Imaging chick embryos with SPIO nanoparticles using SWIFT

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Introduction: Non-invasive imaging techniques, including magnetic resonance imaging (MRI), have been used for studying the dynamics of chick embryo development and growth [1]. This can be repeated observations on the same embryo on a longitudinal basis, using high resolution ultra-high-field (7 Tesla or higher) MR scanners. MRI-based cell tracking using super-paramagnetic iron oxide (SPIO) particles provide an excellent means of cell monitoring in in-vivo [2]. However, SPIO nanoparticles as a T_2* contrast agent are usually associated with signal loss and negative contrast in typical MR images, which may bring difficulties for cell tracking in vivo. Furthermore, differentiation between SPIO nanoparticles and susceptibility artifacts induced by air cavities in a human or animal body is another problem, since air cavities also represent negative contrast. In this work, a novel sweep imaging with Fourier transformation (SWIFT) sequence [3,4] is applied to overcome these challenges and the results are compared with other two conventional pulse sequences such as fast spin echo (FSE) and gradient-recalled echo (GRE).

Methods and Materials: Three MR experiments were conducted using an air-SPIO phantom, an in vivo chick embryo, and an embryo specimen. First, two vials (one empty and one containing aqueous solution of SPIO nanoparticles, 15 nm in size, 125 g/mL in concentration) were embedded into an agar gel phantom. In another experiment, a chick embryo (White Leghorn, at day 12 of incubation) was used for in vivo MR imaging. After in vivo scans, the chick embryo was removed from the eggshell and placed into a container filled with phosphate buffered saline (PBS) solution to make a specimen. Aqueous SPIO nanoparticles suspensions (15 nm in size, 125g/mL) were injected into one eye of the specimen of the chick embryo. Both two-dimensional (2D) and three-dimensional (3D) MR scans were performed using FSE, GRE and SWIFT sequences. Scan parameters were listed in Table 1. All MR images were acquired using a 72 mm ID birdcage coil on a 7T small animal magnet (Agilent, Santa Clara, CA).

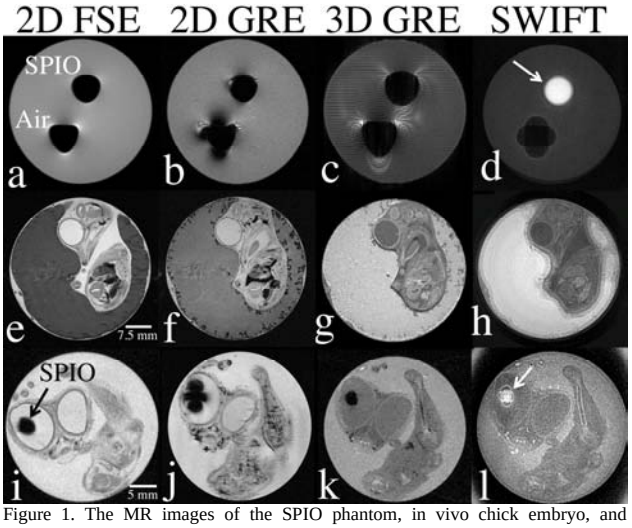

Figure 1. The MR images of the SPIO phantom, in vivo chick embryo, and specimen of the chick embryo are illustrated in the first, second and third rows, acquired with 2D FSE, 2D GRE, 3D GRE and SWIFT sequences (from the first to the fourth columns), respectively.

Results and Discussion: The first row of Fig. 1 shows the MR images of the phantom. By using FSE and GRE pulse sequences, the air cavity and the aqueous solution of SPIO particles are both shown as dark holes in Fig. 1(a-c), which make their differentiation difficult. On the other hand, the SPIO nanoparticles are shown as positive contrast (bright circle) in (d) the SWIFT image, making it a sharp contrast to the air cavity. This is because SWIFT starts to acquire proton signal after only a few microseconds of signal excitation, leading to either a proton density or T_1 weighted image that is immune to signal loss due to short T_2^* values of the scanned material [5]. Anatomical images of in vivo chick embryo are presented in the second row of Fig.1. As shown, for (e) T_2- and (f) T_2^*-weighted images obtained by 2D FSE and 2D GRE sequences, the yolk and organs in the abdomen showed a negative contrast. In the T_1-weighted images acquired by (g) 3D GRE and (h) SWIFT sequences show anatomical details of organs, though the eyes of the embryo appear darker than those in the T_2- and T_2^*-weighted images. Therefore, the T_1-weighted GRE and SWIFT sequences are more suitable for studies of organs in the embryo. Our primary goal is using SWIFT imaging for tracking the stem cells labeled with SPIO nanoparticles, we injected the specimen with aqueous SPIO nanoparticles suspensions in one of the eyes and the images were shown in bottom row. When scanned with (i) FSE and (j-k) GRE sequences, the region of SPIO nanoparticles inside the left eye has a significant signal loss compared with the right eye. In Fig. 1(l), the SPIO injected region appears bright in the SWIFT image of the specimen (indicated with an arrowhead), similar to the results obtained from the phantom study.

	2D FSE	2D GRE	3D GRE	3D SWIFT
Phantom	TR/TE=2000/12ms ETL=8, thk=2mm FOV=40^2mm^2 matrix=256^2 bandwidth=62.5kHz	TR/TE=27/4.6ms =12°, thk=2mm FOV=40^2mm^2 matrix=256^2 bandwidth=50kHz	TR/TE=6.5/3.2ms =12° FOV=50^3mm^3 matrix=256^3 bandwidth=62.5kHz	TR=6.5ms, =12° FOV=50^3mm^3 matrix=512^3 spokes= 96000 bandwidth=62.5kHz
In vivo embryo (egg)	TR/TE=3500/52ms ETL=16, thk=1mm FOV=55^2mm^2 matrix=512^2 bandwidth=100kHz	TR/TE=1000/17ms =60°, thk=0.3mm FOV=55^2mm^2 matrix=512^2 bandwidth=50kHz	TR/TE=5/2.3ms =10° FOV=70^3mm^3 matrix=256^3 bandwidth=62.5kHz	TR=10ms, =8° FOV=70^3mm^3 matrix=512^3 spokes= 128000, bandwidth=62.5kHz
In vitro embryo (specimen)	TR/TE=4000/44ms ETL=16, thk=1mm FOV=40^2mm^2 matrix=256^2 bandwidth=100kHz	TR/TE=1000/20ms =60°, thk=1mm FOV=35^2mm^2 matrix=512^2 bandwidth=50kHz	TR/TE=10/5ms =20° FOV=40^3mm^3 matrix=256^3 bandwidth=100kHz	TR=10ms, =10° FOV=40^3mm^3 matrix=512^3 spokes= 128000, bandwidth=62.5kHz

Table 1. The scan parameters for the pulse sequences that were used to acquire Figure 1.

In summary, the T_1-weighted anatomical scans of the chick embryo were performed using the SWIFT sequence, which demonstrated an equivalent image quality and resolution compared with the traditional FSE and GRE sequences. Additionally, the SWIFT sequence demonstrated its advantage in scanning materials with a short T_2^* value, such as SPIO nanoparticles, and it also allows for a better visualization of some anatomical details than traditional sequences. The positive contrast of the SPIO nanoparticles generated by SWIFT can be easily distinguished from the negative contrast generated by air cavities. This preliminary study provides groundwork for tracking stem cells labeled with SPIO nanoparticles in chick embryos in the future.

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