Magnetic resonance-compatible-spirometry: principle, technical evaluation and application

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ABSTRACT: The aim of this study was to assess the feasibility and accuracy of a novel magnetic resonance-compatible (MRc)-spirometer. The influence of body posture, magnetic resonance (MR)-setting and image acquisition on lung function was evaluated. Dynamic MR imaging (dMRI) was compared with simultaneously measured lung function.

The development of the MRc-spirometer was based on a commercial spirometer and evaluated by flow-generator measurements and forced expiratory manoeuvres in 34 healthy nonsmokers (17 females and 17 males, mean age 32.9 yrs). Mean differences between forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC) were calculated and a sample paired t-test and Bland–Altman plots were generated. A total of 11 subjects underwent different subsequent MRc-spirometric measurements to assess the influence of the components of the MR system on lung function.

The mean (95% confidence interval) difference of FEV₁ and FVC between the two systems was 0.004 (–0.04–0.04) L and 0.018 (–0.05–0.09) L, respectively. In the subgroup analysis, an influence of the MR-system on FEV₁ was found. FEV₁ correlated well with the dMRI measurement of the apico-diaphragmatic distance-change after the first second of forced expiration ($r=0.72$).

In conclusion, magnetic resonance-compatible-spirometry is feasible, reliable and safe. The magnetic resonance-setting only has a small influence on simultaneously measured forced expiratory volume in one second. Dynamic magnetic resonance imaging measurements correlate well with simultaneously acquired lung function parameters.

KEYWORDS: Body posture, dynamic magnetic resonance imaging, lung, lung function tests, magnetic resonance-compatible-spirometry, pulmonary mechanics

Lung function parameters represent an essential tool in diagnosis and management of airway disease. However, global parameters such as forced expiratory volume in one second (FEV₁) and vital capacity are unable to show regional pulmonary function impairment. Early lung disease is characterised by an inhomogeneous regional involvement. Thus, a modality to assess regional lung function impairment could be of major clinical value, in particular for the evaluation of response to local treatment, *e.g.* in patients with cystic fibrosis (CF), severe chronic obstructive pulmonary disease (COPD) and emphysema, after single lung transplantation or radiotherapy for lung cancer.

Dynamic magnetic resonance imaging (dMRI) has been proven to be a reliable tool for visualisation and evaluation of local chest wall movement and

respiratory mechanics in healthy volunteers [1–3] and patients with lung cancer [4].

The introduction of the electrocardiogram as a trigger signal made cardiac magnetic resonance imaging (MRI) possible, allowing for image acquisition at defined time-points of the cardiac cycle. Furthermore, it allowed for images of the lung without cardiac pulsation artefacts. For respiration, a similar signal is the movement of the diaphragm, which is already used for respiratory triggering [5]. However, volume is a more precise trigger signal allowing for image acquisition at defined time-points of the respiratory cycle. Therefore, a parallel examination with spirometry is desirable [6], and an MR-compatible (MRc)-spirometer integrating lung function with simultaneous image acquisition could be highly appreciated.

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Until now this problem has been addressed in various ways. Hoses of different sizes have been used to connect the patient's mouth with the spirometer [1, 7] producing a substantial increase in dead space. In a recent study [8], a small, commercially available Fleisch-type pneumotachograph (2.2×3 cm) was tested for magnetic resonance (MR)-compatibility and used for airflow and volume monitoring during oxygen administration. However, the high frequency emissions and magnetic field of the MR scanner might interfere with the electronic components of the pneumotachograph.

It is known that body posture influences lung function parameters [9, 10]. The influence of the MR-setting on simultaneously acquired lung function can be manifold: supine position; a phased array coil on the chest; and limited space within the magnet bore. These effects must be known before functional MRI can be used to accurately assess and monitor disease progression and therapy response quantitatively, e.g. in COPD or CF.

The purpose of this prospective study was three-fold: 1) to assess the feasibility of a novel MRc-spirometer; 2) to assess the influence of different body positions prior to and during the acquisition of dMRI on lung function; and 3) to correlate dMRI for visualisation of breathing mechanics with simultaneously acquired lung function parameters.

MATERIAL AND METHODS

Characterisation of the MRc-spirometer

An IOS MasterScreen-System (VIASYS Healthcare, Höchberg, Germany) was made MR-compatible for simultaneous data acquisition from MR imaging and spirometry as follows. The Lilly pneumotachograph (VIASYS Healthcare, Höchberg, Germany) of the original system consists of a very fine mesh screen of a defined and precise resistance, covered by a siphon shaped nonmetallic body, adapted with a sealing ring. The pressure difference between both sides of the screen resistor is transduced *via* two small silicon tubes to a differential pressure sensor, followed by amplification of the signal and analogue-to-digital conversion. The resulting flow channel is finally integrated to provide the volume. Previously, silicon tubes of 0.5 m length were used to transmit the pressure from the pneumotachograph to the pressure sensor. Currently, however, devices, including that used for conventional spirometry in the current study, integrate all hardware for pressure detection, amplification, signal conversion and volume integration in a handpiece which is directly connected to the pneumotachograph. Thus, this handpiece is not MR-compatible.

MRc-spirometer

For MR-compatibility, all ferromagnetic components were replaced by nonmagnetic components and the pressure transmission tubes were lengthened. Two 7-m silicon tubes (Rauclair®-E, RAU-PVC 8006, internal diameter 3 mm, gauge 1.5 mm; REHAN AG and Co, Schlauchtechnik, Rehau, Germany) were conducted through a wave guide into the scanner room. Thus, the pneumotachograph can be used in the Radio frequency (RF)-cabin, while the original handpiece, incorporating all electronic components together with the rest of the system, is placed outside (fig. 1a). For better

FIGURE 1. Principle and technical set-up for magnetic resonance-compatible (MRc)-spirometry. a) Elongation of the pressure transmission tubes by two 7-m long silicon tubes (Rauclair®-E; RAU-PVC 8006, internal diameter 3 mm, gauge 1.5 mm) conducted through a wave guide into the scanner room. Thus the pneumotachograph can be used in the MR-scanner and the original VIASYS Healthcare handpiece (Höchberg, Germany), together with the rest of the system, is placed outside the scanner cabin. b) Supine positioning of a volunteer on the couch of the MR-scanner performing MRc-spirometry with coils placed in scanning position. RF: radiofrequency; PC: personal computer.

handling and loss-free pressure difference transmission the pneumotachograph was connected to a second handpiece housing with all electronic parts removed (fig. 1b).

Technical evaluation

A flow generator was used for comparison of the two systems. Standardised American Thoracic Society (ATS) curves 1, 2 and 15 were generated and the deviation of forced vital capacity (FVC) and peak expiratory flow (PEF) were calculated from standard values.

Flow-volume calibration of the pneumotachograph with and without silicon tubes was performed with a 3 L calibration syringe before a specific measurement sequence. In case of deviations of $>2\%$ from the calibrating volume, pressure tightness was controlled and the entire procedure repeated. For linearity checks the 3 L syringe volume was applied at low, mid-range and high flow.

MR compatibility test

The metallic screen of the pneumotachograph was exposed to the static magnetic field of an actively shielded clinical 1.5 T MR system (Magnetom Symphony, Siemens, Erlangen, Germany). Measurements were performed with the screen normal and parallel to the B₀ field axis. RF-induced heating was measured with a balanced gradient echo pulse sequence with true fast imaging with steady-state free precession (trueFISP, repetition time (TR)=3.8 ms, flip angle $\alpha=70^\circ$) over 20 min. This sequence maximises the RF energy deposition (time averaged RF power: 136 W). Temperatures were measured with a fiberoptic, MR-compatible thermometer (Luxtron 3100, St. Clara, CA, USA).

Experimental design

Subjects

The current study was approved by the local ethics committee (University of Heidelberg, Heidelberg, Germany) and conducted according to the guidelines of the institutional review board (DFKZ). Written informed consent was obtained from all volunteers before MR examination.

In total, 34 healthy nonsmokers (17 female and 17 male; mean age 32.9 yrs, median (range) 30 (20–57) yrs) without pulmonary symptoms or contraindications to MRI were recruited for pulmonary function testing using the conventional spirometer and the MRc-spirometer in a supine position. In 32 subjects, additional pulmonary function testing was performed in an upright, sitting position with the conventional spirometer according to the ATS/European Respiratory Society (ERS) guidelines [11].

A subgroup of 11 subjects (six female, five male; mean age 32.2 yrs, median (range) 25 (24–57) yrs) performed additional MRc-spirometry to assess of the influence of various MR-settings on lung function parameters.

Comparison of instruments

All subjects performed spirometry in a supine position with both the conventional spirometer (“supine conventional”) and the MRc-spirometer (“MRc-spirometry”) with nose clips in place. A group of 23 subjects began with supine conventional followed by MRc-spirometry, while 11 subjects started with MRc-spirometry. According to the ATS/ERS guidelines [11], each subject performed three technically acceptable forced expiratory manoeuvres continuously instructed by an experienced operator (M. Eichinger, board-certified pneumologist). Acceptable repeatability was within a range of 5% deviation between measurements. FEV₁ and FVC, reported at body temperature, ambient pressure, saturated with water vapour, were used as parameters for comparison of the two systems. The measurement with the highest sum of FEV₁ and FVC was considered for statistical analysis.

Effects of MR-setting

The subgroup of 11 subjects performed the following additional MRc-spirometry, each within a 2-min interval, in order to assess the effect of differing MR settings on spirometry (fig. 2). 1) “Coils”: MRc-spirometry performed with the subject supine on the couch outside the scanner and the coils placed in scanning position. 2) “Scanner”: MRc-spirometry performed with the subject supine within the bore of the scanner with

coils placed. 3) MRc-spirometry performed with the subject supine in the scanner during dMRI, denoted “dMRI coronal”, “sagittal right”, “sagittal left”, “trachea” and “diaphragm” according to the plane and slice position of image acquisition. To analyse the influence of the MR-setting on lung function, the differences between FEV₁ and FVC measured “supine” and with several sequential MRc-spirometric procedures were calculated.

MRI

A 1.5 T whole body MR-system (Magnetom Symphony) was used for image acquisition. A two-dimensional fast, low-angle, shot-pulse sequence with the following parameters was used: TR/echo time/ α /slice thickness: 2.47 ms/1.03 ms/ 5° /15 mm, parallel acquisition factor 2, temporal resolution 10 images·s⁻¹, 40 s time acquisition and a 400 mm field of view. Images were acquired in coronal (angulated from peak apex to peak diaphragmatic point), sagittal right, sagittal left and transverse (two levels) planes. The volunteers performed forced expiratory manoeuvres during the acquisition of the images with simultaneous registration of MRc-spirometry.

Image analysis

The following lung diameter measurements were taken in the coronal plane using previously published methods [2]. 1) Maximum apico-diaphragmatic diameter (a_1) at maximum inspiration. 2) Apico-diaphragmatic diameter after the first second of the forced expiratory manoeuvre (a_2). 3) Apico-diaphragmatic diameter at end expiration (a_3).

The three diameters were measured for each hemithorax and expressed as the mean value of both hemithoraces. The changes in apico-diaphragmatic length after the first second of the forced expiratory manoeuvre (a ; $a=a_1-a_2$) and at end expiration (A ; $A=a_1-a_3$) were calculated (fig. 3). Finally, the relative length change during forced expiration (T_a) was calculated ($T_a=a/A \times 100$).

FIGURE 2. Experimental flowchart. MRc: magnetic resonance (MR) compatible; dMRI: dynamic magnetic resonance imaging; R: right; L: left. The numbers of subjects performing the procedures are shown in brackets.

FIGURE 3. Image evaluation in the coronal plane. Regional distance measurements at maximal inspiration (a_1), after the first second of forced expiration (a_2) and at end expiration (a_3) for both hemithoraces expressed as mean values. The changes of the apico-diaphragmatic diameter after the first second of the forced expiratory manoeuvre ($a=a_1-a_2$), at end expiration ($A=a_1-a_3$), and the relative distance change after the first second ($T_a=a/A \times 100$) were calculated. Representative images are shown. r: right; l: left.

Statistical methods

Statistical significance was assumed at $p < 0.05$. For assessment of accuracy and reproducibility of MRc-spirometry, mean differences in FEV1 (Δ FEV1) and FVC (Δ FVC) and their respective 95% confidence intervals (CI) were calculated. The one-sample paired t-test was used to test whether the difference was different from zero. Upper and lower limits of agreement [12] and their respective 95% CI between the two systems [13] were derived for FEV1 and FVC, and Bland-Altman plots were generated.

Pearson correlation coefficients were calculated for the correlations between the maximum apico-diaphragmatic diameter (a_1) and the corresponding FVC; the apico-diaphragmatic diameter changes (a , A) with FEV1 and FVC, respectively, as well as the relative diameter change in the first second during forced expiration (T_a) and the relative FEV1 change.

RESULTS

All volunteers completed the forced expiratory manoeuvres with conventional and MRc-spirometry outside and inside the MR scanner as well as during image acquisition. The subjects did not report that the conditions necessary for MR-acquisition restricted or otherwise interfered with the required spirometric manoeuvres.

MRc-spirometer

Technical evaluation

Using standardised ATS curves, the deviation from standard values for FVC was 0.03 L (0.5%) and $0.2 \text{ L} \cdot \text{s}^{-1}$ (1.8%) for PEF. The MRc-spirometer allowed for on-site acquisition of flow by pressure transmission *via* the 7-m long silicon tubes without changes in the pattern of the recorded flow and volume signals. Furthermore, it provided a galvanic isolation between the pneumotachograph and the electronic components next to the pressure transducer. Depending on the length of the tubes, the pressure signal is detected with a time delay of 20 ms at most, measured by sound propagation velocity.

MR compatibility test

No attractive forces were observed when attaching the screen to a thread and positioning it close to the bore entry, where forces acting on paramagnetic objects are expected to be highest. In conventional gradient and spin-echo pulse sequences no image artefacts extending $>5 \text{ cm}$ over the screen were seen. Over the course of the heating experiment no measurable temperature change was observed ($\Delta T < 1 \text{ K}$).

Comparison of instruments

The mean difference between FEV1 “supine conventional” and “MRc-spirometry” was 0.004 L (-0.04 – 0.04) L and non significant. The upper and lower limits of agreement were 0.258 (0.213–0.304) L and -0.250 (-0.295 – -0.204) L, respectively (fig. 4a). The majority of measurements ranged $\pm 200 \text{ mL}$ relative to baseline.

For FVC, the mean difference between supine conventional- and MRc-spirometry methods was 0.018 (-0.05 – 0.09) L and non significant. The upper and lower limits of agreement were 0.438 (0.363–0.513) L and -0.402 (-0.476 – -0.327) L, respectively (fig. 4b); the narrow 95% CIs confirming good agreement between the two systems. The order of examination, *i.e.* whether conventional or MRc-spirometry was performed first, did not influence the results.

Comparison of spirometric parameters in upright sitting and supine positions

The mean (95% CI) difference between sitting and supine positions performed with conventional spirometry was 0.16 (0.1–0.22) L ($p < 0.0001$; fig. 5a) for FEV1 and 0.08 (-0.02 – 0.19) L for FVC (nonsignificant).

Effects of MR setting

The mean differences between FEV1 during forced expiratory manoeuvres during supine conventional spirometry, MRc-spirometry, coils, scanner and dMRI positions were between -0.05 and 0.08 L , (nonsignificant; table 1, fig. 5a). Individual FEV1 comparisons between supine conventional spirometry

FIGURE 4. Bland-Altman plots comparing a) forced expiratory volume in one second (FEV₁) and b) forced vital capacity (FVC) measured using supine conventional- and magnetic resonance compatible-spirometry. The differences of FEV₁ and FVC between the two systems are plotted against the mean of the two measurements. - - - -: mean of the difference and the upper and lower limits of agreement;: baseline.

and coils, scanner, dMRI coronal, sagittal right, sagittal left, trachea and diaphragm revealed a statistically significant difference ($p < 0.02$; fig. 5b).

The mean differences for FVC during the several subsequent forced expiratory manoeuvres were between -0.08 and 0.12 L, (nonsignificant; table 1, fig. 6). The individual comparisons of FVC between supine and sitting conventional spirometry and also between the several MRc-spirometric procedures did not show any significant differences.

Qualitative reproducibility of lung function was well illustrated in the flow-volume loops acquired during the different manoeuvres (fig. 7).

Correlation between lung function and dMRI

Good correlations were found for a_1 and FVC ($r = 0.75$) as well as "a" and FEV₁ ($r = 0.72$). There was a moderate correlation between A and FVC ($r = 0.58$). A good correlation was also found between T_a and the relative FEV₁ change ($r = 0.75$).

TABLE 1 Subgroup analysis of mean differences (Δ) in forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC)

Procedures	Δ FEV ₁ L	Δ FVC L
Subjects n	11	11
Sitting/supine conventional	0.259 (0.17–0.34) [#]	0.18 (-0.01–0.38)
Supine/MRc-spirometry	0.04 (-0.04–0.122)	0.006 (-0.125–0.138)
MRc-spirometry/coils	0.054 (-0.003–0.14)	0.036 (-0.08–0.161)
Coils/scanner	-0.001 (-0.04–0.04)	-0.017 (-0.102–0.06)
Scanner/dMRI coronal	0.045 (-0.04–0.135)	0.07 (-0.049–0.19)
Ccoronal/sagittal R	0.019 (-0.1–0.138)	0.06 (-0.11–0.24)
Sagittal R/sagittal L	0.035 (-0.03–0.1)	0.02 (-0.08–0.13)
Sagittal L/trachea	-0.054 (-0.21–0.104)	-0.09 (-0.29–0.09)
Trachea/diaphragm	0.089 (-0.107–0.29)	0.12 (-0.08–0.33)
Effect of MR setting		
Supine/coils	0.09 (0.01–0.177) [†]	0.04 (-0.06–0.15)
Supine/scanner	0.09 (0.01–0.172) [†]	0.02 (-0.1–0.15)
Supine/dMRI coronal	0.138 (0.07–0.2) [†]	0.09 (-0.01–0.21)
Supine/sagittal R	0.15 (0.01–0.3) [†]	0.16 (-0.09–0.41)
Supine/sagittal L	0.19 (0.05–0.33) [†]	0.18 (-0.02–0.39)
Supine/trachea	0.138 (0.03–0.24) [†]	0.08 (-0.05–0.23)
Supine/diaphragm	0.22 (0.04–0.4) [†]	0.21 (-0.02–0.45)
Image acquisition		
Scanner/sagittal R	0.06 (-0.1–0.23)	0.135 (-0.09–0.36)
Scanner/sagittal L	0.1 (-0.04–0.19)	0.16 (0.305–0.23)
Scanner/trachea	0.04 (-0.1–0.19)	0.06 (-0.09–0.22)
Scanner/diaphragm	0.13 (-0.04–0.31)	0.18 (-0.01–0.39)

Data are presented as mean (95% confidence interval). MRc: Magnetic resonance (MR)-compatible; dMRI: dynamic MR imaging; R: right; L: left.
[#]: $p < 0.0001$; [†]: $p < 0.02$.

DISCUSSION

There were three major findings of the current study. 1) MRc-spirometry is feasible, reliable and safe. 2) The supine position required by the MR-scanner, the coils and the sequences, *i.e.* the MR-setting, alters FEV₁ in comparison with standard measurements performed in a sitting position. 3) MRc-spirometry and simultaneously acquired MR-images show good correlation.

The MRc-spirometer is MR-compatible and technically equivalent to a conventional spirometer. The time lag due to the length of the tubes was estimated from the sound velocity at 28°C ($343 \text{ m} \cdot \text{s}^{-1}$) and the tube length (7 m) to ~ 20 ms. The size and pattern of the signal were correctly transmitted, thus the time delay was negligible.

MRc-spirometry showed good agreement for FEV₁ and FVC with conventional spirometry, demonstrating correct measurement for the novel system [13].

The present study confirms the influence of body posture on lung function with a significant decrease of FEV₁ in supine position [10] and a nonsignificant trend towards a decrease of FVC. These facts have to be considered when comparing results with the standard upright sitting position.

FIGURE 5. Mean forced expiratory volume in one second (FEV₁) differences between a) various conventional- and magnetic resonance-compatible (MRC)-spirometric procedures and b) supine conventional spirometry and differing conventional spirometry settings. Statistically significant differences were detected between supine conventional spirometry and the subsequent MRC-spirometric measurements. dMRI: dynamic magnetic resonance imaging; R: right; L: left. [#]: $p < 0.0001$; [†]: $p < 0.02$.

Two effects of the MR-setting can be highlighted: 1) FEV₁ and FVC did not change significantly during the various procedures, demonstrating that MRC-spirometry is a precise tool for assessment of lung function during MRI; and 2) The MRC-spirometric procedures revealed a flow limitation in healthy

subjects during the course of the study experiment when compared with supine conventional spirometry. There are multiple possible reasons for flow limitation, such as low compliance, large variability of FEV₁ in repeated measurements, reduced mobility or psychological effects in the narrow MR scanner. FEV₁ depends highly on compliance and most likely shows changes during the long course of the experiment, with a minimum of 30 forced expiratory manoeuvres performed at 2-min intervals. Air flow limitation during

FIGURE 6. Mean forced vital capacity (FVC) differences between several conventional- and magnetic resonance compatible (MRC)-spirometric procedures. No significant difference was found between FVC during the different MRC procedures. dMRI: dynamic magnetic resonance imaging; R: right; L: left.

FIGURE 7. Flow-volume loops during different forced expiratory manoeuvres demonstrating good quantitative reproducibility. The traces for expiration and inspiration are represented above and below zero, respectively. Blue: conventional supine spirometry; red: magnetic resonance-compatible-spirometry; green: coils; pink: scanner; yellow: dMRI coronal; black: reference, nominal values ± 2 sd.

repeated forced manoeuvres, as induced in asthmatic patients [14], is unlikely as only healthy nonsmokers were examined in the current study. Although a measurement of muscle strength was not performed, fatigue of respiratory muscles after repeated forced expiratory manoeuvres may have occurred [15].

MRI provides split (right/left) lung analysis. However, for correlation with lung function the regional information was condensed to a global evaluation. A good correlation between lung function and MRI-based measurements was demonstrated, and improvements and extensions of the technique are encouraged. Although a simultaneous measurement of lung function parameters and MRI was accomplished, length changes in two-dimensional are probably not representative of volume changes [2], while three-dimensional data of lung volumes are produced at the cost of lower temporal resolution, which might limit the measurements during forced expiration [16]. Technical improvements in spatial and temporal resolution are anticipated.

In addition, maximal inspiratory distances correlate best with the corresponding lung volumes, while distance changes show lower correlations. A time synchronisation between the scanner and MRc-spirometry may overcome this limitation.

The current study was performed in healthy and cooperative subjects. Since the accuracy and reproducibility of lung function tests depend on patient's compliance, further evaluation with patients in a clinical setting is warranted.

Simultaneous dMRI and MRc-spirometry paves the way for accurate assessment of regional functional impairment as dMRI can visualise and assess regional lung and diaphragmatic motion [2, 17, 18]. The need for regional assessment of the lung is not new and recent studies underline the inhomogeneity of the human lung even under physiological conditions [19]. Most pulmonary diseases develop in certain regions of the lung, sometimes with a typical predilection and heterogeneous distribution pattern. An example is CF, where a discrepancy is found between lung function, which remains preserved over a long period [20, 21], while computed tomography already indicates obvious parenchymal damage. Assessment of regional inhomogeneities is of major interest in this patient group potentially allowing for a targeted and thus more effective therapy.

With the technique presented, the first step towards a complementary spirometric method integrating spirometry and MRI has been accomplished. The next step might be volume gated image acquisition, not only to provide better image quality without breathing artifacts, but also exact timing of image acquisition at functionally important time points of the flow-volume loop and breathing cycle. Regional functional assessment is the third step consisting in dedicated post-processing methods of such data sets.

In conclusion, magnetic resonance-compatible-spirometry is feasible, reliable and safe. The magnetic resonance setting has an influence on simultaneously acquired lung function parameters like forced expiratory volume in one second. Magnetic resonance-compatible-spirometry and simultaneously acquired dynamic magnetic resonance imaging show a good correlation and may become a promising complementary tool for regional assessment of lung disease.

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