In-vivo ^{19}F Imaging of 5-Fluorouracil and its Metabolites in Rat by Two-Element Phased-Array Coil

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Introduction

^{19}F-MRI/MRS has been used in drug-distribution studies of ^{19}F-contained drugs and other ^{19}F-labeled compounds [1-2]. In the drug (e.g. anticancer drug 5-fluorouracil, 5-FU) therapy evaluation by using MRI, it is necessary to obtain not only the drug but also its metabolites images [2-4]. For 5-FU therapy evaluation, we developed a ^{19}F/^{1}H MRI system using a transmit/receive double-tuned RF coil [5], However, the coil sensitivity was not high enough for monitoring the metabolites of 5-FU in tumors. To improve the coil sensitivity in the region of a tumor, we have thus developed a ^{19}F two-element phased-array coil with a transmit ^{19}F/^{1}H dual-tuned linear-birdcage coil. Using this coil, we demonstrated imaging of 5-FU and its metabolite in tumor-bearing rats at 7 T.

Materials and Methods

The developed coils are shown in Fig. 1. For the receive coil, a ^{19}F two-element phased-array coil is used. It is constructed of 2-mm-diameter copper wire on an acrylic half pipe with diameter of 80 mm (Fig. 1A). The size of the two surface coils is 55 × 40 mm. For the transmit coil, a ^{19}F/^{1}H dual-tuned liner-birdcage coil is used. It is constructed of 10-mm copper tape on an acrylic pipe (112 mm in diameter and 200 mm in length) (Fig. 1B).

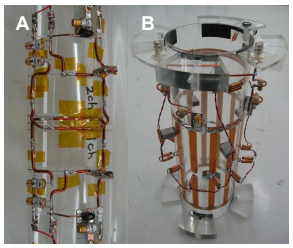

Fig. 1. Developed RF coils. **A:** ^{19}F two-element phased-array coil**; B:** ^{19}F/^{1}H-dual tuned linear birdcage coil.

In an animal experiment, female Wistar rats (body weight: 190 g) bearing Walker 256 tumors were used. The rats were anesthetized with 2-4% isoflurane administered in combination with 30% O_2 through a mask. ^{19}F and ^{1}H MRI images were obtained after intravenous bolus injection of 250-mg/kg 5-FU (Kyowa Hakko Kirin, Japan) into the rats. 5-FU is a metabolic antagonist that is converted into active metabolites (fluorinated nucleosides and nucleotides, Fnuc) and catabolites (α-fluoro-β-alanine, FBAL) in cells by enzymes. These substances contain one fluorine atom in each molecule and have different chemical shifts. The experiment was performed on a 7-T animal MRI system (MRI System, Varian, USA). To obtain the time courses of 5-FU and its metabolite distribution images, ^{19}F coronal images were obtained cyclically after injection by using fast spin echo with frequency-selective pulses of 3-ms Gaussian-shaped pulses, FOV of 400 × 100 mm, matrix size of 64 × 16 without slicing, TR/TE of 1000/7 ms, and ETL of 4. Chemical shifts of 5-FU and its metabolites were selected and interleaved within TR: +5 ppm for Fnuc, 0 ppm for 5-FU, and –19 ppm for FBAL. ^{19}F Imaging was performed about 240 minutes after injection of 5-FU. All ^{19}F images were obtained as 10-minute averaged values. ^{1}H T1-weighted coronal images were obtained by using spin echo, FOV of 200 × 200 mm, matrix size of 256 × 256, 4-mm slicing, and TR/TE of 600/10 ms. ^{1}H T2-weighted coronal images were obtained by using fast spin echo, fat saturation, FOV of 200 × 200 mm, matrix size of 256 × 256 without slicing, TR/TE of 4000/96 ms, and ETL of 16. This projection of a T2 image was obtained to confirm the shape of the tumor obtained by the projection image. All animal studies were conducted in accordance with guidelines for the care and use of laboratory animals.

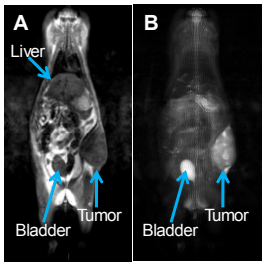

Fig. 2. Anatomical images of the rat. **A:** Slice of T1 SE coronal image; **B:** Projection of T2 FSE fat-saturated coronal image.

Results and Discussion

Figure 2 shows ^{1}H images of a Walker-256-tumors-bearing rat obtained with the transmit coil 250 minutes after injection. These images show that the subcutaneous inoculation of tumor is in the left thigh. Figure 3 shows the time courses of 5-FU, Fnuc, and FBAL distribution images (color), which were overlaid onto the ^{1}H image (Fig. 2A) of the rat. The 5-FU signals were obtained mainly in the liver, kidney, tumor, and bladder regions, and they decreased gradually (with the exception of the bladder). Fnuc signals were obtained only in the tumor region, and the Fnuc image at 90 minutes looks like the shape of the tumor shown by the ^{1}H-T2 image. FBAL signals were obtained mainly in the liver, kidney, and bladder regions, and these signals were increased gradually. The mean signal intensities in the region of the tumor tissue were calculated and plotted (Fig. 4). This graph shows that the signal intensities of 5-FU, Fnuc, and FBAL dramatically changed during the experiment. It suggests that 5-FU was metabolized to Func in the tumor. This result suggests that the efficacy of the anticancer drug 5-FU can be expected. The results of this experiment suggest that the developed ^{19}F two-element phased-array coil facilitates metabolite imaging, and a phased-array coil with more elements has the potential to increase the sensitivity of 5-FU and its metabolite imaging.

Conclusion

We demonstrated that a ^{19}F two-element phased-array coil can be used to obtain the time courses of 5-FU, Fnuc, and FBAL distribution images in Walker-256-tumor-bearing rats. The obtained 5-FU and its metabolite images indicate that the ^{19}F multi-element phased-array coil will make small-animal studies possible in drug research.

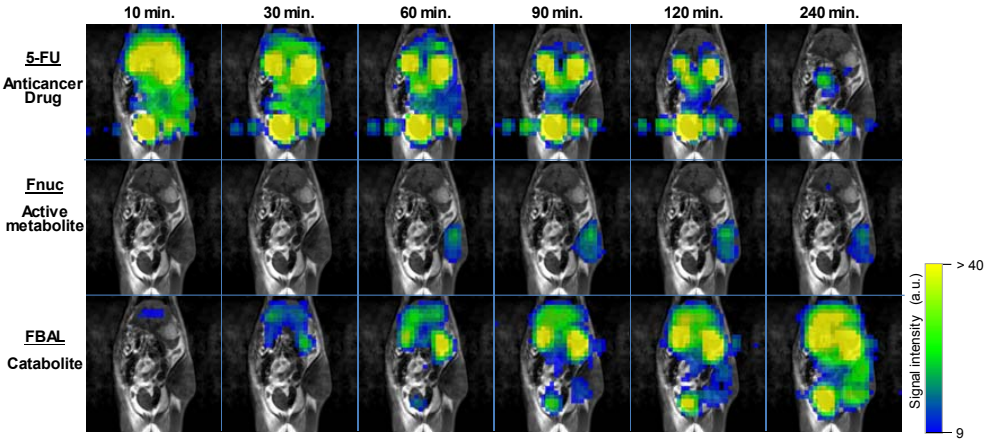

Fig. 3. Time courses of 5-FU, Fnuc, and FBAL distribution images (color), which were overlaid onto the ^{1}H image (gray) of the rat after bolus injection of 5-FU. The color scale ranges from 9 to over 40.

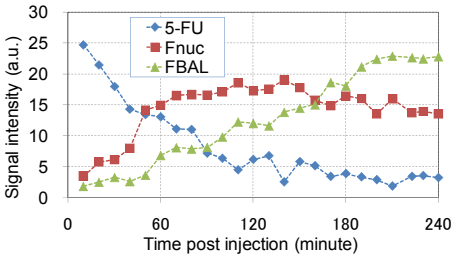

Fig. 4. Plot of signal intensities of 5-FU,Fnuc, and FBAL in the tumor.

Reference

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