Magnetic resonance imaging of lungs using fluorinated gas

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Abstract. Three different pulse sequences (UTE, RARE and FISP) were optimized for 19F-MRI. Coronal slices of respiratory system of laboratory animals (rats) were obtained in 1.5 mm increments and 3D reconstruction of respiratory system of laboratory animals was constructed. For this experiment the animals for 30 minutes breathed with a mixture of fluorinated gas perfluorocyclobutane C4F8 and oxygen in a volume ratio of 70% to 30% using artificial lungs ventilation machine. We showed the possibility to obtain 19F-MRI images of lungs, trachea and bronchi without using breath-holding methods. Such an approach can be especially important for patients with pulmonology diseases (COPD, fibrosis, asthma, etc.). Experiment with a flat wireless coil has shown the possibility of increasing of the intensity of the recorded 19F-NMR signal from the lungs.

1. Introduction

Magnetic resonance imaging (MRI) is a very important diagnostic tool for the human body studying. But MRI of lungs is challenging due to the low proton density and the multiple air-tissue interfaces which leads to fast decay of signal because of significant difference in magnetic susceptibility.

For a long time, specialists used radiography and computed tomography as the modern methods of obtaining anatomical images of lungs. But this methods don't enable comprehensive structural and functional imaging without ionizing radiation. There is an alternative method based on the use of hyperpolarized gases (129Xe, 3He), which allows to obtain highly informative images of lungs [1, 2]. This technique allows researchers to get both anatomical and functional information about lungs. But the method is not widely used in clinical practice due to the high cost and high labor-intensive research.

At the same time, there is a much simpler and not less effective technique, based on the lungs visualisation with MRI in fluorine-19 nuclei. It consists in obtaining images of lungs filled with fluorinated gas. Fluorine-19 has a magnetic moment similar to a proton and its sensitivity is 83% of the sensitivity of proton. The first images in this technique were obtained in 1982 using CF4 in excised rabbit lungs [3]. Then, after a long gap in 19F-MRI reports, breathing of C2F6 in rats was demonstrated [4]. The results of the study of human lungs using a mixture of SF6 and oxygen were published in 2008 for the first time [5]. The quality of such images is lower than the quality of images obtained using hyperpolarized gases. But this method has significant advantages - it is much cheaper and much easier to implement in clinical settings.

Fluorine nuclei are practically absent in living organisms. Therefore, images can be obtained without background signal by using fluorine-containing preparations. Perfluorocarbons (PFCs) are used as such preparations. They are chemically synthesized compounds in which fluorine atoms are bonded to carbon. PFCs are inert, non-toxic and they are not metabolized in human body. In this work,

perfluorocyclobutane (PFCB) C4F8 gas was used as a visualized fluorinated gas. This gas has a number of serious differences from the fluorinated gases studied to date. Its relaxation time T1 is short enough to use ultrashort pulse sequences, such as UTE, and long enough to use pulse sequences based on spin echo (T1~ 50 ms). It is also worth noting that PFCB molecule consists of 4 CF2 groups. It means that it has 8 magnetically equivalent fluorine atoms, which determine the intense singlet NMR spectrum. In addition, this gas is more lipophilic than other fluorinated gases and can be potential agent for assessing lung perfusion.

2. Materials and methods

This work was carried out in the Magnetic Tomography and Spectroscopy Laboratory of the Fundamental Medicine Faculty at Lomonosov Moscow State University on Bruker BioSpec 70/30 USR MRI scanner with a constant magnetic field of 7 T, intended for MRI studies of small laboratory animals.

Images were obtained using 1H / 19F volume receiving-transmitting radiofrequency coil with an inner diameter of 72 mm. Pre-shimming was performed on a phantom sample — a 25-ml sealed vial partially filled with liquid PFCB.

MRI was applied in in vivo studies with laboratory animals – intact mature rats. Rats were anaesthetized with chloral hydrate at a dosage of 300 mg / kg of weight. All experimental procedures with animals were carried out in accordance with Principles of Good Laboratory Practice.

3. Results

3.1. Comparisons of pulse sequences for obtaining high-quality images of rat lungs

First of all, it is necessary to determine which pulse sequences are best for obtaining images of the lungs in vivo. UTE, RARE, and FISP sequences were selected to compare. The UTE and FISP sequences are based on the gradient echo technique. However, UTE allows to set an extremely short TE, but not a very short TR, and FISP makes possible to set longer TE, but short TR. The RARE pulse sequence is based on the spin echo technique, and in some studies it can provide more information than other sequences.

Images were obtained in coronary projection for 10 seconds with the following scanning parameters: FOV=10×10 cm2, MTX=64×64. The TR repetition time for the UTE, RARE and FISP sequences was set to 10 ms, 40 ms, 2.7 ms, respectively. TE for the UTE, RARE and FISP sequences was set 68 μs, 4.86 ms, 1.35 ms respectively. For the RARE sequence, the RARE factor is 2. For UTE and FISP sequences, the deviation angle is 30° FA.

The result of the experiment is presented in figure 1.

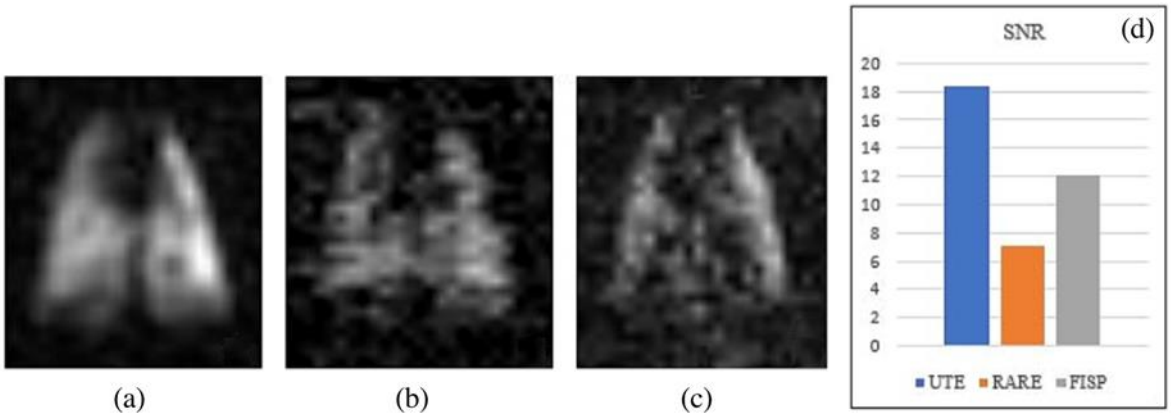

Figure 1. 19F-MRI images of the rat lung obtained using UTE (a), RARE (b) and FISP (c) pulse sequences; d - a diagram showing the SNR values on the resulting images.

The experiment shows that the image obtained using UTE sequence is much better than the image obtained using FISP sequence, judging by the signal-to-noise ratio (18.4 and 12.1, respectively). This is due to the fact that UTE allows to set shorter TE that is necessary, because the PFCB relaxation times are very short. Also the work of the FISP sequence was strongly affected by the heterogeneity of the field in the lungs.

However, pulse sequences, based on the gradient echo technique, do not give image detailing sufficient for carrying out a qualitative analysis of the obtained images. Probably this is due to the technology of receiving the echo signal. In the case of a gradient echo, the echo signal is obtained by applying a reverse polarity gradient, and in the case of a spin echo, it is obtained by using an additional 180° pulse. In the first case, the signal is highly sensitive to inhomogeneities of the magnetic field, and in the second case the inhomogeneity of the field has almost no effect on the quality of the MRI images obtained.

Despite the fact that RARE pulse sequence gives images with poorer quality than UTE and FISP, it is based on the spin echo technique, and although the signal-to-noise ratio for an image obtained using this sequence is the smallest (SNR = 7), RARE sequence still needs to be used for the reason that some studies are carried out using sequences based only on spin echo.

3.2. Study of the possibility of obtaining images from other parts of the respiratory system (trachea, bronchi)

Three-dimensional reconstruction of the respiratory system of rat was obtained using 3DTrueFISP pulse sequence. Scanning parameters for 19F-MRI were as follows: TR=2.6 ms, TE=1.3 ms, FOV=4.8×4.8×3 cm3, MTX=32×32×20, FA=30°, EXPT=28 min. The resulting image is shown in figure 2.

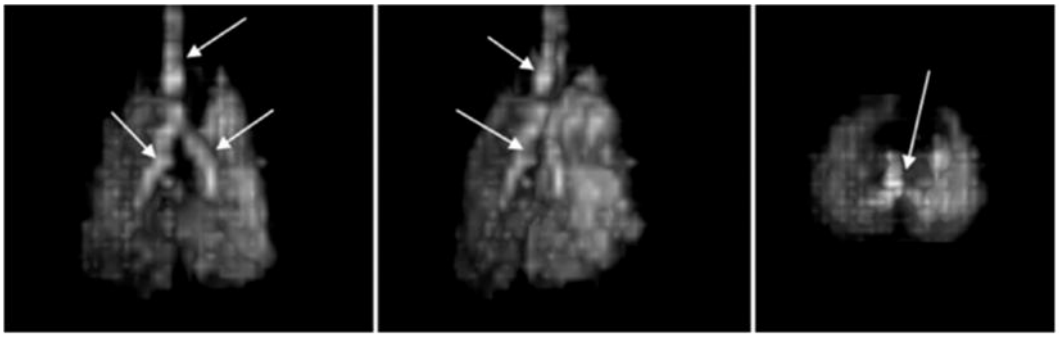

Figure 2. Three-dimensional reconstruction of rat lungs. Trachea and bronchi are marked by arrows.

The study showed that three-dimensional 19F-MRI of the respiratory system of laboratory rats allows to visualise not only the lungs, but also trachea and bronchi (indicated by arrows in figure 2).

This experiment showed that trachea and bronchi can be visualised only by using 3D scanning technique. 2D scanning techniques do not allow to receive images of the trachea and bronchi (figure 1). One of the possible reasons for this is the difference in data collection with 2D and 3D scanning techniques. To detect the gas flow, for example, in the trachea, it is necessary to obtain sections in the form of a stack in a plane perpendicular to the trachea itself, when registering images using 2D sequence. However, the presented images were obtained in such a way that the selection sections are parallel to the trachea, and 2D scanning technique became insensitive to the flow.

3.3. Comparison of ventilated lung volume with their anatomical image

In this study, images were obtained using 3DTrueFISP pulse sequence. Scanning parameters for 19F-MRI were as follows: TR=2.6 ms, TE=1.3 ms, FOV=4.8×4.8×3 cm3, MTX=32×32×20, FA=30°, EXPT=28 min. For classic 1H-MRI 2D Multi Slice Multi Echo (MSME) pulse sequence was used.

Images were obtained in coronary projection with the following scanning parameters: TR=550 ms, TE=11 ms, FOV=4.8×4.8 cm2, MTX=160×160, number of slices 20, slice thickness 1.5 mm, EXPT=12 min.

Figure 3 shows joint 1H- and 19F-MRI images of the rat respiratory system. For different slices, the signal-to-noise ratio on 19F-MRI images is on the order of 4–8. Respiratory synchronization was not used to obtain 19F-MRI images of the respiratory system. In general, it is logical to scan an animal for a certain period of time in order to prevent artifacts of chest movement. On the other hand, any delay leads to an increase in the total scan time. As can be seen in figure 3, there are no artifacts caused by movement due to the breathing of the experimental animal.

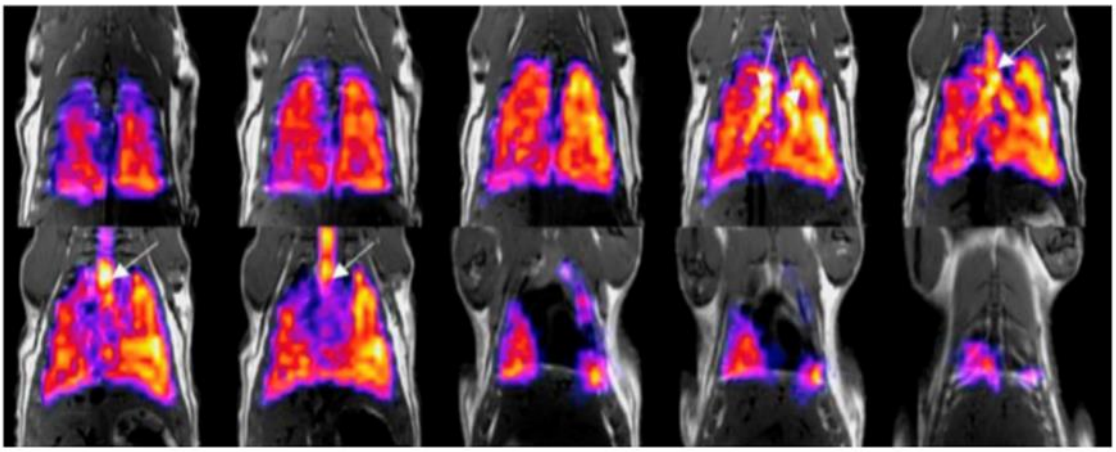

Figure 3. Joint 1H- and 19F-MRI images of the rat respiratory system. Trachea and bronchi are marked by arrows.

This images show both the anatomy of the lungs (1H-MRI images) and their ventilation (19F-MRI images). This rat is absolutely healthy and no violations of the ventilation of the lungs in the images have been identified. Also since in this case 3D scanning technique was used, other elements of the rat respiratory system (trachea and bronchi) were visualised.

3.4. Amplifying of the recorded NMR signal from the respiratory system using a flat wireless coil

Previous experiments have shown that visualization of PFCB in the lungs is a realizable task for magnetic resonance imaging. However, this technique is less sensitive than, for example, hyperpolarized MRI. Therefore, the question of how to increase the sensitivity of the 19F-MRI method requires a solution. This paper proposes a method by which the signal obtained by imaging the lungs using 19F-MRI can be increased. It is based on the use of an inductively coupled coil system — resonator and wireless coil. A wireless coil is an oscillating circuit having its own resonant frequency and acting as an antenna in MRI studies. The operation of such coils is based on the phenomenon of mutual induction. Surface wireless coils allow to locally increase the magnetic field, and therefore to increase the signal. In magnetic resonance imaging, the signal recorded by the tomograph is proportional to the root of the number of accumulations. Therefore, if the coil allows to increase the recorded signal by 2 times, then the number of accumulations (and hence the scanning time) can be decreased by 4 times to get an image of the same quality.

In the experiment, the coil was located on the chest of the rat, fixed, then images were obtained. Images were obtained using UTE pulse sequence, the main scanning parameters were as follows: TR=20 ms, TE=0.4 ms, FOV=10x10 cm2, MTX=64x64, FA=40°, EXPT=1 min. The result is shown in figure 4.

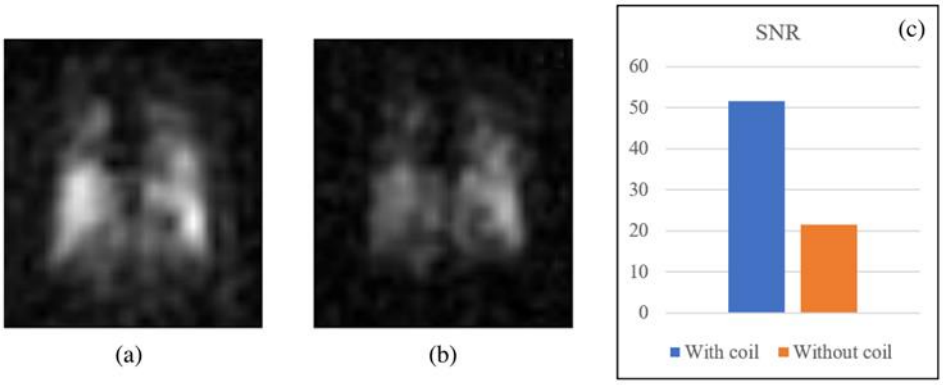

Figure 4. 19F-MRI images of a rat lungs taken within a minute using a wireless coil (a) and without using a wireless coil (b), c - a diagram showing the SNR values on the resulting images.

Experiment showed, that the signal-to-noise ratio in images obtained using a wireless coil turned out to be 2.4 times greater than in images obtained without using it. Thus, it becomes possible to obtain an image of the same quality, but 5.76 times faster.

4. Conclusions

Visualization of the lungs is not the easiest task for researchers. All existing methods are either not sufficiently informative, or can harm human health due to the radiation used. Therefore, the search for new solutions in this area is a socially significant task.

The work showed that fluorinated gas PFCB can be used to obtain informative 19F-MRI images of the lungs. Also other elements of the respiratory system (trachea and bronchi) of laboratory rats can be visualised using PFCB. The resulting images allow to evaluate the ventilation of the lungs. The quality of the recorded images can be enhanced by using an inductively coupled coil system — resonator and wireless coil. In the future, it is planned to conduct studies on laboratory animals with various pathologies to assess whether the 19F-MRI method is suitable for their detection.

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