Appl Magn Reson
DOI 10.1007/s00723-017-0934-5

Applied
Magnetic Resonance

ORIGINAL PAPER

Visualization of Digestion Process Using ^{19}F MRI

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Received: 31 July 2017 / Revised: 24 August 2017

Abstract Tracing parameters of digestion process could help in setting more accurate diagnosis for patients with gastrointestinal diseases. For this purpose, we suggest a new type of food tracer. By soaking liquid perfluorocarbon in dry rodent food, each step of digestion process can be visualized on ^{19}F-magnetic resonance (MR) images. Compared with liquid contrast agents, food is able to fill organs of gastrointestinal tract more tightly and yield properties of digestion process. However, rats, participating in such study, should be set on a water diet before experiment. ^{19}F-MR images are obtained with volume scanning (3D) pulse sequence based on multiple spin echo methodic with minimal time intervals between echoes. Gastrointestinal ^{19}F-magnetic resonance imaging (MRI) visualization is a harmless real-time tracking method which could be easily transferred into clinical practice. Moreover, it does not apply ionizing radiation, so in the combination with reference ^{1}H-MRI this method could become very useful in treatment process assessment.

1 Introduction

The ability to visualize the process of food digestion is the key to a comprehensive study of the physiological conditions of the gastrointestinal (GI) tract. The main diagnostic methods are computerized tomography (CT) and magnetic resonance imaging (MRI). CT over MRI has some advantages: less scanning time, higher spatial resolution, wide availability, and lower cost [1].

In gastrointestinal CT studies barium porridge is a commonly used contrast agent. The main disadvantage of CT is ionizing radiation, which significantly limits the time and number of diagnostic sessions, which does not allow measuring

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Published online: 02 September 2017

dynamic properties of digestion [2]. MRI, in turn, is not limited by the radiation dose on the object of study. It has only specific absorption rate (SAR) limitation for tissues, which is less strict [3].

The problem of obtaining proton MRI (^{1}H-MRI) of GI tract is a strong ^{1}H-nuclear magnetic resonance (NMR) signal produced by the surrounding tissues of abdomen. To solve this problem, contrast agents based on gadolinium chelates (Magnevist®, Gadovist®, etc.) were implemented [4]. Their effect is based on changes of relaxation times of tissues, mainly pathological, leading to change of the contrast on T1-weighted images. However, it could not help in food visualization because it is hard to interpret small low-signal areas on MR images of abdominal cavity. For this, an unequivocal method is needed.

In case of fluorine-19 NMR signal registration (^{19}F-MRI), there is no background signal from other tissues, because fluorine-19 nuclei are almost absent in the living organism [5]. On the other hand, there are organofluorine compounds—perfluorocarbons (PFCs), in which hydrogen atoms are substituted by fluorine atoms [6]. These substances are chemically and biologically inert and in an undiluted condition give a strong ^{19}F NMR signal [7]. Thus, in vivo ^{19}F MRI represents localizations related only to injected PFCs. Anatomical correlation can be made by algebraic addition of ^{1}H MR images, obtained in the same region.

Perfluorodecalin (PFD) was chosen as a contrast agent, because it was previously probed in studies with animals [8]. Besides, it is the main fluorine containing component of the drug Perftoran®, permitted for clinical trial in Russian Federation [9].

In this article, the possibilities of in vivo ^{19}F MRI food visualization in laboratory animals are discovered. As a contrast agent, any liquid PFC providing strong enough NMR signal could be used. For experiments with PFD, we suggest to apply the volume scanning pulse sequence RARE (rapid acquisition with relaxation enhancement) with minimal TE between echoes. The required amount of contrast agent depends on the number of food pellets. We determined that seven average pellets absorb 2 ml of PFD. In this way, concentration of contrast agent will constitute approximately 34.8 mM/kg for adult rats. ^{19}F NMR spectroscopy confirmed the absence of a contrast agent in rats in 3 days after injection. The behavior and physiological state of rats did not change after experiments.

2 Materials and Methods

MRI experiments were carried out on 7T MRI scanner Bruker BioSpec 70/30 USR, designed for small laboratory animals (mice and rats). A Bruker birdcage coil was modified for work on both frequencies (proton and fluorine-19).

The central part of PFD ^{19}F-NMR spectrum is wide (25 ppm) and consists of four doublets. Taking this into account, we previously optimized parameters of scanning pulse sequence: 3D spin echo pulse sequence, RARE factor = 8, TR/TE = 500/5.9 ms, slice thickness in coronary projection is 3.125 mm [10]. ^{19}F-MR images were obtained in the coronary projection. The reference ^{1}H-MR images were

Fig. 1 Food for laboratory animals soaked in perfluorodecalin

obtained in the same geometry. Then, ^{1}H- and ^{19}F-MR images were fused (algebraically added) in the ImageJ software.

The main group of subjects included 10 adult male Wistar rats. They were set on a water diet for 2 days before PFD injection. Dry rodent food was filled with PFD in proportion 2 ml on seven pellets (Fig. 1). MR images were obtained 10 min, 25 min, 3.5 h, and on the following day after preparate introduction. Besides, there were two groups of five adult male Wistar rats each one. The first group got 2 ml PFD oral administration.

These experiments were performed in accordance with Russian and international regulations: the order of the Health Ministry of the Russian Federation No. 708n dated January 23, 2010 "On approval of the rules of good laboratory practice" and the document "Guide for the Care and Use of Laboratory Animals" [11]. The main criteria in the evaluation of the general state of animal health were behavioral factors, the appetite, color of skin, mucous membranes condition, cleanliness, absence of visible signs of disease.

3 Results and Discussion

Dry pellets are used typically as food for laboratory animal. Due to its composition, each pellet can absorb a huge amount of liquid. In our study, we soaked pellets in PFD—a food tracer for ^{19}F-MRI. For this, dry rodent pellets were submerged in the container with PFD for 1 min. Thereafter, they were brought from the container to the box with rats. The rats were kept on a water diet for 2 days before experiment. Being hungry, the rats ate the food given to them. Although it was hard to make laboratory animals to eat food with chemical compounds, this problem is not expected in clinical studies.

In vivo ^{19}F-MRI food tracking was successfully performed in all subjects. The digestion process was traced during the first day after introduction. Figure 2 represents ^{19}F-MR images of rats in 10 min, 25 min, 3.5 h, and on the following day after the subject took in seven pellets.

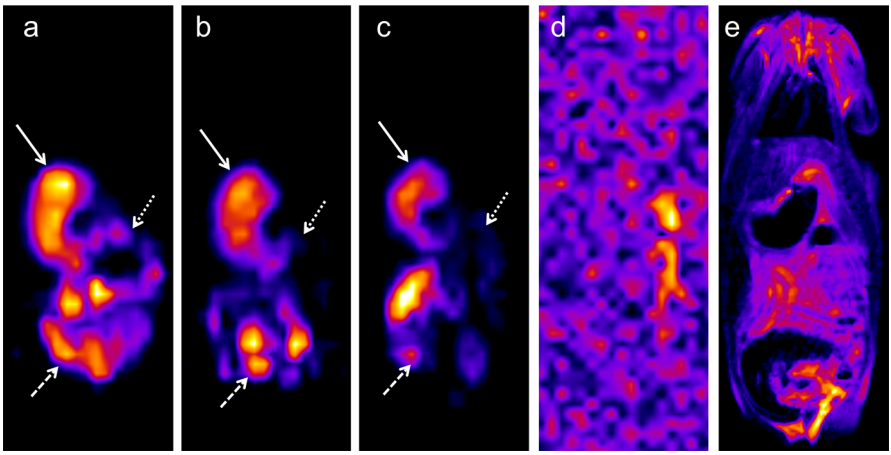

Fig. 2 ^{19}F-MR images of rat obtained in 10 min (**a**), 25 min (**b**), 3.5 h (**c**), on the next day (**d**) after receiving seven pellets soaked in PFD. **e** Reference ^{1}H-MR image. The *solid arrow* indicates stomach, the *pointed arrow* duodenum, the *dashed arrow* small intestine

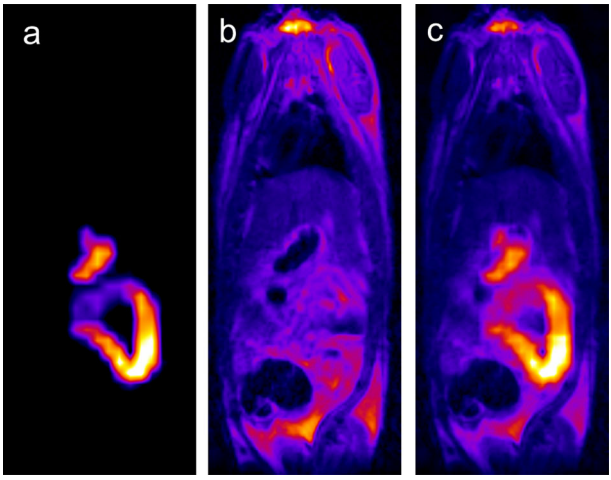

Fig. 3 **a** ^{19}F-, **b** ^{1}H-, **c** ^{19}F + ^{1}H-MR images of rat obtained in 10 min after 2 ml PFD perioral injection

The results of the experiments show that introduction of food with contrast agent inside it provides unique information about digestion process in GI tract, as compared with MR images obtained after perioral administration of liquid fluorinated substances (Fig. 3). Unlike liquids, food fills digestive organs more tightly—particularly noticeable 10 and 25 min after injection. At Fig. 2a the stomach, duodenum and small intestine are clearly located. After 3.5 h ^{19}F NMR signal from the PFD is still retained in the stomach, duodenum and small intestine. The next day, ^{19}F NMR signal from the PFD is almost not observed (Fig. 2d).

Thus, using a simple technology with soaking dry food in liquid contrast agents (e.g., PFD), highly detailed ^{19}F-MRI images of the internal organs of GI tract could be obtained, especially for stomach, duodenum and small intestine. Moreover, it is possible with this technique to observe in vivo the natural digestion process, to quantify the amount of remaining food in the digestive tract after absorption, as well as to evaluate the functional capacity of the digestive tract. From a medical point of view, this method is certainly promising.

Acknowledgements The study was carried out on the equipment of the MSU Collective Using Center "Biospectrotomography" and supported by RFBR grant No.17-02-00465-a.

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