Multinuclear magnetic resonance imaging in biomedical experiments

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Abstract. The detection of nuclei other than protons can significantly enhance the opportunities of MRI method. Thereby one of the most promising nuclei in this field is fluorine-19. We showed that it is possible to visualize lungs, gastrointestinal tract and inflammation regions by 19F MRI without complicated and expensive specific technics. Moreover, the use of other nuclei in multinuclear applications is also possible and it is a promising direction in this field.

1. Introduction. Purpose
Magnetic resonance imaging (MRI) is usually used for visualization of internal organs to elicit its pathologies, which appear as variances in geometrical proportions (morphological changes) and tissues composition. Last is elicited on MRI images by contrast changes. The contrast control in MRI is provided with setting parameters of impulse sequences, choice of which allows to improve imaging tissues with short or long relaxation times. To solve these challenges, MRI method on hydrogen nucleus (proton) – detection of NMR signals from hydrogen-contained compounds (water, fat, etc.) – is used. This method is very sensitive to protons due to its high gyromagnetic ratio and 100% nature abundance.

2. Materials and methods
The additional information about internal organs can be also obtained from other magnetic nuclei, which are contained in organic molecules. However, they have much less sensitivities because of their small gyromagnetic ratios. So, only the detection of phosphorus 31P and sodium 23Na (beside 1H) nuclei is applied in up-to-date MRI. The detection of such nuclei as 13C, 15N, 17O, 2D, etc. is usually applied for studying metabolic processes, whose labels are isotope-enriched compounds. The preliminary hyperpolarization of these compounds is applied to achieve the maximal sensitivity.

The typical configuration of medical MRI scanner is aimed to the detection only protons. However, in some cases, its hardware may be adjusted to detect nuclei other than protons. We described in our previous studies [1-4] how 0.5T medical MR scanner Bruker Tomikon S50 has been adjusted for
detection not only protons, but also 19F, 31P, 13C, 23Na, 11B, 2H, 35Cl nuclei. Herewith 19F NMR spectroscopy and MRI were applied in in vivo studies with laboratory animals – rats, mice. The studies of the perfluorocarbon compound Perfloranum® (well-known as a blood substitute with efficient gas transmission function) were performed.

3. Results
With use of the 0.5T MRI scanner, we were able to detect the 19F MRI signals in the study of human gastrointestinal tract. The figure 1 a, b shows 19F and 1H MRI images of healthy volunteer, who has swallowed the capsule filled with perfluorodecalin (PFD). These images were obtained using 3D-gradient echo (GE). Scanning parameters for 19F MRI were followed: FA=300, TR/TE=600/4.6 ms, BWT/BWR=0.7/125 kHz, EXPT=20 min, MTX=128×128×16, FOV=30×30×35 cm.

Figure 1. 19F-, 1H- and (19F+1H)-MRI images of the capsule filled with perfluorodecalin (as marked by the arrow) in gastrointestinal tract.

The combination of 1H and 19F MRI images allows to specify the localization of the capsule with PFD relatively to the anatomical structures. One hour after swallowing, this capsule was found (as it’s shown in the Figure 1) in the stomach, at the entrance to the duodenum. Capsule shell with 1-ml internal volume was made from gelatin and polyacryl.

Scientific research MRI scanners intended for small laboratory animals (rats, mice, etc.) investigations are more suitable for multinuclear experiments. One of such scanner is 7T MRI device Bruker BioSpec 70/30 USR, in which we have studied metabolic processes using 13C and 31P NMR spectrometry. Acceptable results were also obtained by the detection of deuterium 2H with help of NMR spectroscopy and MRI methods [5].

An important direction in multinuclear MRI is lung visualization. Hyperpolarized gases, whose atoms are polarized to almost 100% condition by specific methods, are usually used for this purpose. The hyperpolarization condition is nonequilibrium and has practical interest only in the case of weakly interacting atoms, whose translations in the equilibrium condition occur for a long time. As such substances, the inert gases (3He, 199Xe, 36Kr, etc.) and gases, which contain nuclei with low gyromagnetic ratio (for example, isotope-enriched by 13C carbon dioxide) can be.

Because preparation of the hyperpolarized gases is technically complicated and consequently available to only few number of laboratory in the world, the fluorine-contained compounds can be used for this purpose as an alternative to hyperpolarized gases.

The detection of 19F NMR signal is promising method because its sensitivity is comparable to proton sensitivity. Herewith in the case of 19F MRI, there is no background from normal tissues on fluorine images, because the extremely little fluorine amount is contained in these tissues. Also because of the same reason, it is enough to apply only one impulse sequence – not two, three or more as it is in the case of 1H MRI – to differentiate the tissues by measuring 19F signals.

Since NMR resonance frequencies of protons and fluorine-19 are very close, it is possible to use the same technical hardware (receiver-transmitter, NMR signal detector) to detect these nuclei. For 0.5T MRI scanner, we used proprietary receive coils, whose tuning range was enough to work with
both of the nuclei (19F, 1H). However proprietary transmitting coil could work only on protons. Therefore one of the quadrature channels of the receive coil was adjusted to transmit RF power.

For 7T MRI scanner, the proprietary resonator designed to detect only hydrogen was adjusted for detecting the fluorine-19 nuclei. Because the additional capacity and commutator were installed in this resonator circuitry, the own resonator’s frequency could be switched depending on the fact which nuclei (hydrogen or fluorine) are needed to detect.

The interesting results were obtained using 19F frequency resonators with inductively (i.e. by wireless way) included coils in the program of creating so-called implant systems. The main purpose of such implant (the plane one-loop coil fine-tuned to the Larmor frequency) is to transmit and receive NMR signals at the region which is very close to the required specific organ. Thereby the level of RF field strength in the region can be significantly enhanced in the implant region reaching the best sensitivity [6]. Wireless coils were used in our studies to detect 19F MRI signals, but it is absolutely clear that such coils can be useful for other multinuclear applications.

The results (Figure 2) which show the effectiveness of fluorocarbon compounds as the contrast agent and different markers for imaging separate internal organs, gastrointestinal tract, lungs and inflammation regions were obtained by 19F MRI method in the in vivo studies of perfluorocarbon compounds injected to the body of laboratory animals. The rats “Wistar” as laboratory animals were used in these experiments.

Figure 2. A - liver, spleen and thymus of rat after intraperitoneal injection of Perfloranum®; B - visualization of cellulitis of rat after intravenous injection of perfluorotributylamine (C12F27N); C - gastrointestinal tract of rat after oral administration of Perfloranum®; D - Lung of rat after inhalation of perfluorocyclobutane (C4F8).

A number of these obtained data are not obvious. Note, the concentration of Perfloranum® after its intraperitoneal injection became apparent not only in liver and spleen, but also in thymus as it is seen on the fragment A of the Figure 2. However, after intravenously injection, the Perfloranum® accumulates only in liver and spleen.

4. Discussion. Conclusions
Detection of nuclei other than protons can significantly expand opportunities of MRI method. Thereby, especially significant prospects relate to the application of 19F MRI. However the use of
other nuclei in multinuclear applications presents also promising direction in this line. Such applications become possible using relatively simple technical resources (for example – implant coils) without isotope enrichment of sounding compounds or their hyperpolarization.

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