DIFFUSION WEIGHTED IMAGING OF ZEBRAFISH EMBRYOS USING DEDICATED RADIO FREQUENCY COILS

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INTRODUCTION: Image quality can be enhanced by: (A) improving signal-to-noise ratio (SNR) with an increase in static magnetic field strength [1]; (B) by using strong spatial encoding fields (i.e. magnetic field gradients) to increase resolution; (C) by reducing the size of the radio frequency (RF) coil [2]; and (D) by decreasing the sample size provided the RF coil is ideally positioned near the sample, but this is not always feasible. When these variables are optimized, MR images with isotropic resolution of micro meters (µm) can be achieved [3]. RF coil susceptibility, or magnetic field changes caused by a conductor immersed in a magnetic field, increases with the magnetic field strength, which can be problematic with the use of high-field instruments [4, 5]. Susceptibility based artifacts induced in images appear as signal loss and a reduction in image quality. The extent of which can be as large as the loss of information as a consequence of a signal void. For this reason, different methods have been used to minimize susceptibility artifacts. For example, RF coils have been built using zero susceptibility materials [6], or they were immersed in a solution that matches conductor susceptibility [7]. In addition, specifically made susceptibility matched liquid plugs have been employed to fix samples in the imaging region of the RF coil [8]. Such approaches reduce susceptibility-induced effects, but are tedious, time-consuming and often impractical for use in general imaging applications. The aim of our work is to create dedicated solenoid RF micro-coils, for imaging of very small samples (< 1mm^3). While the acquisition of micron resolution MR images of various samples has been achieved before, the evaluation of coil configuration and materials used is lacking [9]. In this study, we tested seven different 1.4mm diameter RF solenoid coils built using different conductors and coatings. We quantitatively analysed the impact of susceptibility of the various RF coils using images acquired on a 16.4T MRI scanner. Finally, we used our coil to acquire high-resolution MR diffusion-weighted images of zebrafish embryos. Zebrafish embryos are important models for vertebrae and drug development, because they are transparent during early development and can absorb chemicals from water [10].

METHOD: Seven coils with a diameter of 1.4mm were built using various conductors and coatings. Different wires had enamel, polyurethane, silver and Teflon (HFTE) coatings. The conductor diameters varied between 0.10mm to 0.49mm. Coil specifications are provided in Table 1. These conductors were chosen as they have different susceptibilities and signal carrying properties as determined by their skin effect [11]. The glass tubes were filled with a liquid comprising 80% deuterium (D_2O), 20% water (H_2O) and 0.1% copper sulphate ($CuSO_4$). Instead of water, our samples mainly included deuterium to avoid signal saturation. $CuSO_4$ was added to shorten relaxation times; this allowed a reduction in scan times. The glass tubes filled with the liquid were centrifuged for a few seconds prior to solenoid fixing to remove air bubbles, which can otherwise lead to large unwanted air-material susceptibility artifacts.

Coil	Diameter (mm)	Conductor (coating)	Mean SNR	Max CV [%]	SD of CV
1	0.30	copper (enamel)	73.33	2.62	0.54
2	0.10	copper (polyurethane)	113.64	4.12	0.15
3	0.14	copper (uncoated)	61.27	4.82	0.04
4	0.18	copper (HTFE)	66.53	4.99	1.04
5	0.25	silver (enamel)	88.94	5.92	1.22
6	0.11	silver (enamel)	61.51	3.29	0.14
7	0.49	composite (matched)*	76.22	8.08	2.19

Table 1. The specifications of the various 1.4mm solenoid RF coils. Coil number two provided the best performance, as measured by SNR, coefficient of variation and how it varied across contiguous image slices. We also used a susceptibility matched (*) wire as used for high-frequency Bruker Biospin RF coils.

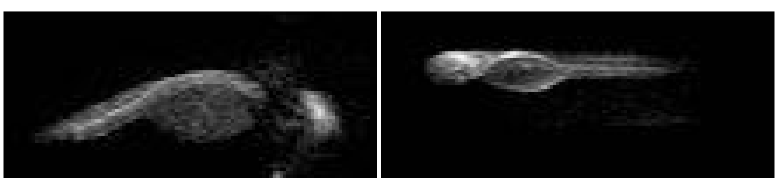

Figure 1. Diffusion images of zebrafish embryos (left) 24 hours and (right) 48 hours post fertilization obtain with coil number two. Images have a 33 micron isotropic resolution.

Data acquisition: Raw MRI data of the liquid mixture was acquired using all coils using a 16.4T Bruker® scanner interfaced to a computer running Paravision version 4 [12]. For coil performance analysis a spin echo sequence was used: T_R = 500ms, T_E = 11ms, matrix size = 256×256, slice thickness = 0.2mm, bandwidth = 50,000Hz and FOV = 1×1cm². Three-dimensional contiguous data with a field-of-view of $0.4456 \times 0.1604 \times 0.1604$cm^3 was acquired for the zebrafish embryos. The standard scanner supplied diffusion sequence was used without acceleration and with the following parameters: matrix size = $128 \times 48 \times 48$, TE = 15.1404ms, TR = 700ms, number of averages = 5 and bandwidth = 50,000Hz.

Embryo preparation: Embryos were embedded in 0.7% low-melting temperature agarose (NuSieve GTG Agarose from FMC BioProducts, Rockland, ME) and 0.2% triciane in a medium comprising 5mM NaCl, 0.17mM KCl, 0.33mM $CaCl_2$ and 0.33mM $MgSO_4$. The embryo in agarose was placed in the end of a 145mm glass pasteur pipette. Approximately a 12-15mm length of the glass pipette end was cut off, with the embryo in the middle, before insertion in the RF coil and then the scanner.

Data analysis: The reconstructed images, saved as digital imaging and communications in medicine (DICOM) files, were used to calculate the SNR with our in-house MATLAB® program [13]. We quantified SNR and the impact of susceptibility to find the coil with the best performance. For each coil the SNR map was calculated, and in the analysis, we considered various regions of interest (ROIs) across the liquid sample. The SNR map is an indicator of coil sensitivity, and the signal variation across different ROIs can be used to assess performance. To establish spatial variations across an image slice, the standard deviation (SD) of the SNR map was calculated for each slice. Furthermore, we computed the SD of the coefficient of variation (CV) between image slices, to assess variations across the sample. Together, these measures allowed us to quantify the influence of conductor material and diameter on the SNR and coil uniformity.

RESULTS: In Table 1 we highlighted coil number two, which has the largest mean SNR and a reasonable CV. Given the three levels of analysis, we concluded that a copper conductor with polyurethane coating provides the best performance out of materials tested. We used the copper (polyurethane) coil to acquire high-resolution diffusion images of 24 hour and 48 hour zebrafish embryos, which we illustrate in Figure 1. We were able to achieve around 30 micron isotropic resolution, enabling visualization of the clearly visible developing spinal cord in the 24-hour embryo. The ability to image embryos with this level of detail can possibly provide a tool to test the efficacy of pharmacological compounds.

References

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