2712
Effects of temperature in the estimation of inhomogeneous magnetic transfer (iHMT) in post-mortem human brain

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Synopsis
Inhomogeneous magnetic transfer (iHMT) is more sensitive to myelin macromolecules than standard MT proxies. Measuring iHMT in the multi-parameter mapping protocol allows calculating iMT from MT saturation (MTsat) maps and thus inherently correct for the undesired dependencies on flip angle and the longitudinal relaxation rate. Further validation of this new iMT metric requires measurement of MPM-based iMT of human post-mortem material. Here, we showed that iMT of a whole human post-mortem brain is feasible but can lead to temperature increase in the specimen, which is particularly pronounced in white matter.

Introduction
Measuring inhomogeneous magnetic transfer (iHMT) in the multi-parameter mapping (MPM) protocol hereafter called iMT-MPM protocol at 3 T, allows us to calculate iMT from MT saturation (MTsat) maps and thus inherently correct for the fluctuation of flip angle, B0 longitudinal relaxation rate and B0. The advantage of iMTsat over MTsat maps is thought to be its direct sensitivity to the phospholipids of myelin. Validation, however, requires further post-mortem experiments using human brain tissue. Such measurements are not restricted to acquisition time and SAR. However, the absorption of the radio-frequency (RF) power by the conductive material inside the specimen causes a temperature increase. This is particularly pronounced in white matter. We acquired iMTsat maps of postmortem human whole-brain specimens. The absence of perfusion leads to measurable temperature increase during the RF intensive iMTsat measurements, which requires measurement of MPM-based iMT of human post-mortem material. Here, we showed that iMT of a whole human post-mortem brain is feasible but can lead to temperature increase in the specimen, which is particularly pronounced in white matter.

Methods
Ex vivo specimen: One post-mortem human brain, without any neurological disease reported (63 years old, post-mortem interval: 18h), was dissected at autopsy with prior informed consent (WF-74/16) and fixed with 4% paraformaldehyde (PFA) in a buffered aqueous solution.

Acquisition: Whole brain imaging was performed on a 3 T PRISMA fit MRI (Siemens Healthcare, Erlangen, Germany) with a Siemens 32-channel receiver head-coil. These images were acquired using the MPM1 protocol, which consists of a B1+ calibration and a 3D echo-spoiled fast low-angle shot (FLASH) sequence with three different signal weightings (T1, T2, MT, and proton density), PD0, that allow the PD0, the FWHM effective transverse relaxation rate (R2*) and MTsat. An MPM-MTM protocol requires the acquisition of four MW images instead, using four pairs of Gaussian subpulses with equal or different frequency offsets (± and –) (Figure 1A). In this work, we also acquired two scans with single MT saturation pulse at opposite frequency offsets (+ and –). This MPM-MTM protocol (T1, T2, PD0, and 6 MW images) was acquired three times with each MT saturation pulse of 1 ms or a single 1 ms duration, a flip angle of 464°, and a frequency offset of 3 kHz, at the same TR of 25 ms. The other imaging parameters are reported in Table 1. Temperature was estimated using the logarithm of the MD. The MD maps were acquired in between MTw images and in between repetitions (the latter with a cool down period of 7.5 min), using a set of diffusion-weighted spin echo images (duration ~1 min at 35% SAR) were acquired (b-values: 0 and 1000 s/mm², 6 diffusion-weighted directions).

Results and Discussion
The log(MD) increases linearly after the acquisition of each MTw image. This increment is observed equally in the outer-specimen solution and in the ventricles (Figure 2A, top plot). As expected, the rate of the log(MD) (Figure 2A, bottom plot) in ROI #1 is approximately constant, since the SAR was kept equal across acquisitions. However, the rate varied strongly in ROI #2, indicating a non-linear heat exchange in the centre of the specimen. The 7.5 minutes pause was not sufficient in cooling down the specimen (log(MD) slope ~0). Importantly, the estimated iMTsat maps increased with increasing temperature (white boxes in Figure 3A and 3B). The highest variance in temperature was observed in WM, with an increment of 10% in the mean iMTsat, from 0.215 to 0.235 μm, and shifted distribution to higher iMTsat values (Figure 3C, second histogram).

Conclusion
We acquired iMTsat maps of postmortem human whole-brain specimens. The absence of perfusion leads to measurable temperature increase during the RF intensive iMTsat measurements, which particularly affects the iMTsat parameters in white matter. Thus, robust postmortem iMTsat measurements require either short acquisition time or extra precaution to control the temperature of the specimen.

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References

Figures
Figure 1: Sketch of inhomogeneous magnetisation transfer (iHMT) protocol and estimation. (A) The MPM protocol is modified such that 4 different magnetisation-weighting images (MW) are acquired using subpulsed pairs with equal and opposite frequency offsets (± and –) and a set of diffusion-weighted spin echo images (duration ~1 min at 35% SAR). Nine subpulsed pairs with opposite frequencies were also acquired (+ and –). From the analysis, R1, R2*, PD0 and PD are obtained and also MTsat for each MTw acquired. (B) The iMTsat map is the difference of two MTsat averages, from equal frequency offsets (+ and –) and from different offsets (+ and –).
Figure 2: Variation of the temperature proxy in the embedding solution of the post-mortem brain. (A) As a heuristic proxy of temperature, the logarithm of the mean diffusivity (log(MD), first plot) and its slope (second plot) are shown across repeated acquisition of MTw-images (dash lines). (B) Two ROIs are covering the specimen's solution: the outer edge (ROI #1, blue curves in A) and in the ventricles (ROI #2, orange curves in A). In both ROIs, the median increases linearly across measurements with a similar slope. The green boxes (in A) represent the 7.5 minutes cool down.

Figure 3: Comparison of the ihMT maps between first and last repetition of the ihMT-MPM protocol. (A and B) The ihMT values increased locally from the first to the last measurements, predominantly close to the ventricles (white boxes). (C) The increased ihMT is observed as a shift of the first histogram (blue bars) as compared to the second histogram (orange bars) in white matter (second histogram). But, it is not observed in grey matter (third histogram) and to a lesser degree in the entire brain (first histogram).

Figure 4: Correlation between ihMT variation and logarithm of the mean diffusivity (log(MD)) due to temperature increase in the post-mortem brain. The estimated median ihMT in white matter (WM) increased linearly with the median log(MD) (R²: 0.984, top plot) in comparison to grey matter (GM), where it is no observable dependency (bottom plot).

Table 1: ihMT-MPM sequence protocol parameters list.