PE. Iterative motion compensation reconstruction ultra-short TE (iMoCo UTE) for high-resolution free-breathing pulmonary MRI. Magn Reson Med 2020;83:1208-1221.

10. Mendes Pereira L, Wech T, Weng AM, et al. UTE-SENCEFUL: First results for 3D high-resolution lung ventilation imaging. Magn Reson Med 2019;81:2464-2473.

11. Tibiletti M, Paul J, Bianchi A, et al. Multistage three-dimensional UTE lung imaging by image-based self-gating. Magn Reson Med 2016;75:1324-1332.

12. Tibiletti M, Kjørstad A, Bianchi A, Schad LR, Stiller D, Rasche V. Multistage self-gated lung imaging in small rodents. Magn Reson Med 2016;75:2484-2485.

13. Ma W, Sheikh K, Svenningsen S, et al. Ultra-short echo-time pulmonary MRI: Evaluation and reproducibility in COPD subjects with and without bronchiectasis. J Magn Reson Imaging 2015;41:1465-1474.

14. Lederlin M, Crémillieux Y. Three-dimensional assessment of lung tissue density using a clinical ultrashort echo time at 3 Tesla: A feasibility study in healthy subjects. J Magn Reson Imaging 2018;48:839-847.

15. Weiger M, Wu M, Wurnig MC, et al. Rapid and robust pulmonary proton ZTE imaging in the mouse. NMR Biomed 2014;27:1129-1134.

16. Takizawa M, Hanada H, Oka K, Takahashi T, Yamamoto E, Fuji M. A robust ultrashort TE (UTE) imaging method with corrected k-space trajectory by using parametric multiple function model of gradient waveform. IEEE Trans Med Imaging 2012;32:306-316.

17. Glover GH, Pauly JM. Projection reconstruction techniques for reduction of motion effects in MRI. Magn Reson Med 1992;28:275-289.

18. Paul J, Divjakovic E, Wundrak S, et al. High-resolution respiratory self-gated golden angle cardiac MRI: Comparison of self-gating methods in combination with k-t SPARSE SENSE. Magn Reson Med 2015;73:292-298.

19. Weick S, Breuer FA, Ethes P, et al. DC-gated high resolution three-dimensional lung imaging during free-breathing. J Magn Reson Imaging 2013;37:727-732.

20. Doumes G, Yaabek J, Benhassen W, et al. 3D ultrashort echo time MRI of the lung using stack-of-spirals and spherical k-space coverages: Evaluation in healthy volunteers and parenchymal diseases. J Magn Reson Imaging 2018;48:1489-1497.

21. Thickman D, Kressel HY, Axel L. Demonstration of pulmonary embolism by magnetic resonance imaging. Am J Roentgenol 1984;142:921-922.

22. Noll DC, Pauly JM, Meyer CH, Nishimura DG, Macovskj A. Deblurring for non-2D Fourier transform magnetic resonance imaging. Magn Reson Med 1992;25:319-333.

23. Velthoen S, Weng AM, Knapp J, et al. Self-gated non-contrast-enhanced functional lung MR imaging for quantitative ventilation assessment in patients with cystic fibrosis. Radiology 2016;283:242-251.

24. Bauman G, Puderbach M, Deimling M, et al. Non-contrast-enhanced perfusion and ventilation assessment of the human lung by means of Fourier decomposition in proton MRI. Magn Reson Med 2009;62:656-664.

25. Kaufman H-U, Ebert M, Kreitner K-F, et al. Helium-3-MRT of the lung: Ventilation—first clinical applications. RoFo-Fortschritte auf dem Gebiet der Röntgendiagnostik und der bildgebenden Verfahren, Vol 166. Stuttgart, New York: Georg Thieme; 1997. p 192-198.

26. Woodhouse N, Wild JM, Paley MN, et al. Combined helium-3/proton magnetic resonance imaging measurement of ventilated lung volumes in smokers compared to never-smokers. J Magn Reson Imaging 2005;21:365-369.

27. Löffler R, Müller CJ, Peller M, et al. Optimization and evaluation of the signal intensity change in multislice oxygen-enhanced MR lung imaging. Magn Reson Med 2000;43:860-866.

28. Naish JH, Parker GJ, Beatty PC, et al. Improved quantitative dynamic regional oxygen-enhanced pulmonary imaging using image registration. Magn Reson Med 2005;54:464-469.

29. Fischer A, Weick S, Ritter CO, et al. Self-gated non-contrast-enhanced functional lung imaging (SENCEFUL) using a quasi-random fast low-angle shot (FLASH) sequence and proton MRI. NMR Biomed 2014;27:907-917.

30. Johnson G, Wadghiri YZ, Tumbull DH. 2D multislice and 3D MRI sequences are often equally sensitive. Magn Reson Med 1999;41:824-828.

31. Chan TF, Vese LA. Active contours without edges. IEEE Trans Image Process 2001;10:266-277.

32. Rasche V, Binner L, Cavagna F, et al. Whole-heart coronary vein imaging: A comparison between non-contrast-agent-and contrast-agent-enhanced visualization of the coronary venous system. Magn Reson Med 2007;57:1019-1026.

33. Zapke M, Topf H-G, Zenker M, et al. Magnetic resonance lung function—a breakthrough for lung imaging and functional assessment? A phantom study and clinical trial. Respir Res 2006;7:106.

34. Myronenko A. MIRT — Medical image registration toolbox for Matlab. 2018. https://sites.google.com/site/myronenko/research/mirt

35. Kjørstad A, Corteville DM, Fischer A, et al. Quantitative lung perfusion evaluation using Fourier decomposition perfusion MRI. Magn Reson Med 2014;72:558-562.

36. Pracht ED, Arnold JF, Katas M, Flentje M, Jakob PM. Assessment of pulmonary perfusion in a single shot using SEEPAGE. J Magn Reson Imaging 2008;27:63-70.

37. Pracht ED, Fischer A, Arnold JF, Katas M, Flentje M, Jakob PM. Single-shot quantitative perfusion imaging of the human lung. Magn Reson Med 2006;56:1347-1351.

38. Biederer J, Mirsadraee S, Beer M, et al. MRI of the lung (3/3) — Current applications and future perspectives. Insights Imaging 2012;3:373-386.

39. Fink C, Puderbach M, Biederer J, et al. Lung MRI at 1.5 and 3 Tesla: Observer preference study and lesion contrast using five different pulse sequences. Invest Radiol 2007;42:377-383.

40. Karimi R, Tornling G, Forsslund H, et al. Lung density on high resolution computer tomography (HRCT) re-flame inflammation in smokers. Respir Res 2014;15:23.