T2* and phase contrast in marmoset brain

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Introduction: The common marmoset (Callithrix jacchus) has a gray-to-white-matter volume ratio close to that of humans, making it an ideal nonhuman primate for visualizing, *in vivo* and noninvasively, myelinated structures [1]. Thus, the marmoset has been increasingly studied with MRI. To date, there have been no studies of the soft tissue contrast in marmoset brain using T_2^* and phase information.

Materials and Methods: *In vivo* brain images of anesthetized marmosets were acquired on a 7T/30cm MRI scanner (Bruker-Biospin) using a custom-built birdcage transmission coil and a phased-array receiver coil. Two sequences were performed: three-dimensional (3D), high-resolution, T_1-weighted magnetization-prepared rapidly acquired gradient echo (MPRAGE) with isotropic voxel size = 150 μm^3, and 3D multi-gradient-echo (MGRE) with isotropic voxel size = 300 μm^3, 32 echoes spaced 1.71 ms apart. In one monkey, the MGRE sequence was repeated in 2D mode with higher in-plane resolution (150 μm^2), thicker slices (600 µm) and a different orientation (coronal). T_2^* maps were obtained by a mono-exponential fit over all the echoes. Phase maps were obtained by correcting for phase wrap and by performing a linear fit of the phase variation in the temporal domain. The generated frequency maps were then high-pass filtered by applying a Gaussian filter and subtracting the original frequency maps. Regions of interest (ROIs) were drawn manually in both white matter (WM) and grey matter (GM). Mean and standard deviation (mean ± SD) were calculated in each ROI for both T_2^* relaxation time and frequency values. In addition, an *ex vivo* 3D high-resolution (150μm^3 isotropic) DTI experiment was performed on one fixed brain using the same magnet.

Results/Discussion: Typical T_2^* values in WM (corpus callosum = 22.4 ± 3.8 ms) and GM (cortical GM = 33.4 ± 4.6 ms and deep GM = 36.5 ± 6.9 ms) are close to those reported in human brain at same field strength [2]. Although WM appears homogeneous on T_1-weighted images (Figs 1A, 1E), the posterior WM shows a strikingly heterogeneous pattern on T_2^* images (Figs 1B, 1F). Indeed, the internal part of posterior WM has significantly elevated values (T_2^* = 34.2 ± 6.2 ms) as compared to the edges (T_2^* = 24.4 ± 3.2 ms) interfacing with cortical GM. Such a pattern is also observed on phase images (Figs 1C, 1G) where there is a significant negative frequency shift (up to -3.3 Hz) between the internal part and the edges of the posterior WM. Similar to human brain [3], GM shows a slightly positive frequency shift relative to water (+ 0.3 ± 0.7 Hz). To explain the origin of the observed T_2^* and phase contrasts, different sources can be potentially considered, including fiber orientation relative to the main field [4-5]. As illustrated by the color-encoded FA maps (Fig 1D, 1H), the white matter of marmoset brain has a highly structured fiber architecture, especially in the posterior WM areas. Local tissue composition and microstructure are also other possible sources of contrast [6-7]. Indeed, T_2^* is highly sensitive to the degree of myelination, which typically varies across the cortical GM of marmoset brain (Figs 2A, 2B), especially in the medial temporal (MT) area [8]. Note that gross specimen tissue (Fig 2C) also shows a heterogeneous pattern in the posterior WM, which may suggest the presence of other chemical species (potentially magnetic).

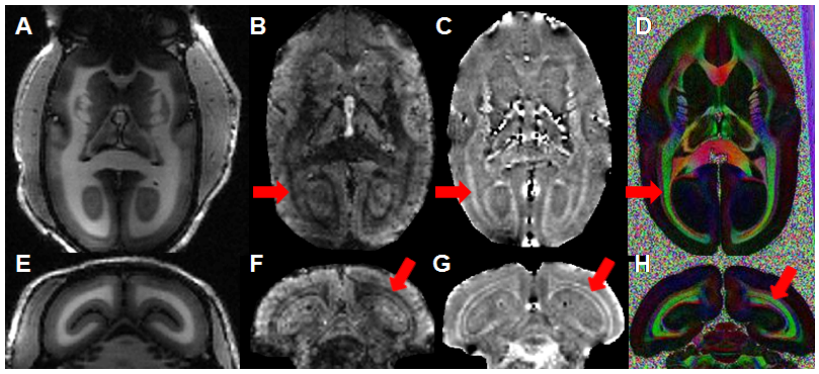

Fig 1: (A,E) T_1-weighted MPRAGE images; (B,F) T_2^* contrast images acquired in 3D mode; (C,G) Corresponding phase contrast images; (D,H) Color-encoded FA maps acquired *ex-vivo*. Top and bottom rows correspond to axial and coronal views, respectively. Red arrows point to posterior WM areas discussed in the text.

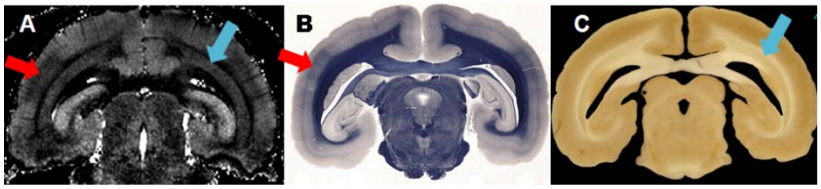

Fig 2: (A) T_2^* map acquired in 2D mode; (B) Weil stain (for myelin) photograph from http://udn.nichd.nih.gov/aboutatlas.html; (C) Gross specimen photograph from http://marmoset-brain.org:2008/ (Tokyo Metropolitan Institute for Neuroscience). Red arrows point to highly myelinated MT area. Blue arrows point to posterior WM areas discussed in the text.

Conclusions: T_2^* and phase contrast were investigated in marmoset brain. A striking heterogeneous pattern, potentially related to fiber orientation, was observed in posterior WM areas. The marmoset brain is therefore an interesting system in which to study the mechanisms of T_2^* and phase contrast.

References: [1] Newman *et al*., Brain Res Rev 2009;**62**:1-18. [2] Li *et al.*, Neuroimage 2006;**32**:1032-1040. [3] Duyn *et al*., PNAS 2007;**28**:11796-11801. [4] Bender and Klose, NMR Biomed 2010; **23**:1071-6. [5] Lee *et al.*, PNAS 2010;**11**:5130-5. [6] Fukunaga *et al.*, PNAS 2010; **8**:3834-9. [7] He and Yablonskiy, PNAS 2010; **32**:13558-13563. [8] Bock *et al.*, J Neurosci Methods 2009;**185**:730-6.