

Human post-mortem brain phantom as a standardization model for multicentre MRI studies

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Introduction

Multicentre MRI studies are essential for enrolling large and diverse patient cohorts, as required for the investigation of heterogeneous neurological diseases such as multiple sclerosis (MS). However, intensities and contrasts in conventional T1, T2, and proton density (PD) weighted images are not only related to tissue characteristics, but also depend on various parameters such as the sequences used, the choice of timings (e.g. TR and TE) and the sensitivity profiles of the radiofrequency (RF) coils¹. In general, water phantoms are used for long-term and/or inter-site quality assessment. However, these phantoms hardly mimic the structure, shape, size or tissue types of human brain. The aim of this study was to validate the long-term stability of a human post-mortem brain phantom, as an intra- and inter-site quality measure, using quantitative mapping of T1, T2, PD, and the magnetic transfer ratio (MTR).

Methods

Scans were performed on the brain of a 71-year old woman (cause of death: pneumonia) with a post-mortem interval of 20 hours. The brain was fixated in 4% formalin for 3 months, subsequently washed out for 24 hours using Galdan and embedded in Paraplast. The brain phantom was scanned 6 times over a period of time between 4 and 32 weeks post fixation in Paraplast at a constant room temperature of 21.5°C using a 3T whole body scanner with an 8 channel receive head coil. T1 maps were derived from two 3D spoiled gradient echo (GE) data sets acquired with FLASH-EPI hybrid readout (TR/TE=16.4ms/6.7ms, isotropic spatial resolution of 1mm) and excitation angles of 4° and 24°². Data were corrected for effects of B1 inhomogeneities and residual transverse coherences³. PD maps were derived by correcting the GE data set acquired with 4° for T1 and T2* relaxation effects and inhomogeneities of the receive coil³. T2 mapping was based on fast spin echo imaging (TR=10s, spatial in-plane resolution 1mm, slice thickness 2.5 mm, TE=[17.86,103,120,188]ms). MTR mapping was performed with an in plane resolution of 1mm and a slice thickness of 3mm as described in the literature⁴. The generated T1, T2 and MTR maps were segmented to grey matter (GM) and white matter (WM) masks. Mean values of T1, T2 and MTR in GM and WM masks (averaging across the whole brain) and the PD GM/WM quotient were calculated for each time point. To verify the stability of T1 over time, voxel-based comparisons were carried out for each time interval on the segmented GM and WM maps. These were generated from the T1 maps using SPM8.

Results

Figure 1 shows the time course of average PD, MTR, T1, and T2 values in GM and WM following fixation. MTR, PD and T2 are stable. T1 was found to decrease from 267/236 ms to 234/216 ms in GM/WM within the first 11 weeks after fixation. Over the following 5 months period, T1 values were found to stabilize around 206/180 ms in GM/WM. Calculated statistical *t*-maps from VBM analysis indicate that there were no significant changes of T1 values in GM over time. However, in WM, the voxel-based comparisons indicate the presence of a periventricular rim artefact in the proximity of the right ventricle which reduced in size over time and its effects were found to vanish after 24 weeks following fixation (Figure 2; Table 1).

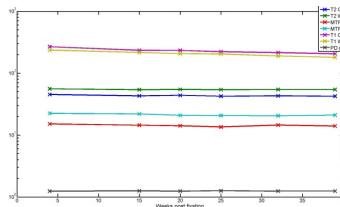


Figure 1: T1, T2, MTR and PD relaxation times plotted overtime.

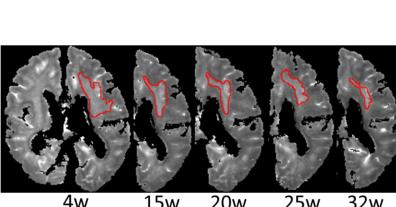


Figure 2: Right periventricular rim artefact in WM. This was found to reduce in size overtime.

Discussion

The post-mortem brain offers similar structural characteristics as an *in-vivo* brain and provides a measurable contrast between GM and WM tissue. Thus, it can be used as a valid model for multi-centre MRI study standardization. Excess dehydration of brain tissue and formalin fixation may account for the observed ongoing slight decrease in T1 tissue relaxation times over time, in particular since T1 times are mainly linked to water mobility⁵. Moreover, we assume that the washout of residual formalin from the brain accounts for the rim artefact viewed in the proximity of the right ventricle. It is unlikely; however, that this artefact interferes with the extraction of volumetric measures from the post-mortem brain as it is restricted to a limited WM region. Therefore, the impact of this artefact on the results of brain tissue segmentation and volumetric extraction should be low. We conclude that brain phantoms prepared in a similar fashion are sufficiently stable starting 4 weeks following fixation in Paraplast to be used for intra-and inter-site standardization.

References

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Weeks post fixation	T1 mean [ms]	#voxels
4	132	825
15	173	570
20	182	528
25	177	480
32	190	276

Table 1: mean T1 and number of voxels enclosed within the observed rim artefact region overtime.