Effect of embedding media on post-mortem MRI of formalin-fixed brain tissue at 7.0 T

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Target audience: Basic MR Researchers, imaging and clinical scientists, radiologists, pathologists, neurologists, ultra-high field experts

Purpose: It is well known that formalin fixation of post-mortem material affects its MR characteristics[1]. It is not clear, however, how image quality and relaxation times of brain tissue are affected by the medium which accommodates the post-mortem material during MR investigation. Previous studies in fixed rat hearts demonstrated that iso-osmotic agarose provides an embedding medium suitable for MR exams[2]. For post-mortem imaging of neurological diseases, quantification of relaxation times and exact delineation of lesions are important. We compared different embedding media for post-mortem MRI of formalin fixed brain slices. Our goal was to analyze whether the embedding medium affects the relaxation times T_1, T_2, and T_2^* of brain grey matter (GM) and white matter (WM) and which embedding medium gives best contrast between GM and WM and best lesion delineation.

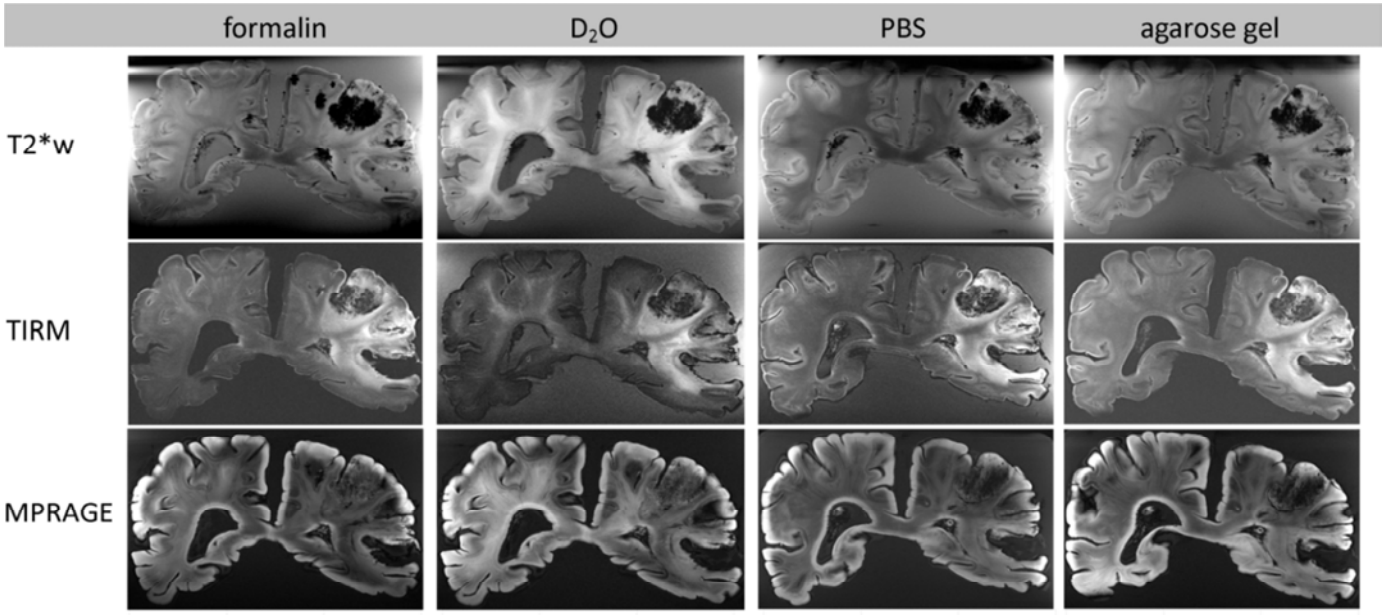
Methods: A coronal brain slice from a patient (female, 82 yrs) with a hemorrhagically transformed ischemic stroke in the left hemisphere, fixated in formalin for 3 months, was used. The brain slice was scanned in 4 embedding media: formalin, deuterium oxide (D_2O), phosphate-buffered-saline (PBS), and 1.5% low-melting point agarose gel prepared in PBS. It was immersed in the particular embedding media 3 hours before scanning and covered by a plexi-glass plate to prevent movement in the fluid during the MR exam. The scanning was performed on a 7.0T whole body MRI system (Magnetom, Siemens Healthcare, Erlangen, Germany). For T_1 mapping a turbo spin echo inversion recovery (TSE-IR) sequence (TE=7 ms, TR=10 s, 7 inversion times logarithmically spaced from 40ms to 5120 ms) was employed. T_1 was calculated offline using a three-parameter fit. For T_2 mapping a multi-echo spin echo sequence (TR=3000 ms, 32 equidistant echoes ranging from 14 ms to 448 ms) was applied. For T_2^* mapping, a multi-echo gradient echo (GRE) sequence (TR=500 ms, α=35°, 7 equidistant echoes ranging from 4.6ms to 47.2 ms) was used. T_2 and T_2^* times were computed online using the scanner software. T_1, T_2 and T_2^* times were averaged over 3 regions of interest (ROI) placed in GM (cortex) and 3 ROIs positioned in the WM of the unaffected hemisphere. High spatial resolution imaging was performed to visually compare GM/WM contrast, image quality and delineation of ischemic/hemorrhagic lesions using: T_2^* weighted GRE (TR=100 ms, TE=15 ms, α=35°, resolution 0.2x0.2x1.5 mm^3, 30 averages, scan time 00:35:14 h), TIRM (turbo inversion recovery magnitude, TR=8000 ms, TE=85 ms, α=128°, TI= 1600ms, resolution 0.3x0.3x1.5 mm^3, 15 averages, scan time 02:36:02 h) and MP-RAGE (TR=2300 ms, TE=4.3 ms, α=9°, TI= 700ms, resolution 0.3x0.3x1.5 mm^3, 15 averages, scan time 4:26:50 h).

Results: All of the embedding media provided images of high quality, as shown in the Fig.1. Differences in relaxation times were observed as surveyed in the table attached to Fig.1. T_1 relaxation times did not differ between embedding media. T_2 relaxation times were lower, while T_2^* relaxation times were higher in GM for PBS and agarose gel compared to formalin and D_2O. There were negligible differences in T_2 and T_2^* relaxation times in WM. The contrast between T_2 relaxation times of GM and WM was similar with all embedding media. The contrast between T_2^* relaxation times of GM and WM was higher with formalin and with D_2O compared to PBS and agarose gel. Visual inspection of the high resolution images showed that delineation of hemorrghagic tissue in T2* weighted images and overall anatomy details in MP-RAGE images were comparable for all embedding media. However, best delineation of ischemic tissue, contrast between GM and WM and least artifacts was achieved with D_2O for the T_2^* weighted GRE sequence and with agarose gel for TIRM sequence.

Discussion: Differences in T_2, and T_2^* relaxation times suggest that embedding media can change MR tissue characteristics of GM, supposedly by means of washing out the free fixative[2]. Interestingly, no changes were found for WM. Contrary to previous results our study did not confirm the advantage of embedding tissue in PBS for the sake of normalizing the relaxation times and increasing the GM/WM contrast[3].

Conclusion: Characteristics of post-mortem brain tissue change with different embedding media. Our results suggest that D_2O provides excellent GM/WM contrast in T_2^* weighted sequences while scanning in agarose gel provides good tissue and tissue-to-lesion contrast with least artifacts for TIRM imaging. Our results suggest that the optimal embedding medium is subject to the sequence used and should be chosen accordingly.

References: [1] Schmierer, K. et al., Magn. Reson. Med., 2008, 59(2), 268–77. [2] Hales, P. W. et al., NMR in Biomedicine, 2011, 24(7), 836–43. [3] Shepherd, T. M. et al., MRM, 2009, 62(1), 26–34.



	GM	WM
T1 (ms)	898±28	771±39
T2 (ms)	70.6±5	83.7±6
T2* (ms)	17.9±6	30.3±3

	GM	WM
T1 (ms)	875±84	738±43
T2 (ms)	67.8±6	81.9±7
T2* (ms)	22.5±4	29.4±4

	GM	WM
T1 (ms)	891±10	841±35
T2 (ms)	58.8±4	76.8±3
T2* (ms)	28.4±2	29.5±3

	GM	WM
T1 (ms)	921±23	766±34
T2 (ms)	58.4±3	71.5±5
T2* (ms)	28.2±3	31.1±5