A method to improve the quality of diffusion MRI with rapid histological correlation in a murine model

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TARGET AUDIENCE: Researchers who are interested in preclinical MRI or diffusion MRI.

PURPOSE: MRI of small animal models is used extensively in biomedical research. The interpretation of functional imaging is important for monitoring the tissue microenvironment in vivo. However, correlating MR images with tissue samples is challenging because of the distortion of MR images and the differences in section orientation. Diffusion MRI is susceptible to the inhomogeneity of the magnetic field, resulting in signal loss and geometrical distortions. Optimal cutting temperature (OCT) compound is a water-soluble embedding medium that consists of glycols and resins to be used as a specimen matrix for cryostat sectioning. In this study, we embedded part of an animal in OCT prior to MRI examination to improve field inhomogeneity and reduce the geometric distortion in diffusion MRI. Simultaneously, animals embedded in OCT can be sectioned directly for histological examination in an orientation that matches the imaging plane.

METHODS: MRI experiments were performed using a 7-Tesla animal MRI scanner (ClinScan, Bruker). ***Phantom experiment:*** A cubic phantom with 1.2% agarose gel was examined to analyze the effect of OCT on the field inhomogeneity. To mimic areas with susceptibility differences, a fixed air bubble was introduced inside the gel. The MRI of the phantom was acquired for three conditions: stand-alone, embedded within Fluorinert (a proton-free perfluorinated electronic liquid),[1] and embedded within OCT. Diffusion-weighted imaging (DWI) was acquired using a single-shot EPI technique with b-values = 0 and 1000 s/mm^2. The B_0 field maps of the corresponding slices were obtained using a gradient dual echo sequence (TR/TE=1000/ 7 and 10 ms). Field inhomogeneity was calculated from the phase difference between the images with different TEs. [2] ***Animal experiment:*** Six mice with transgenic mouse prostate adenocarcinoma (TRAMP)-C1 implanted underwent MRI experiments. Animal was placed prone on a board, which served as a guide for the coronal plane for both the MRI and tissue section. OCT embedding was performed by covering the lower half of the animal in a polypropylene container filled with OCT (Fig. 1). DWI was acquired with identical imaging parameters with the phantom study. Transversal and coronal planes were obtained with continuous slices to cover the entire tumor. The coronal images were prescribed parallel to the plastic board on which the animal rested. Anatomic MR images were acquired using a turbo spin echo T2 weighted (TSE-T2W) sequence. The extent of the geometric distortion was quantified by calculating the overlap percentage between the ADC and TSE-T2W images. ***Tissue section:*** Following MRI experiments, the mice were immediately snap-frozen in liquid nitrogen. The sectioning plane of the tissue was orientated in parallel with the board, which corresponded to the coronal MR images

RESULTS: Fig. 2 shows strong field differences surrounding the air bubble and edges of the phantom, resulting in severe shape distortions in the corresponding DWI. When embedded in Fluorinert, the shape distortion along the edge of the phantom was reduced; however, the distortion and signal dropout remained prominent near the air. Homogeneous B0 fields were identified following OCT embedding, which reduced the distortion along both the edges and the air in the corresponding DW images. Fig.3 shows that the overlay percentages between the ADC and TSE-T2W images for the animals with the OCT envelope were significantly greater than those for the animals without the OCT envelope in both the axial (93.3 ± 2.6% vs. 82.3 ± 2.6%; p = 0.031) and coronal planes (87.4 ± 1.9% vs. 74.2 ± 2.4%; p = 0.031). Fig.4 shows that following OCT embedding, the distortion in DWI was reduced, which corresponded well to the TSE-T2W images. The histological specimens of the OCT-embedded animals were visually complementary to the coronal planes of the DW images in a slice-to-slice fashion at the matched depth.

DISCUSSION: We have demonstrated that the use of an OCT envelope reduces the geometric distortion in diffusion MRI and simplifies the coregistration of the images and histological specimens in an animal model. The proposed method is straightforward and robust for use in preclinical MRI, which might improve the quality of diffusion MRI and simultaneously provide histological information to serve as image biomarkers.

REFERENCES: 1.Neufeld A, et al. Susceptibility-matched envelope for the correction of EPI artifacts. Magn Reson Imaging. 2005;239:947-51.
2. Jezzard P, Balaban RS. Correction for geometric distortion in echo planar images from B0 field variations. Magn Reson Med. 1995;341:65-73

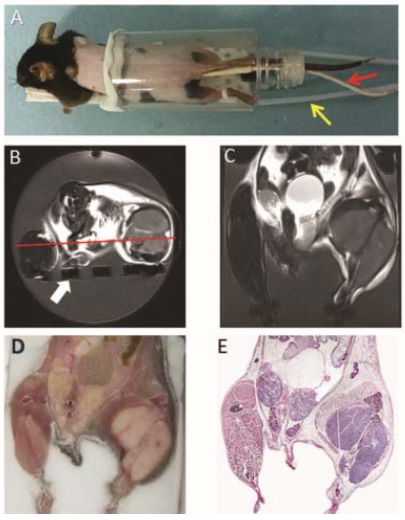


Fig.1. (A) Experimental setup of a mouse placed in a container in which half of the body was embedded in OCT. Red arrow: the rectal probe to monitor body temperature. Yellow arrow: the tube with circulating warm water. (B) Axial T2W image. Red line: the prescribed orientation of the coronal planes, which was parallel to a board (white arrow). (C) Coronal T2W image. (D) Depth-matched tissue section that corresponded to the MRI scan. (E) Histology of the tissue section with hematoxylin and eosin staining.

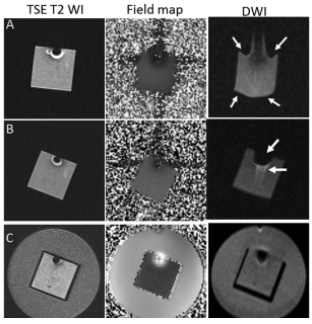
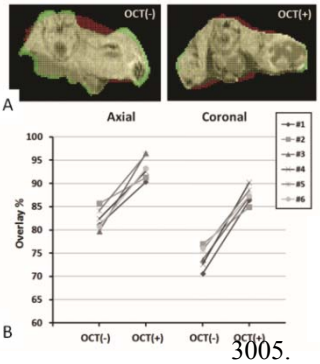


Fig. 2. TSE-T2WI, Field map and DWI of a phantom with air filled. (A) Not embedded. (B) Embedded with Fluorinert. (C) Embedded with OCT. Arrows indicate distortion artifacts.



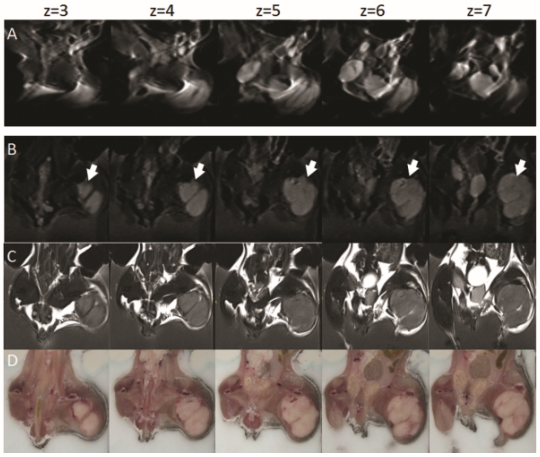


Figure 4. MR images of a mouse and the depth-matched tissue sections. (A) DW images without OCT embedding. (B) DW images after OCT embedding; white arrows indicate the tumor. (C) Anatomical TSE-T_2W images with corresponding slice locations. (D) Tissue section images were matched to the depth of the corresponding MR images. The z numbers represent the acquired slice numbers of the DW images.

Fig.3. (A) Overlay images of the ADC and TSE-T2W images of a mouse. Red and green represent the T2W and ADC images respectively, whereas yellow represents the overlap area of the two images. (B) Comparisons of overlay percentages before and after OCT embedding in axial and coronal planes.