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Brief Communication

High-resolution 3D-MRI of postmortem brain specimens fixed by formalin and gadoteridol

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ABSTRACT

Purpose: The purpose of this investigation was to compare magnetization-prepared rapid gradient echo (MP-RAGE) images with T1-weighted images (T1WI) and T2-weighted images (T1W2) of postmortem brain tissue fixed by admixtures of formalin and gadoteridol. We additionally sought to explore the feasibility of using fixed brain magnetic resonance imaging (MRIs) in forensic practices.
Methods: Specimens included in the study were eight whole brains that had been removed during forensic autopsy. Brain specimens were randomly divided into three groups and MRIs were performed either (A) the day of autopsy ($n = 2$) on unfixed tissue, (B) after immersion fixation in 20% formalin ($n = 3$), or (C) after immersion fixation in 20% formalin mixed with 4 mL/L ProHance® (gadoteridol) ($n = 3$). T1WI, T2WI, and MP-RAGE images of all group samples were acquired with a 3T clinical MR scanner. Gray and white matter contrasts of the cortex and basal nucleus in every fixation group and image sequence were then visually compared.
Results: Gray/white matter contrasts of the cortex were good in all images obtained by MP-RAGE, and T1WIs of specimens fixed by formalin and gadoteridol-mixed formalin. Additionally, gray/white matter contrast in the basal nucleus was sufficient in the MP-RAGE sequence of specimens fixed by gadoteridol-mixed formalin.
Conclusions: MRI of brains immersion-fixed in formalin and gadolinium could serve as a promising tool for neuropathological assessment in forensic practices.

1. Introduction

In forensic research and practice, various imaging modalities are used to explore postmortem tissues, including roentgenography [1,2], computed tomography (CT) [3–14], magnetic resonance imaging (MRI) [10,11,15–18], and ultrasonography [19,20]. Although whole body CT scans are widely used in forensics to determine the cause of death [4,6–10,14], an eviscerated organ can also be imaged postmortem [21,22]. During a forensic autopsy, pathologists are required to remove and examine the whole brain [23] after a fixation period of 2–4 weeks [24]. MRIs of fixed brain tissue can then be performed in order to complement the autopsy examination [25,26], and to provide a 3D image of the specimen to pathologists.

However, in order to apply MRIs of fixed tissue effectively to forensic practice, it is necessary to achieve a high-quality image, with optimum contrast and resolution; moreover, these images should favorably compare with the cut surface of the brain following sectioning. Currently, the technology available for scanning fixed brain tissue is limited, offering poor contrast and resolution. Therefore, a procedure other than the conventional scan sequence should be considered, such as T1- (T1WI) or T2-weighted imaging (T2WI) and a modified fixation approach.

In the current study, we focused on a method proposed by Johnson et al. [27] in which mice were perfused by an admixture of fixative and contrast medium before postmortem MR scanning. This technique allowed MRIs of the fixed brain to yield high

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contrast and good spatial resolution within a shorter scan time. Although fixation via perfusion can be accomplished on postmortem human brain tissue [28], it is not necessarily a general method used during forensic autopsies since human brains can be adequately fixed by immersion in formalin. Consequently, immersion of postmortem brain tissue in an admixture of fixative and contrast medium should yield optimum MR images when scanned using magnetization-prepared rapid gradient echo (MP-RAGE) sampling [29,30], a technique developed to obtain high contrast brain images.

Here, we demonstrate the feasibility of acquiring high spatial resolution images of human brain tissue immersion-fixed in formalin and gadolinium contrast agent via a 3.0 Tesla clinical MR scanner. The purpose of this investigation, therefore, was to compare MP-RAGE imaging with T1WI and T2WI as conventional techniques used to evaluate postmortem brain tissue fixed by formalin and gadoteridol, and to consider the feasibility of fixed brain MRIs in forensic practice.

2. Materials and methods

2.1. Samples

Eight whole brains were derived from forensic autopsies at the National Defense Medical College and the Tokyo Medical Examiner Office. Causes of death in all cases were lesions that were either thoracic or abdominal in nature. Brain specimens were randomly divided into three groups and MRIs were performed either (A) the day of autopsy ($n = 2$) on unfixed tissue, (B) after immersion fixation in 20% formalin ($n = 3$), or (C) after immersion fixation in 20% formalin mixed with 4 mL/L ProHance® (gadoteridol) ($n = 3$).

In group (A), samples were adequately fixed by 20% formalin after MR scanning. All samples were then sectioned in the coronal plane based on general neuropathology techniques [31] and a photo of every cut surface was acquired.

We obtained approval of our study from the ethics committees of both the National Defense Medical College and the Tokyo Medical Examiner Office.

2.2. MRI

Before performing MRI, we inverted brain samples for 5 min in a plastic bowl filled with water.

The MR apparatus was a Philips' MR Systems Achieva 3T Medical System with an 8-channel head coil. Three sequences were used in this study, and the acquisition parameters are as follows: (1) MP-RAGE: TE = 3.5 ms, TR = 7.8 ms, Slice thickness = 0.5 mm, Matrix = 480 × 480, Flip angle = 8, FOV = 240 × 240 mm, Turbo factor = 384, pixel size = 0.5 × 0.5 mm, (2) T1W VISTA: TE = 12.7 ms, TR = 500 ms, Slice thickness = 1.0 mm, Matrix = 256 × 256, Flip angle = 90, FOV = 256 × 256 mm, Turbo factor = 20, pixel size = 1.0 × 1.0 mm, and (3) T2W VISTA: TE = 124.8 ms, TR = 4000 ms, Slice thickness = 1.0 mm, Matrix = 256 × 256, Flip angle = 90, FOV = 256 × 256 mm, Turbo factor = 85, pixel size = 1.0 × 1.0 mm. Averages in all sequences were one, and the total scan time for one sample was 30 min.

2.3. Image assessment

Nine different combinations between fixation methods (A, B, and C) and MR sequences (MP-RAGE, T1WI, and T2WI) were acquired during MRI. From the data that we obtained, we compared image contrast between gray (GM) and white matter (WM) among the different combination groups. One forensic pathologist with 9 years of experience and one magnetic resonance technological specialist who had 15 years of experience visually and semi-quantitatively evaluated contrast between GM and WM in the cortex and basal nucleus through the mammillary body according to a three level scale (poor, fair, and good).

3. Results

All results are express as means ± standard deviation (SD). Postmortem interval at autopsy was 1.2 ± 0.4 days. Fixation times were 9.0 ± 1.7 days in (B) and 9.3 ± 2.9 in (C).

There were no macroscopic lesions detected in any of the samples (left line in Fig. 1). Coronal T1 W VISTA, T2 W VISTA, and MP-RAGE images through the mammillary body are shown in Fig. 1 as the second line, third line from the left, and right line, respectively. Image assessments between GM and WM contrasts across every fixation and sequencing group are described below.

3.1. T1W VISTA

The images of unfixed brain tissue had high intensity and poor contrast of GM and WM. In addition, it was inevitable that unfixed specimens would become deformed so MR images of slices were asymmetrical. Signal intensities of formalin-fixed brain images were reduced by approximately half in the WM, and slightly increased in the GM compared to unfixed tissue. Consequently, contrasts were good at the cortex and fair in the basal nucleus.

The border between GM and WM could be adequately observed in formalin-fixed brains, and the contrast of images obtained from ProHance and formalin-fixed brains were good at the level of the cortex and fair at the basal nucleus.

3.2. T2W VISTA

In unfixed brain tissue, the signal intensities derived from GM using T2W VISTA were higher than signals from WM, and the contrasts ranged from poor to fair in the cortex and fair at the basal nucleus.

Signal intensities and contrasts of formalin-fixed specimens were qualitatively the same as those of unfixed brain tissue; however, the contrast was qualitatively reduced compared to that of unfixed brains. In ProHance and formalin-fixed brain tissue, the signal intensity in the putamen was high; however, signal intensities in the rest of the brain were low and yielded poor contrast in the GM and WM. Therefore, anatomical identification of areas using this imaging sequence was very difficult in formalin-fixed and ProHance and formalin-fixed specimens compared to when we used the other two sequences.

3.3. MP-RAGE

Using the MP-RAGE sequence, the unfixed brain image produce a reversal of signal intensity between GM and WM compared to all other images. The contrasts were good at the level of the cortex and poor at the basal nucleus. In MRIs of unfixed brain, contrasts of MP-RAGE were highest.

In formalin-fixed specimens, signal intensities in the GM were higher than WM. Additionally, the signal intensities of both GM and WM were increased compared with unfixed tissue specimens. However, signal intensities in the mammillary body, hypothalamus, and caudate nucleus were inappropriately high. Contrasts were good at the level of the cortex and poor in the basal nucleus.

In ProHance and formalin-fixed specimens, GM signal intensities were higher than those of WM, and the contrast of both GM