High resolution multi-echo FLASH MRI of fixated human brain with combined magnetization transfer (MT) and T2* weighting

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Introduction

Formaldehyde fixation strongly alters the relaxation times of brain specimens and thus their appearance on standard T1- or T2-w(eighted) MRI (1) while, on the other hand, the amount of structural material is only moderately increased (2). Thus, proton density (PD)-weighted techniques have been widely used as recommended in (3). The drawbacks of PD-w are insensitivity to bleeding, anisotropic voxels (with spin-echo) and or low signals and thus long measurement times. Here, we present a time-efficient high resolution 3D technique based on averaging gradient echoes where PD-w contrast was enhanced by a magnetization transfer (MT) pre-pulse.

Methods

Fixated human brains (>3 weeks in phosphate-buffered saline with 3.7% formaldehyde) were scanned on a 3T Siemens TIM TRIO. Non-infectious specimens were immersed top-down in a bowl and scanned in an 8-channel head receive array, or otherwise sealed in plastic bags placed in a quadrature birdcage knee coil. Care was taken to minimize air pockets during preparation and prevent folding artefacts from overlapping with brain (Figs. 3,4).

First, a T1-w anatomical dataset at 0.8 mm³ was acquired (3D MP-RAGE; TI=600ms) followed by non-selective 3D FLASH MRI (256 axial partitions of 384x384 pixels at 0.5 mm resolution). Eight gradient echoes at TE = 2.46, 4.92, …19.68 ms (500 Hz/pixel) were averaged to increase SNR (4) and yielded the R2* relaxation rate by regression of log signals (not shown). The off-resonance MT presaturation (at +1.2 kHz, 9.984 ms Gaussian, 500°) increased TR from 23 ms to 39 ms. A flip angle of 16° was chosen to increase SNR at the cost of a moderate degree of T1-weighting. Measurement time was 35 mins with 6/8 partial Fourier acquisition in phase and partition direction; 4 averages with quadrature coil. Images were converted to NIFTI format and aligned along the intercommissural line using the T1-w dataset as temporary individual template.

Results

Signal loss at air-water interfaces was observed at long TE (Fig. 1), but ameliorated on the averaged images (Figs. 2-4). The fixation margin was reduced at longer TE, where effects of T1 and T2* relaxation partly cancelled. It showed large individual variations, but could be unequivocally discerned from anatomical features due to its continuous appearance. The PD-w contrast between gray and white matter (GM/WM) was enhanced by application of the MT-pulse (Fig. 2). The average TE of 11ms was sufficient to render major vessels and bleeding sites (Fig. 3) and highly ordered WM tracts (Fig. 4) as distinct hypointensities (5). The contrast of subcortical edema in severe trauma and GM was strongly reduced (Fig. 3). At 0.5mm resolution numerous anatomical details emerged in the basal forebrain (Fig. 3), deep brain, pons and brainstem (Fig. 4). Depiction of cortical substructures in the calcarine sulcus and cerebellar folia were at the limit of resolution (Fig. 4).

Discussion

The multi-echo-averaging approach was even more SNR efficient than in vivo (4), due to rapid T1 relaxation in fixated tissue and the additional TR provided by the MT-module. For comparison, 16 hour measurements have been reported to achieve 0.5 mm resolution with conventional PD-w FLASH (6). The MT-ratio was not calculated, because it has lower SNR and is strongly influenced by T1 at long TR (7). Though the high bandwidth reduces B_0-related distortions, some signal loss was observed at air-water interfaces. Since the early echoes are little affected by T2*, the blooming effect may be reduced by weighted averaging. On the other hand, the sensitivity of averaged signals to residual heme iron may prove useful to address pathology related to bleeding, e.g. for forensic purposes. The effect of micro-bleeds in Alzheimer's disease still needs to be studied and possibly optimized.

References

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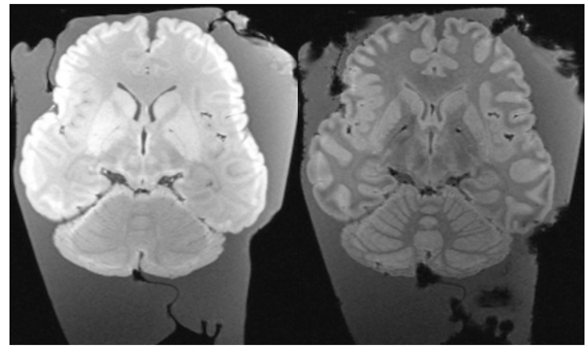

Figure 1: Influence of TE (left: 2.46 ms; right: 19.68 ms, consistent windowing) on brain contrast and air pockets.

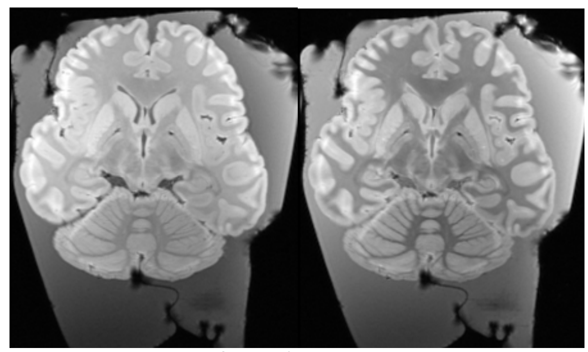

Figure 2: MT-pulse before 16° excitation (right: TR = 39 ms; left: no MT, TR = 23 ms) enhances the PD-w contrast.

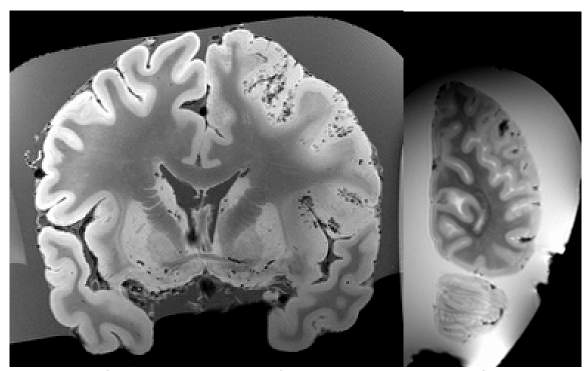

Figure 3: Cortical bleeding after severe trauma (left) and multi-focal septic-ischemic encephalitis (right). Note the structures in basal forebrain and deep white matter.

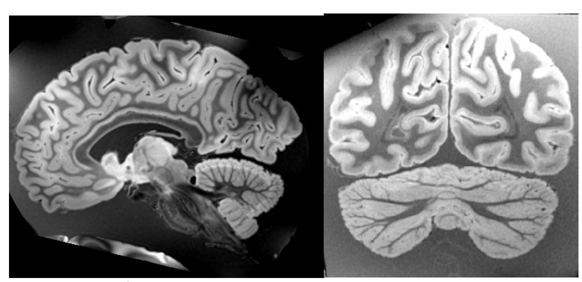

Figure 4: Left: sagittal view showing hypointense tracts and hyperintense nuclei in deep brain and brainstem. Right: The Gennari stria in calcarine sulcus and resolution of cerebellar foliae are faintly visible in coronal view.