Influence of respiration-induced signal variations on the quantification of pulmonary perfusion parameters in free-breathing MRI

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Introduction

Background: Recently, the feasibility of **free-breathing dynamic contrast-enhanced (DCE) MRI** for pixelwise quantification **of lung perfusion** has been shown [1], and even a better reproducibility compared to breath-hold DCE-MRI could be demonstrated. [2,3]

Purpose: The purpose of the present study was to analyze the **influence of breathing-induced signal variations** of the lung parenchyma **on the accuracy and precision of calculated perfusion parameters**.

Methods

MR imaging: We analyzed breath-hold and free-breathing lung DCE-MRI data sets of 5 healthy male volunteers (acquisitions of 40 3D volumes with 128 × 128 × 36 matrix and a temporal resolution of 1.3 s/volume using a fast view-sharing gradient echo sequence, flip angle: 15°; contrast agent: 0.1 mmol/kg bodyweight gadobutrol) to determine typical signal intensities of lung tissue pixels, noise levels, signal amplitudes of breathing-induced density variations, respiratory frequencies, and to define a typical arterial input function (AIF).

Simulation: Based on these experimental data, we simulated signal curves in lung tissue using a 1-compartment model; the (true) perfusion parameters were set to a plasma flow of 200 mL/100 mL/min and a plasma volume of 10 mL/100 mL according to the results presented in [1]. Breathing-related signal variations were derived from a sinusoidal lung-volume variation: $V(t) = V_0 + \frac{1}{2} V_T \sin \omega t$ yielding

$$S(t) \propto \frac{1}{V(t)} \approx S_0(t) \cdot (1 - \frac{V_T}{2V_0} \sin \omega t).$$

Complex image noise was added followed by magnitude calculation and signal discretization to integer values. Perfusion parameters were estimated from these tissue curves by fitting the data to a 1-compartment model; simulations were repeated 50,000 times.

Evaluation: Systematic and statistical deviations from the initial "true" perfusion parameters were assessed as median value and the range from 16th to 84th percentile (normalized to the true value) over all 50,000 simulations.

Results

In vivo measurements: The typical signal of lung tissue in our DCE-MRI data sets was about 4 a. u. (pre-contrast), the maximum signal of the AIF in the pulmonary artery about 120 a. u., and the noise level about 0.5 . . . 1 a. u., yielding a contrast-to-noise ratio (CNR) of about 100 . . . 200 relative to the maximum AIF signal (higher signals, limiting the dynamic range, were found in subcutaneous fat). Respiration periods ranged from 2.5 to 5 s/respiratory cycle; typical signal variations due to respiration were about twice as large as the noise level (2 a. u.).

Simulations: Examples of simulated data are shown in Fig. 1. The results of the perfusion-model fitting are summarized in Fig. 2: Without noise ("CNR: ∞"), the statistical variations show clearly the influence of respiration-induced signal variations. Generally, the effect increases for larger relative tidal volumes (color-coded in adjacent bars), and the estimated flow is also more sensitive to slow than to fast breathing.

In the presence of noise ("CNR: 200", "CNR: 100"), the influence of respiration becomes smaller and is relevant only for flow estimation at slow, relatively deep breathing.

The *systematic* deviations of the median over all examined parameter sets are very low and range between −0.44 % and +2.1 % for the plasma flow and between −1.0 % and +0.83 % for the plasma volume.

Discussion

Our results indicate that the influence of signal variations in the lung tissue due to respiratory proton-density changes is relatively low compared to the influence of image noise for realistic values of the CNR. Image noise alone accounts for statistical variations in the order of 10 % to 20 % for the plasma flow and of 6 % to 12 % for the plasma volume (cf. the separate blue reference bars in Fig. 2). Only at slow (7 s/respiratory cycle) and deep respiration, the further increase of the statistical variation is relevant.

The result can be explained by the model-fitting approach being rather insensitive to sinusoidal signal variations in the investigated frequency range, which increase the sum of squared residuals but – only to a much lower degree – influence the resulting model parameters.

Conclusions

The pixelwise quantitative evaluation of **free-breathing DCE-MRI of the lung is *not* very sensitive to respiration-induced periodic lung-volume changes** and subsequent MR signal variations. If possible, patients should be asked to breathe shallowly and not too slowly to further reduce the effect of breathing on estimated perfusion parameters.

References

[1] Maxien D et al. RoFo 2013; 185: 1175.
[2] Ingrisch M et al. Proc ISMRM 2013; 21: 591.
[3] Ingrisch M et al. Invest Radiol 2014 (in press, epub) (DOI: 10.1097/RLI.0000000000000020)

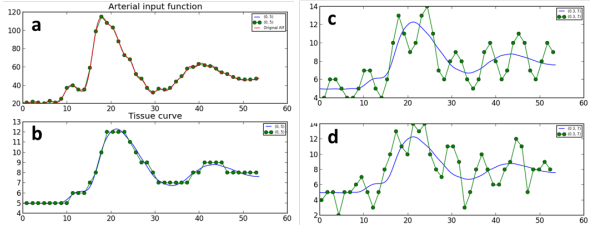

Fig. 1: (a) Representative arterial input function (AIF) determined from in vivo measurements; **(b)** simulated tissue curve **without** noise and breathing (for plasma flow: 200 mL/100 mL/min, plasma volume: 10 mL/100 mL) **(c)** tissue curve (and 1-compartment fit) **with** breathing, **(d)** tissue curve (and 1-compartment fit) **with** noise and breathing.

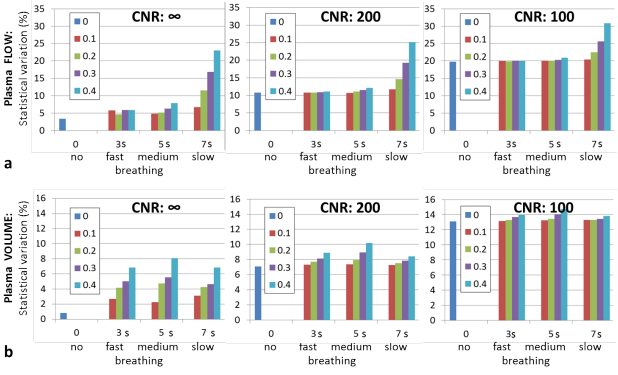

Fig. 2 Statistical variation (range from 16th to 84th percentile) of **(a)** estimated flow (top) and **(b)** volume (bottom) parameters for five different relative tidal volumes $V_T/2V_0$ (color-coded in adjacent bars from 0.1 to 0.4), 3 different respiratory rates (respiratory cycles of 3 s, 5 s, and 7 s), and 3 different CNRs (relative to maximum arterial signal of AIF). The separate blue bar on the left of each diagram is the reference value without breathing.