ОРИГИНАЛЬНАЯ СТАТЬЯ

FREE BREATHING DYNAMIC 19F MR IMAGING OF LUNGS USING OCTAFLUOROCYCLOBUTANE AT 1.5 T

Gulyaev M.V.[1], Pavlova O.S.[1,2], Rudenko A.Yu.[3], Ozhiganov R.M.[4], Dmitriev D.S.[5], Pistrak A.G.[5], Ryabikov K.N.[5], Tarasov V.P.[5,6], Pirogov Y.A.[2]

1 – Faculty of Medicine, Lomonosov Moscow State University. Moscow, Russia.
2 – Faculty of Physics, Lomonosov Moscow State University. Moscow, Russia.
3 – Belozersky Institute of Physico-Chemical Biology, Lomonosov Moscow State University. Moscow, Russia.
4 – Higher Chemical College of the Russian Academy of Sciences, Mendeleev University of Chemical Technology of Russia. Moscow, Russia.
5 – «S.P. HELPIC» LTD. Moscow, Russia.
6 – Federal Research Center of Problems of Chemical Physics and Medicinal Chemistry Russian Academy of Sciences. Moscow region, Chernogolovka, Russia.

Purpose. To obtain the information about lung function in humans with octafluorocyclobutane (C_4F_8, OFCB) using ^{19}F MRI at 1.5 T.

Materials and methods. We carried out this work on a laboratory bench with a 1.5 T magnet and open source software. The resonant frequency of the conventional 1H RF coils (~63.8 MHz) has been retuned to the resonant frequency of ^{19}F (~60 MHz). To minimize the consumption of fluorinated gas, a gas mixture installation was designed and tested on one healthy volunteer. Two methods for assessing pulmonary function were implemented: wash-in/wash-out dynamics and single-breath imaging. The wash-in/wash-out dynamics technique was implemented using short breaths of the gas mixture (70% OFCB and 30% O2) and then air, respectively. The single-breath imaging was realized on one prolonged inhalation and exhalation of the gas mixture.

Results. The τ-maps (effective time maps) and FV-maps (fractional ventilation maps) of the lungs were constructed. The FV values of the lungs were calculated: $FV_{wash\text{-}in} = 0.30 \pm 0.06$ and $FV_{insp} = 0.34 \pm 0.06$ (for the wash-in and single-breath method, respectively); $FV_{wash\text{-}out} = 0.35 \pm 0.04$ and $FV_{exp} = 0.45 \pm 0.06$ (for the wash-out and single-breath method, respectively).

Discussion. This work builds on our previous work that assessed lung function with OFCB using ^{19}F MRI at 0.5 T. In this paper, we implemented the ^{19}F MRI studies for the assessment of pulmonary function on a 1.5 T MRI scanner. We solved the problem of retuning the RF coils to the ^{19}F resonant frequency and developed a gas delivery system that can be used repeatedly for different patients – just replace the nozzle to inhale/exhale the gas mixture. We showed that the FV values calculated for a healthy volunteer are standard and were obtained previously using another fluorinated gas perfluoropropane.

Conclusion. We conclude that the use of OFCB provides informative ^{19}F MR images for the assessment of pulmonary function at 1.5 T.

Keywords: ^{19}F MRI, lungs, octafluorocyclobutane, wash-in, wash-out, single-breath.

Corresponding author: Gulyaev M.V., e-mail: gulyaev@physics.msu.ru

For citation: Gulyaev M.V., Pavlova O.S., Rudenko A.Yu., Ozhiganov R.M., Dmitriev D.S., Pistrak A.G., Ryabikov K.N., Tarasov V.P., Pirogov Y.A. Free breathing dynamic 19F MR imaging of lungs using octafluorocyclobutane at 1.5 t. REJR 2024; 14(2):57-68. DOI: 10.21569/2222-7415-2024-14-2-57-68.

Received: 08.02.24 **Accepted:** 05.04.24

ДИНАМИЧЕСКАЯ 19F МРТ ВИЗУАЛИЗАЦИЯ ЛЕГКИХ С ИСПОЛЬЗОВАНИЕМ ОКТАФТОРЦИКЛОБУТАНА В МАГНИТНОМ ПОЛЕ 1.5 ТЛ

Гуляев М.В.[1], Павлова О.С.[1,2], Руденко А.Ю.[3], Ожиганов Р.М.[4], Дмитриев Д.С.[5], Пистрак А.Г.[5], Рябиков К.Н.[5], Тарасов В.П.[5,6], Пирогов Ю.А.[2]

1 – Факультет фундаментальной медицины, Московский государственный университет им. М.В. Ломоносова. г. Москва, Россия.
2 – Физический факультет, Московский государственный университет им. М.В. Ломоносова. г. Москва, Россия.
3 – Научно-исследовательский институт физико-химической биологии им. А.Н. Белозерского Московского государственного университета им. М.В. Ломоносова. г. Москва, Россия.
4 – Высший химический колледж Российской академии наук, Российский химико-технологический университет им. Менделеева. г. Москва, Россия.
5 – ООО «С.П. ГЕЛПИК». г. Москва, Россия.
6 – Федеральный исследовательский центр проблем химической физики и медицинской химии Российской академии наук. г. Черноголовка, Россия.

Цель. Получение данных о функциональном состоянии легких человека с помощью октафторциклобутана (C_4F_8, ОФЦБ) методом ^{19}F МРТ в магнитном поле 1.5 Тл.

Материалы и методы. Работа проведена на лабораторном стенде 1.5 Тл МР-томографа с открытым программным обеспечением. Резонансная частота стандартных (фирменных) радиочастотных катушек, работающих на резонансной частоте ядер 1H (~63,8 МГц), перенастроена на резонансную частоту ядер ^{19}F (~60 МГц). Для минимизации потребления фторированного газа спроектирована и испытана установка газовой смеси на одном здоровом добровольце. Реализованы два метода оценки функционального состояния легких, основанные на получении серий ^{19}F МРТ изображений, которые отражают накопление и вымывание фторированного газа при свободном дыхании (wash-in и wash-out процессы соответственно), а также при одиночном дыхании газовой смеси (методика single-breath). Методика wash-in/wash-out реализована с использованием коротких вдохов газовой смеси (70% ОФЦБ и 30% O2), а затем воздуха, соответственно. Методика single-breath осуществлена на одном продолжительном вдохе и выдохе газовой смеси.

Результаты. Построены τ-карты (карты эффективного времени) и FV-карты (карты частичной вентиляции) легких. Рассчитаны значения частичной вентиляции легких: $FV_{wash\text{-}in} = 0.30 \pm 0.06$ and $FV_{insp} = 0.34 \pm 0.06$ (для метода wash-in и single-breath соответственно); $FV_{wash\text{-}out} = 0.35 \pm 0.04$ и $FV_{exp} = 0.45 \pm 0.06$ (для метода wash-out и single-breath соответственно).

Обсуждение. Данная работа основана на результатах нашей предыдущей работы, в которой оценивалось функциональное состояние легких человека методом ^{19}F МРТ в магнитном поле 0.5 Тл с помощью фторированного газа ОФЦБ. В этой статье мы провели ^{19}F МРТ исследования для оценки функции легких на МР томографе с величиной магнитного поля 1.5 Тл. Мы решили проблему перестройки 1H РЧ катушек на работу на резонансной частоте ядер ^{19}F и разработали систему подачи газовой смеси, которую можно использовать неоднократно для разных пациентов – достаточно заменить насадку для вдоха/выдоха. Мы показали, что значения частичной вентиляции легких (FV), рассчитанные для здорового добровольца, являются типовыми и были получены ранее с использованием другого фторированного газа перфторпропана.

Заключение. Применение газа ОФЦБ позволяет получать информативные ^{19}F МРТ- изображения легких для оценки их функционального состояния в магнитном поле 1.5 Тл.

Ключевые слова: ^{19}F МРТ, легкие, октафторциклобутан, накопление, вымывание, одиночное дыхание.

Контактный автор: Гуляев М.В., e-mail: gulyaev@physics.msu.ru

Для цитирования: Гуляев М.В., Павлова О.С., Руденко А.Ю., Ожиганов Р.М., Дмитриев Д.С., Пистрак А.Г., Рябиков К.Н., Тарасов В.П., Пирогов Ю.А. Динамическая ^{19}F МРТ визуализация легких с использованием октафторциклобутана в магнитном поле 1.5 Тл. REJR 2024; 14(2):57-68. DOI: 10.21569/2222-7415-2024-14-2-57-68.

Статья получена: **08.02.24** **Статья принята:** **05.04.24**

The effectiveness of pulmonary diagnostics in magnetic resonance imaging (MRI) can be improved by inhaling inert fluorinated gases [1,2]. In this case, MRI study is performed at the Larmor frequency of fluorine-19 nuclei (19F), which is not a standard function for clinical MR scanners. This feature significantly narrows the capabilities of the 19F MRI method, however, it can be realized on different MRI scanners due to the following statements.

The gyromagnetic ratio γ for the 19F nucleus is 40.05 MHz/T, which is only 6.3% less than γ for the 1H nucleus (42.57 MHz/T). This causes a slight difference in the resonance frequencies for 19F and 1H nuclei on clinical MR scanners [3]. So, for example, in a magnetic field of 1.5 T, the difference in frequencies for 19F and 1H nuclei is only ~3.78 MHz. Thus, the standard radiofrequency (RF) coils, originally produced to operate at the resonant frequency of 1H, can be used for 19F MRI. Only minor modifications to their oscillating circuit are required, for example by changing the capacitor values (usually by increasing the capacitance) and then adjusting the reflection coefficient S11 and transmission coefficient S21. Additionally, it is preferable to have a broadband transmitter, as well as the ability to change the operating frequency in the software.

The gases initially used in 19F MRI of the lungs were originally utilized in the treatment of retinal detachment. In 1969, Norton E. pioneered the intravitreal injection of an expanding gas, sulfur hexafluoride (SF6), for prolonged adaptation at the edge of a retinal tear [4]. Subsequently, perfluorinated gases such as perfluoromethane (CF4), perfluoroethane (C2F6), perfluoropropane (C3F8), perfluorobutane (C4F10), and octafluorocyclobutane (C4F8) were incorporated into ophthalmic practice [5]. These gases are colorless, odorless and chemically inert, rendering them invaluable in vitreoretinal surgery, as endorsed by the Ministry of Health of the Russian Federation through Order No. 902n dated November 12, 2012.

The most commonly used fluorinated gases in 19F MRI of the lungs are sulfur hexafluoride (SF6) and perfluoropropane (C3F8, PFP). Using these gases, the functional properties of the lungs are determined by calculating the percentage of ventilation defects, assessing regional ventilation, constructing fractional ventilation maps (FV-maps), ventilation/perfusion maps (V/Q-maps), effective time maps (τ-maps) of gas accumulation (wash-in) and its removal from the lungs (wash-out) [6-11]. The studied parameters were assessed both in healthy volunteers and in patients with COPD, asthma, cystic fibrosis, etc [12-14]. Significant differences in the studied parameters were shown for healthy lungs and lungs with pathologies.

Our previous studies of the lungs in magnetic fields of 0.5 T (in humans) and 7 T (in laboratory rats) showed that octafluorocyclobutane (C4F8, OFCB, Russian Freon R318C) is a promising fluorinated gas for 19F pulmonary MRI [15,16]. Being domestically produced in Kirovo-Chepetsk, OFCB turns out to be more convenient to use than SF6 and C3F8. In addition, the favorable relaxation times (T1 ≈ T2 ≈ 50 ms) are well suited to the 19F MRI technique, thereby reducing the requirements for gradient system and pulse sequences. Safety information regarding OFCB can be accessed in a research paper from 1960 [17]. In our previous work, we demonstrated the great potential of using OFCB gas for assessment of lung function in humans at 0.5 T [18].

In this paper, we report the usage of OFCB gas in 19F MRI of human lungs at 1.5 T. The main tasks that are solved in this work is the retuning of the operating frequency of the transmit-receive path of the MR scanner; the development and production of a specialized system for delivering respiratory mixture (OFCB and O2) to the human lungs; the construction of τ-maps and FV-maps of the lungs of a healthy volunteer.

Materials and methods.

MRI system. The work was carried out at «S.P. HELPIC» LTD (Moscow, Russia), where the laboratory stand of the MR scanner XGY SuperScan 1.5 T (Ningbo Xingaoyi Magnetism Corporation Ltd., China) is located. The MR scanner is equipped with an MSM-TN-150AM-D 1.5T magnet (Mitsubishi Electric Corp., Japan), an EVO spectrometer (MR Solutions Ltd., UK) and a QDCM-800 gradient amplifier (Performance Control Inc., USA) with a maximum gradient amplitude of 30 mT/m. The MR scanner is operated using open software, which is controlled with a software shell created by the employees of «S.P. HELPIC» LTD.

RF coils. For 19F pulmonary studies, two RF coils were used. One RF coil is a whole-body transmitter, inserted into the bore of the magnet. Another RF coil is a body receiver that surrounds the chest.

The transmitter RF coil is a high-pass quadrature birdcage coil with an internal diameter of 60 cm. It has 16 strings and, accordingly, 16 capacitors on upper and lower rings. These capacitors determine the resonant frequency of the transmitter RF coil. For 1H (~63.8 MHz), the value of each capacitor is 78 pF (two capacitors of 39 pF connected in parallel). The frequency tuning of the transmitter RF coil to ~60.0 MHz was carried inside the RF copper screen (for imitation the RF screen located in the magnet) with the help of vector network analyzer Rohde&Schwarz ZNB4 (Germany). As a result, 15 pF was added for each capacitor, so that the total capacitance was 93 pF (two capacitors of 39 pF and one capacitor of 15 pF connected in parallel). For a precise adjusting of the coefficients S11 and S21, pieces of non-magnetic coaxial cable were used as additional capacitors. This solution has sufficient flexibility in the choice of capacitor values and sufficient dielectric strength. At 19F resonant frequency (~60.0 MHz), S11 was better than -15 dB. Decoupling between the ports of the tuned RF coil was more than 30 dB.

The power divider (90° hybrid coupler) was rebuilt by changing the values of inductances. As a result, at 19F resonant frequency the decoupling between the ports was more than 30 dB, S11 and S22 were better than -20 dB, amplitude imbalance was less than 0.1 dB.

The receiver RF coil is a 4-channel Rx coil. The frequency tuning was carried out under the load, which was a plastic container filled with ~10 L water. The impedances of the ports at ~60.0 MHz were measured with the help of the Rohde&Schwarz ZNB4 and new matching RF circuits were calculated and then changed. The decoupling between the channels in the coil's design is frequency-independent – therefore, it did not have to be changed.

In vitro 19F MRI. The operation of all RF communication elements (transmit-receive path, amplifier) and RF coils (transceiver, receiver) at ~60.0 MHz was tested on a phantom, which was an inflatable balloon of ~7L filled with OFCB gas. The 19F MR images of the balloon were obtained using 2D spoiled gradient echo (RF-spoiled GRE) pulse sequence with the following scan parameters: TR: 15 ms, TE: 5.4 ms, FA: 40°, number of slices: 1, slice thickness: 35 cm, FOV: 50 cm × 50 cm, matrix: 200 × 200, spatial resolution: 0.25 cm × 0.25 cm, number of repetitions: 4, bandwidth: 25 kHz , scan time: 12 s. 19F MR images of the phantom were obtained in axial, coronal and sagittal projections.

Gas delivery system. To minimize the consumption of OFCB, as well as to avoid excessive emissions of fluorinated gas into the atmosphere (the gas is a greenhouse gas), a specialized system for delivering respiratory mixture to the human lungs has been developed and produced. The block diagram of a system for delivering respiratory mixture (70% OFCB and 30% O_2) to the human lungs is presented in Fig. 1.

It is a closed breathing circuit and consists of the following blocks connected in series: an oxygen concentrator, a fluorinated gas cylinder, an oxygen gas analyzer, a gas mixture reservoir, breathing tubes, a moisture collector, a carbon dioxide absorbent, control shut-off valves and inhalation/exhalation valves, and a breathing mask. Oxygen was produced using a JAY-10 concentrator (Longfian Scitech Co, Ltd, China) with a purity of 95%. OFCB (refrigerant R318C) with a purity of 99.99% was purchased from «Fire Safety Center LLC» (Russia).

Oxygen concentrator and the cylinder with OFCB are connected through flexible tubes to a gas mixture reservoir – oxygen pillow □42 L (Matwave, USA). Control shut-off valves are installed at the outlet of the oxygen concentrator and the OFCB cylinder. Mixing of gases occurs under the control of the oxygen gas analyzer PKG-4 N-K-P (JSC Eksis, Russia), which measures the concentration of O_2 in the gas mixture reservoir. Adjustment of inhalation from the reservoir is carried out using manual control, implemented by a flexible tube at the end of which there is a syringe with a volume of 20 ml. This design allows, by moving the piston up/down in the syringe, to open the flow of the gas mixture during inhalation and close it during exhalation, respectively. After the manual control valve, there is one of the flexible tubes (inspiratory tube) of the breathing circuit (internal diameter 22 mm), connected to the Y-shaped connector of the inspiratory and expiratory tubing. The output of the Y-connector is connected to a non-vented nasal mask JOYCE clinic FF (Löwenstein Medical, Germany) of a specific size (S, M, L) depending on the volunteer being studied. The exhalation tube is connected to a moisture collector and to the container with soda lime absorbent (Alba Healthcare, USA) to absorb exhaled CO_2, after which it is connected to the gas mixture reservoir. During the 19F pulmonary MRI, the oxygen content in the gas mixture reservoir is constantly measured (using the oxygen gas analyzer PKG-4 N-K-P). If the oxygen content in the gas mixture drops, then for the next experiment the oxygen is added through the oxygen concen

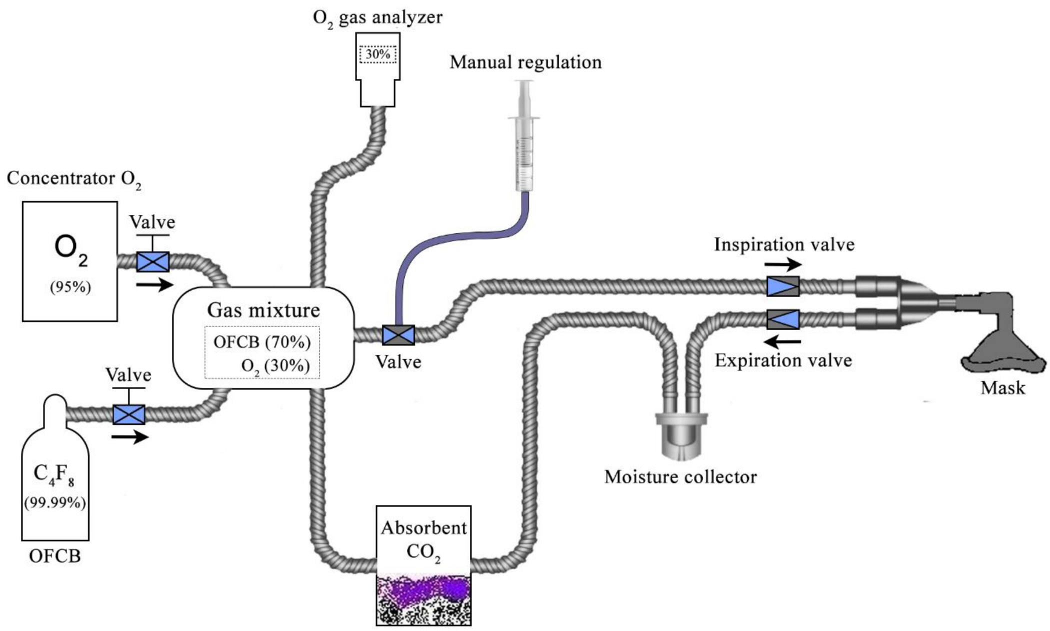

Fig. 1 (Рис. 1)

Fig. 1. Diagram.

Block diagram of a system for delivering respiratory mixture to the human lungs.

Рис. 1. Диаграмма.

Структурная схема системы доставки дыхательной смеси в легкие человека.

trator to 30% in the gas mixture.

In vivo 19F MRI. In vivo 19F MRI studies were conducted on one healthy volunteer – a 19-year-old man, without bad habits and acute/chronic lung diseases. Before conducting 19F MRI of the lungs, his written informed consent was obtained regarding voluntary participation in the experiment. In all other respects, we were guided by the principles of the World Medical Association Declaration of Helsinki from 1964: ethical principles for medical research involving human subjects.

Two methods were implemented to assess the lung function, based on obtaining a series of 19F MR images of the lungs: wash-in/wash-out dynamics and single-breath imaging. For both techniques, the 19F MR images were acquired in the coronal projection using RF-spoiled GRE with the following scan parameters: TR: 6 ms, TE: 2.0 ms, FA: 30°, number of slices: 1, slice thickness: 35 cm, FOV: 35 cm × 35 cm, matrix: 60 × 60, spatial resolution: 0.58 cm × 0.58 cm, number of repetitions: 14, bandwidth: 25 kHz, scan time: 5 s.

Wash-in/wash-out dynamics. Wash-in/wash-out dynamics reflects the accumulation of the fluorinated gas in the lungs during free breathing of the gas mixture and its removal from the lungs during free breathing of air. To implement the wash-in/wash-out technique, during the first scan (~5 s) the volunteer took a normal breath of the gas mixture and held his breath; during the next scan (~5 s) he exhaled slowly. In total, the volunteer took seven inhalations and exhalations of the gas mixture. As a result, fourteen 19F MR images of inhalations/exhalations were obtained to evaluate the wash-in process. After, the volunteer took nine inhalations and exhalations from the air. In this case, eighteen 19F MR images were obtained to evaluate the wash-out process. The total scan time was 2 min 40 s.

Single-breath imaging. The single-breath technique was proposed by us in our paper on the use of OFCB at 0.5 T [18]. It is carried out in one respiratory cycle without holding the breath, while the subject takes the deepest and longest possible breath of the gas mixture, after which he makes the same deep and long expiration. The total time of this study depends on the subject, in our case it was 1 min 20 s (□40 s for inhalation and ~40 s for exhalation), during which a series of sixteen 19F MR images was obtained.

Image Processing and Analysis. The analysis of the obtained data was carried out in Python 3.8. To evaluate the wash-in/wash-out dynamics, only the 19F MR images obtained during inhalation of the gas mixture/air were used. For single-breath imaging, the entire series of 19F MR images was applied.

First, the effective time maps reflecting the effective time of accumulation of the 19F NMR signal in the lungs ($\tau_{wash-in}$-maps and τ_{insp}-maps) and its washout from the lungs ($\tau_{wash-out}$-maps and τ_{exp}-maps) were calculated. Then, the fractional vantilation maps were built: $FV_{wash-in}$-maps and FV_{insp}-maps ($FV_{wash-out}$-maps and FV_{exp}-maps) reflecting the amount of gas inhaled (exhaled) to a unit volume of lungs per unit of time.

A description of the methodology for calculating τ-maps and FV-maps has been presented previously in several papers [8,12,18,19] and is presented in a short form here.

To analyze the obtained data, the entire series of 19F MR images was divided into two series corresponding to the wash-in or single-breath inspiration process and wash-out or single-breath expiration process, after which the signal was approximated using the following functions:

$$\begin{cases} S_{in} = S_0(1 - \exp(-{}^{t}/_{\tau_{in}})) + S_{noise} \\ S_{out} = S_0 \exp(-{}^{t}/_{\tau_{out}}) + S_{noise} \end{cases} \quad (1),$$

where S_{in} and S_{out} are the signal intensity during wash-in or single-breath inspiration process and wash-out or single-breath expiration process, respectively; S0 and S_{noise} are approximation constants corresponding to the maximum intensity of the fluorinated signal in the lungs and the noise signal, respectively; τ_{in} and τ_{out} are the effective time of accumulation of the fluorinated signal in the lungs (wash-in or single-breath inspiration process) and its wash-out (or single-breath expiration process) from the lungs, respectively.

The signal intensity in a series of MR images can also be described using the following system of equations:

$$\begin{cases} S_{in} = S_0(1 - (1 - FV_{in})^{n_{in}}) + S_{noise} \\ S_{out} = S_0(1 - FV_{out})^{n_{out}} + S_{noise} \end{cases} \quad (2),$$

where FV_{in} and FV_{out} are the fractional ventilation parameters corresponding to the ratio of the amount of «new» gas entering a voxel at each breath during the wash-in or single-breath inspiration process and during the wash-out or single-breath expiration process, respectively, to the total amount of gas in each voxel; nin and nout are the number of breaths during the wash-in or single-breath inspiration process and wash-out or single-breath expiration process, respectively.

As the first MR images (during first inspiration) were obtained after 5 s, using formulas (S2) we can obtain the following equation:

$$FV_{in/out} = 1 - \exp(-{}^{5}/_{\tau_{in/out}}) \quad (3)$$

The SNR values in the 19F MR images were estimated in the ImageJ 1.51j8 software [20] according to the following formula:

$$SNR(i,j) = \frac{(S(i,j) - S_{noise})}{\sigma_{noise}} \quad (4),$$

where S(i,j) – is the signal intensity in the measured voxel (i,j), S_{noise} – is the value of noise measured in the background region, σ-noise – is the standard deviation of the noise in the given background region.

Results.

Fig. 2a shows a photo of a phantom located inside the receiver RF coil in the MR scanner. In Fig. 2b-2d, the 19F MR images obtained from the phantom are presented in three orthogonal projections. The images were obtained without visible distortions and artifacts with a maximum SNR = 120 (Fig. 2e). The 19F NMR signal registration area corresponds to the internal dimensions of the receiver RF coil and is sufficient to scan human lungs. According to the reference data [21,22], the average dimensions of a human lung are: 180-210 mm (height) × 100-123 mm (width) × 127-180 mm (depth).

Fig. 3a and Fig. 4a show the 19F MR images of the lungs of a healthy volunteer obtained during the implementation of the wash-in/wash-out and single-breath techniques, respectively. The graphs of the relative intensity of the 19F NMR signal in a time series of 19F MR images are shown in Fig. 3b and 3c for the wash-in and wash-out processes, respecively, as well as in Fig. 4b and 4c – for the one deep inspiration and expiration phases of the single-breath imaging technique, respectively.

The τ-maps of the effective time of the accumulation/excretion of the OFCB gas in the lungs of a healthy volunteer were constructed, the results are presented in Fig. 5a. In Fig. 5b, the FV-maps are shown. Density distribution histograms of the FV values in the lungs are presented in Fig. 6. Table №1 shows the calculated mean and median FV values obtained for the wash-in/wash-out dynamics experiment and for single-breath imaging technique.

Discussion.

This work builds on previous studies that proposed assessing lung function using 19F MRI. The technique consists of breathing a gas mixture (fluorinated gas and O2) at certain points in time, simultaneously with MR scanning of the lungs. This requires a multinuclear MR scanner, a specialized fluorinated gas and a system for delivering respiratory mixture.

Fluorine-19 nucleus has a huge advantage over other MR active nuclei because it

Fig. 2 a (Рис. 2 а)

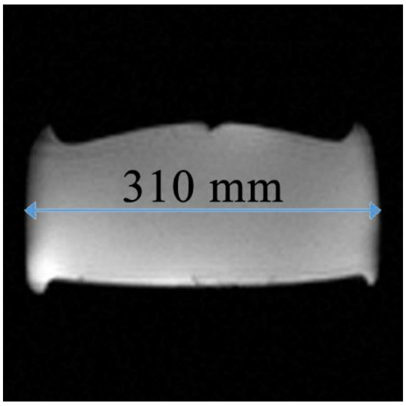

Fig. 2 b (Рис. 2 б)

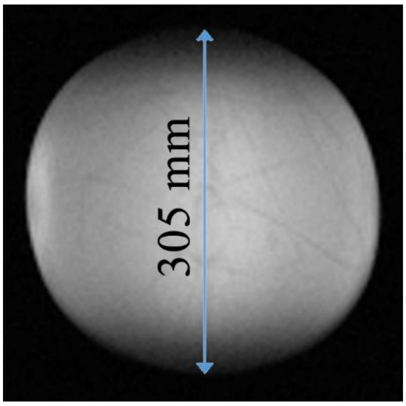

Fig. 2 c (Рис. 2 в)

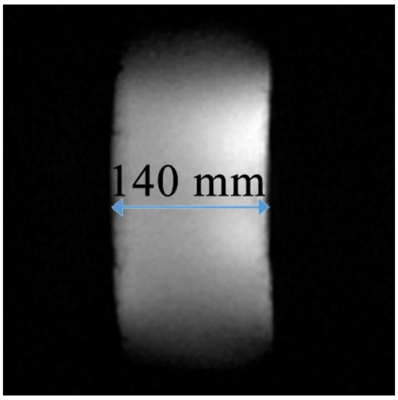

Fig. 2 d (Рис. 2 г)

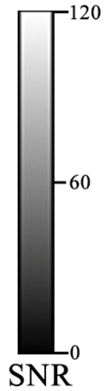

Fig. 2 e (Рис. 2 д)

Fig. 3. The results of in vitro 19F MRI studies.

a – Photo of a phantom – an inflatable ballon filled with OFCB and located in the MR scanner.

b-d – 19F MR images of the phantom in axial, coronal and sagittal slices, respectively.

e – Scale of the SNR values in 19F MR images of the phantom.

Рис. 3. Результаты in vitro 19F МРТ исследований.

а – Фотография фантома – надувной баллон, заполненный газом ОФЦБ и расположенный в МР-томографе.

б-г – 19F МРТ-изображения фантома в аксиальной, корональной и сагиттальной плоскостях, соответственно.

д – Шкала значений SNR на 19F МРТ-изображениях фантома.

resonates at a frequency that is only 6% lower than that of 1H nuclei. Therefore, if the MR scanner is not a multinuclear (as in our case), the following problems arise. It is necessary to find out whether the transmitter can emit at the resonant frequency of 19F and determine whether it is possible to change the operating frequency of the MR scanner? These capabilities were present for our device. The next point is the presence of RF coils operating at the resonant frequency of 19F. The manufacturers of the MR scanners usually offer such coils, but if it is not possible to purchase them, then the conventional 1H RF coils can be used for these purposes. It is enough to make minor changes to the RF elements of the oscillating circuits of the RF coils, as well as additional RF components, in our case it was the power divider.

The choice of the fluorinated gas is the next important issue for pulmonary 19F MRI. Sulfur hexafluoride (SF6) and perfluoropropane (C3F8, PFP) are the most common gases used for this purpose [1,13,23]. Recently, another fluorinated gas was used for 19F MRI of lungs – octafluorocyclobutane (C4F8, OFCB). Our works at 0.5 T and 7 T [15,18,24] and a work by other authors at 3 T [25] have shown great potential for its application not only for lung imaging, but also for assessing pulmonary function. In this paper, we report on the use of OFCB gas in a

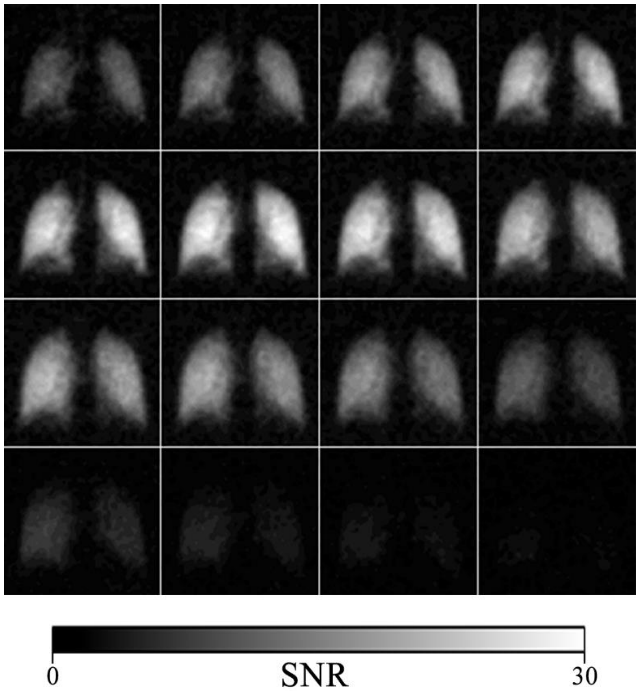

Fig. 3 a (Рис. 3 а)

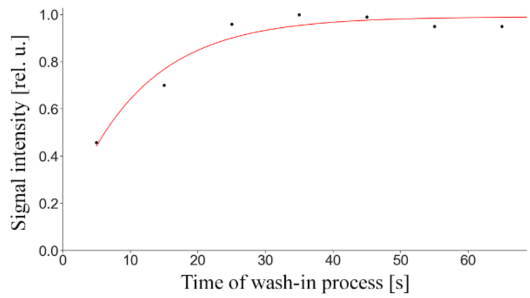

Fig. 3 b (Рис. 3 б)

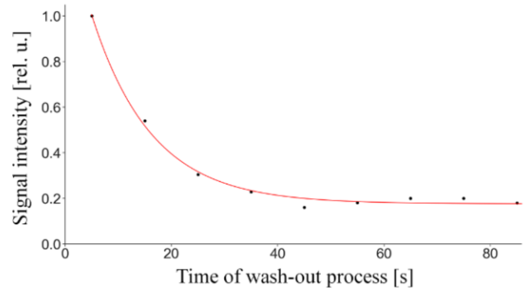

Fig. 3 c (Рис. 3 в)

Fig. 3. The results of the wash-in/wash-out experiment – accumulation of the OFCB gas in the lungs during free breathing of the gas mixture and its removal from the lungs during free breathing of air.

a – A series of 19F MR images of the OFCB gas within the lungs obtained during short breaths of gas mixture (first seven images) and air (subsequent nine images).

b,c – Graphs of the relative intensity of the 19F NMR signal in one of the pixels versus time during the wash-in and wash-out processes, respectively.

Рис. 3. Результаты эксперимента wash-in/wash-out – накопление газа ОФЦБ в легких при свободном дыхании газовой смесью и выведение газа ОФЦБ из легких при дыхании воздухом.

а – Серия 19F МРТ-изображений газа ОФЦБ в легких, полученных во время коротких вдохов газовой смеси (первые семь изображений) и воздуха (последующие девять изображений).

б, в – Графики относительной интенсивности 19F сигнала ЯМР в одном из пикселей в зависимости от времени для методики wash-in и wash-out, соответственно.

magnetic field of 1.5 T.

Note that the fluorinated gases are inert and safe for the living organism. However, they are greenhouse gases, and therefore it is advisable to limit their release into the environment. In this regard, in this work, a system for delivering a gas mixture (70% OFCB and 30% O2) to the human lungs was designed and produced. It operates on the principle of a closed breathing circuit, used in particular during artificial ventilation of the lungs, thereby minimizing the consumption of fluorinated gas. The gas delivery system is practical and can be used for different patients – just replace the nozzle to inhale/exhale the gas mixture, which is in direct contact with the patient's mouth.

The supply of the respiratory mixture to the lungs is controlled manually by moving the piston up/down in the syringe. The advantage of this design is that the volunteer controls the gas mixture supply and inhales as much gas mixture as he can inhale. The disadvantage is the lack of synchronization with the supplied pulse sequence. With synchronization, the process of obtaining the 19F MR images is greatly simplified, and the results of the study are more rigorous. Without the synchronization, the patient must be additionally explained at what point in time he should inhale and exhale the gas mixture.

To assess pulmonary function, we used one of the well-known wash-in/wash-out dynamics method [11] and proposed by us single-breath imaging technique [18]. In wash-in/wash-out experiment, the volonteer took short inhalations and exhalations of the gas mixture, followed by short inhalations and exhalations of the same duration with air. In our case, the 19F MR scanning was carried out within 10 s for one respiratory cycle (5 s to in

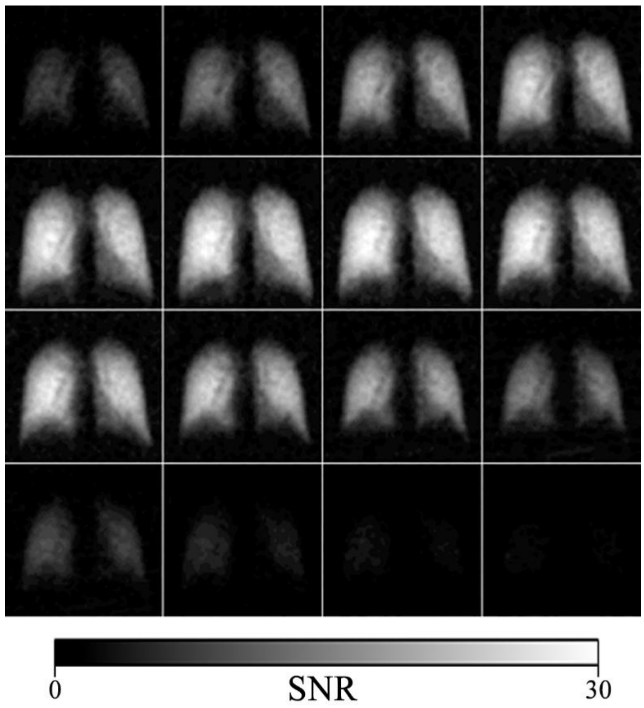

Fig. 4 a (Рис. а)

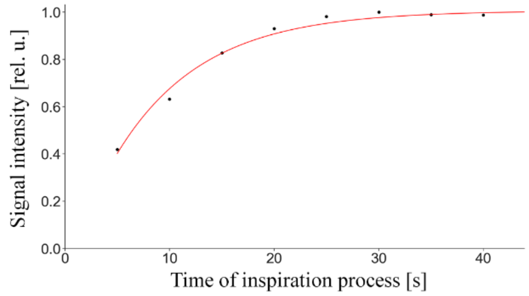

Fig. 4 b (Рис. б)

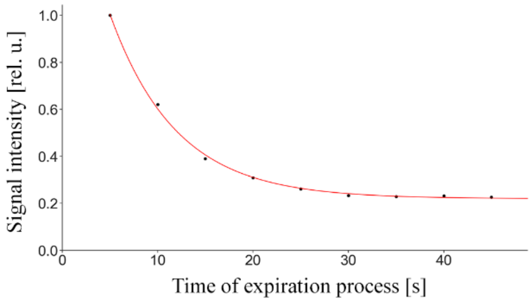

Fig. 4 c (Рис. 4 в)

Fig. 4. The results of the single-breath imaging experiment – accumulation of the OFCB gas in the lungs during one prolonged inhalation of the gas mixture and its removal from the lungs during one prolonged exhalation.

a – A series of 19F MR images of the OFCB gas within the lungs obtained during short breaths of gas mixture (first seven images) and air (subsequent nine images).

b,c – Graphs of the relative intensity of the 19F NMR signal in one of the pixels versus time during the wash-in and wash-out processes, respectively.

Рис. 4. Результаты эксперимента single-breath – накопление газа ОФЦБ в легких на одном продолжительном вдохе газовой смеси и выведение газа ОФЦБ из легких на одном продолжительном выдохе газовой смеси.

а – Серия 19F МРТ-изображений газа ОФЦБ в легких, полученных на одном глубоком вдохе газовой смеси (первые восемь изображений) и на одном глубоком выдохе газовой смеси (последующие восемь изображений).

б, в – Графики относительной интенсивности 19F сигнала ЯМР в одном из пикселей в зависимости от времени во время одного глубокого вдоха и одного глубокого выдоха, соответственно.

hale and 5 s to exhale, respectively). In single-breath experiment, the volonteer took one long and deep inhalation and then one long and deep exhalation. It took him 1 min 20 s (40 s to inhale and 40 s to exhale, respectively). According to the feelings and perceptions of the volunteer, the single-breath technique is easier to implement, since although it requires stretching the inhalation/exhalation phases, it allows to avoid holding breath, of which there are quite a lot, despite their short duration.

Note the comparable FVwash-in and FVinsp values calculated for the wash-in/wash-out dynamics and single-breath imaging techniques, respectively, as well as higher FVexp values for the single-breath imaging technique. The latter is likely due to a deeper and longer exhalation compared to the wash-in/wash-out method, in which inhalation and exhalation with air are short and alternating. At the same time, the density distribution of the FV values for both methods looks comparable – one mode is observed, and the distribution of the FV values is close to normal. The FV values calculated for a healthy volunteer are standard and were obtained previously using PFP gas [26,27].

It is of interest to compare the results obtained by using wash-in/wash-out dynamics method and single-breath imaging technique in magnetic fields of 0.5 T [18] and 1.5 T. Note higher SNR values in 19F MR images of the lungs at 1.5 T – more than 3 times, as well as

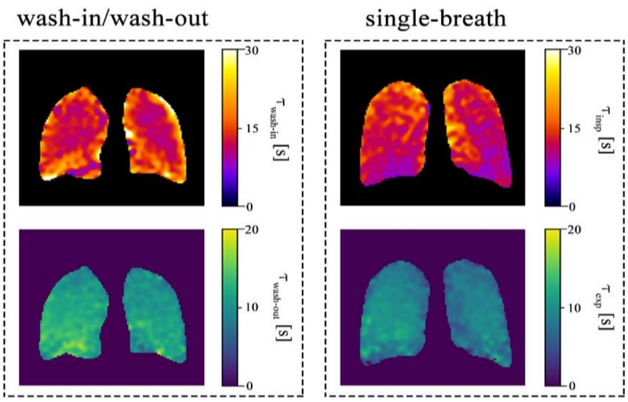

Fig. 5 a (Рис. 5 а)

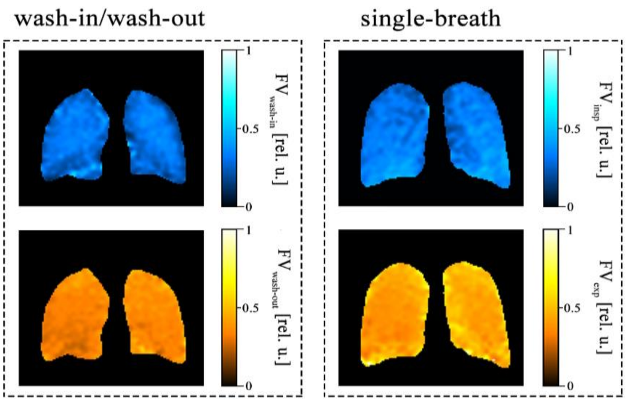

Fig. 5 b (Рис. 5 б)

Fig. 5. Parametric maps of pulmonary function for a healthy volunteer.

a – τ-maps of the effective time of the accumulation of the OFCB gas within the lungs (top row) and its excretion from the lungs (bottom row), constructed for the wash-in/wash-out dynamics experiment (left) and for single-breath imaging technique (right).

b – FV-maps of the accumulation of the OFCB gas within the lungs (top row) and its excretion from the lungs (bottom row), constructed for the wash-in/wash-out dynamics experiment (left) and for single-breath imaging technique (right).

Рис. 5. Параметрические карты функции легких здорового добровольца.

а – τ-карты эффективного времени накопления газа ОФЦБ в легких (верхний ряд) и его выведения из легких (нижний ряд), построенные для методики wash-in/wash-out (слева) и single-breath (справа), соответственно.

б – FV-карты накопления газа ОФЦБ в легких (верхний ряд) и его выведения из легких (нижний ряд), построенные для методики wash-in/wash-out (слева) и single-breath (справа), соответственно.

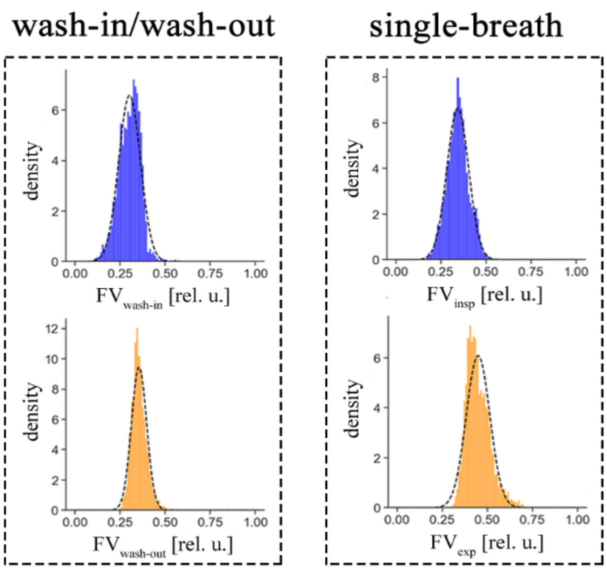

Fig. 6 (Рис. 6)

Fig. 6. Statistical data on measurements of FV values.

Density distribution histograms of the FV values within the lungs for wash-in/wash-out dynamics experiment (left) and single-breath imaging technique (right), respectively.

Рис. 6. Статистические данные по измеренным значениям частичной вентиляции легких (FV)..

Гистограммы распределения плотности значений FV в легких для методики wash-in/wash-out (слева) и single-breath (справа), соответственно.

the absence of the need to carry out additional processing of the obtained images (apodization of data) in order to increase the SNR values. The FVwash-in values at 0.5 T and 1.5 T are comparable, in contrast to the FVwash-out values, which are underestimated at 0.5 T. We believe that this may be due to the fact that when breathing air at 0.5 T, the 19F NMR signal in the lungs decreases faster, since initially the SNR values in them are low and after several breaths of air the signal decreases faster in the lungs and becomes comparable to noise, which leads to an underestimation of the FVwash-out values. For the single-breath imaging technique in a magnetic field of 0.5 T, the FV values were not calculated and are presented only in this work.

Table №1. The FV values in the FV-maps for wash-in/wash-out dynamics experiment and single-breath imaging technique.

Process phase	wash-in/wash-out		single-breath	
	$\mu + \delta$	*Me* (q1-q3)	$\mu + \delta$	*Me* (q1-q3)
$FV_{wash\text{-}in}$ (FV_{insp})	0.30 ± 0.06	0.31 (0.26-0.34)	0.34 ± 0.06	0.34 (0.30-0.38)
$FV_{wash\text{-}out}$ (FV_{exp})	0.35 ± 0.04	0.35 (0.33-0.38)	0.45 ± 0.06	0.44 (0.40-0.48)

Abbreviation: μ and δ, mean and standard deviation, respectively; *Me*, median values; q1-q3, first and third quantiles of the distribution of the *FV* values.

Conclusion.

19F MR images of human lungs were obtained and lung function was assessed in a healthy volunteer using C4F8 fluorinated gas at 1.5 T. 19F MR images were obtained without visible distortions and artifacts using a developed system for delivering a respiratory gas mixture to the human lungs. 19F MRI studies of human lungs were carried out using wash-in/wash-out dynamics method (with free breathing of a gas mixture/air) and single-breath imaging technique (with deep breathing during one respiratory cycle). Both methods were used to assess lung ventilation, which was carried out by constructing effective time maps (τ-maps) and fractional ventilation maps (FV-maps). The use of OFCB provides informative 19F MR images for the assessment of pulmonary function at 1.5 T. However, to confirm the calculated FV values in human lungs, additional experiments with a larger number of volunteers need to be performed.

Funding.

This work was supported by a Russian Science Foundation grant (21-75-10038). The Authors declare that there is no conflict of interest.

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