Feasibility of ^{13}C-MRI of the lung using $^{13}CO_2$ gas

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Introduction: Recently, sophisticated techniques for visualizing intrapulmonary gas using hyperpolarized ^{129}Xe [1] or ^{3}He [2, 3], or fluorinated gas compounds [4-6] have been developed. However, when compared with respiratory gases like N_2, O_2 and CO_2 all of theses MRI contrast gases differ in their physical and physiological properties. O_2 enhanced MRI [7] uses paramagnetic properties of oxygen to enhance relaxation of tissue but demonstrates a complex relation between ventilation and signal intensity.

A direct visualization of respiratory gases may be preferable. While nitrogen and oxygen have isotopes with spin ≠ 0 their gyromagnetic ratios are extremely low. Moreover, relaxation times of these gases are extremely short. Therefore, MRI of these two gases is difficult. ^{13}C, however, has spin ½ and a sufficiently high gyromagnetic ratio. It is a nucleus used in many spectroscopic NMR studies.

It was the aim of this study to test the feasibility of ^{13}C-MRI of the lung using isotopically enriched and thermally polarized $^{13}CO_2$ gas as a physiologic contrast gas.

Materials and Methods: MRI was performed at 1.5 T using a Siemens Magnetom Vision Experimental (50 mT/m, 160 mT/m/ms) whole-body MRI system equipped with non-proton imaging capabilities. A homebuilt Birdcage design resonator (8 leg, lowpass) with a length of 140 mm and an internal diameter of 80 mm was used for radiofrequency transmission and signal reception.

MRI was performed on phantoms containing 100 % isotopically enriched $^{13}CO_2$ (99 atom % ^{13}C, Westfalen AG, Münster, Germany). Moreover, the feasibility of ^{13}C-MRI of the lung using $^{13}CO_2$ was tested in three rats post mortem. For this purpose rats were tracheotomized and $^{13}CO_2$ was washed in by repeated application of the gas using a 20 mL syringe.

After adjustment of the MRI system to the resonance frequency of ^{13}C (15.98 MHz) a spoiled gradient-recalled echo pulse sequence (TE=0.5ms, bandwidth 2080 Hz/pixel, number of signal averages, NEX=150; imaging matrix, MA=64x64; field of view, FoV = 500 x 500 mm, no slice selection) was used for imaging. To determine the optimal repetition time TR, TR was varied between 5 ms and 100ms. To measure the T2* relaxation time in a next step, TE was varied between 0.5 ms and 15 ms (TR = 100ms). Optimization of the readout bandwidth was performed using pulse sequences with a bandwidth of 65 Hz/pixel (TE=11ms), 130 Hz/pixel (TE=5ms) and 260 Hz/pixel (TE=4ms). TR and NEX were set to 24ms and 75, respectively. The resulting scan time was 1:57 min in these measurements.

TrueFISP imaging was performed using a two-dimensional pulse sequence with TR/TE/NEX = 6.32ms/3.0ms/10 at MA=64x64 and FoV = 500 x 500 mm^2 (no slice selection). The total scan time for this pulse sequence was 4.1 sec.

Measurement of the intrapulmonary $^{13}CO_2$ distribution was performed using the bandwidth-optimized (130 Hz/pixel) gradient echo-pulse sequence with a total scan time of 53min.

Because of the limited spatial resolution the peak signal-to-noise ratio (pSNR) was calculated by measuring the peak signal intensity within the $^{13}CO_2$ containing object divided by the mean signal intensity of noise outside the phantom or lung.

Results: ^{13}C-MRI of isotopically enriched $^{13}CO_2$ proved feasible on phantoms as well as in rat lungs post mortem. The variation of TR demonstrated that an increase of the TR beyond 20 ms resulted in no significant signal increase (Fig. 1a). Therefore this TR was considered optimal in the course of this study. Variation of TE yielded a transverse relaxation time of $T_2^* = 6.57 \pm 0.26$ ms (R = 0.9976, c.f., Fig. 1b). Variation of the readout bandwidth resulted in pSNR values of 36.2, 36.2, and 27.2 at a bandwidth of 65 Hz/pixel, 130 Hz/pixel and 260 Hz/pixel, respectively. Because of the shorter TR achievable at 130Hz/pixel, this readout bandwidth was considered optimal for this study (Fig. 1c). Although the scan time of the TrueFISP pulse sequence was only 4.1 sec, a pSNR of 7 was obtained on axial slices on the phantom. Using the 130 Hz/pixel bandwidth spoiled gradient echo pulse sequence visualization of the intrapulmonary distribution of $^{13}CO_2$ in a rat lung was feasible (Fig. 1d).

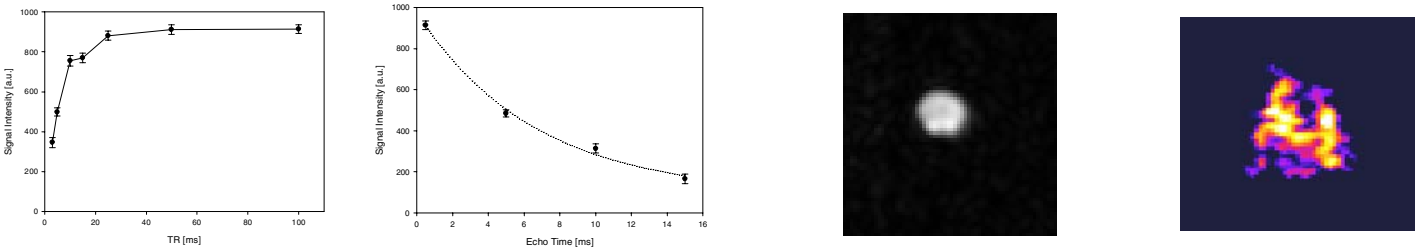

Fig. 1: *Variation of the ^{13}C signal intensity as a function of* ***a)*** *TR and* ***b)*** *TE. The solid line in b) is a nonlinear Marquardt fit assuming a monoexponential decay of the magnetization.* ***c)*** *Axial ^{13}C image of a phantom containing 100% $^{13}CO_2$ using a gradient echo pulse sequence with a readout bandwidth of 130 Hz/pixel. The pSNR is 36.2* ***d)*** *Coronal image of a rat lung post mortem. The pSNR is 6.2.*

Discussion: The results of this study demonstrate for the first time that MRI of intrapulmonary $^{13}CO_2$ is feasible with acceptable scan times. The T_2 relaxation time is long enough to acquire the MRI signal after excitation. Scan times are currently on the order of those required for ^{19}F MRI of fluorinated gas compunds in animals of the same size [5]. Experience with ^{19}F MRI has shown, however, that breath hold scan times can be achieved in larger objects such as pigs [6]. It may be speculated that this may become feasible in the future for ^{13}C-MRI of isotopically enriched $^{13}CO_2$ although physiologic effects introduced by the contrast gas need to be investigated before performing such studies *in vivo*.

In conclusion, ^{13}C-MRI of isotopically enriched $^{13}CO_2$ is feasible. This is the first time that a gas with physiologic and physical characteristics almost identical with respiratory gases is used for direct imaging of gas space. Future studies need to evaluate the potential of this new technology for assessment of lung physiology and pathophysiology.

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