Towards Quantitative Magnetic Resonance "Angstromscopy"

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Introduction: A principle theme in magnetic resonance imaging research has been the quest to visually resolve or discriminate anatomical structures which although being compositionally similar are functionally distinct. One such example are the thalamic nuclei, which despite projecting to differing regions of the cortex and relaying disparate somatosensory, motor, language and other cognitive information are difficult to identify on a typical T_1 or T_2-weighted MR image. Correlation of structure with function, as garnered from functional MRI, positron emission tomography or electrophysiology, would serve to increase our understanding of neuro-development, under both 'normal' and disease conditions. With the proliferation of high field strength (3T and above) scanners combined with purpose-built multi-channel radio-frequency (RF) coil arrays, acquisition of images with voxel volumes less than $1mm^3$ has become commonplace, permitting the discrimination of fine anatomical divisions, such as the Line of Gennari in the visual cortex[1]. While much of this imaging has been performed with conventional T_1-weighted imaging, *quantitative* T_1 mapping has demonstrated additional image contrast between neighboring functionally distinct regions, such as amongst the thalamic nuclei[2], due to the removal of confounding proton density (ρ), T_2, T_2* and RF receive coil effects on the measured signal. The development of rapid T_1 mapping methods, such as Driven Equilibrium Single Pulse Observation of T_1 (DESPOT1)[3] and the associated DESPOT1 with High-speed Incorporation of Field Inhomogeneities (DESPOT1-HIFI)[4] which corrects for B_1^+ field inhomogeneities at high field, T_1 maps can now be acquired with comparable efficiency as conventional T_1-weighted images. Here we explore the present state-of-the-art of *in vivo* quantitative T_1 and ρ "microscopy" performed on a clinical 3T scanner with a commercial 8-channel RF coil arrays.

Methods: With DESPOT1[3], T_1 and ρ are derived from two or more spoiled gradient recalled echo (SPGR) images acquired with constant repetition time (TR) and varied flip angle (α). DESPOT1-HIFI[4] involves the supplemental acquisition of an inversion prepared (IR)-SPGR image with matched field of view (FOV), echo time (TE) and TR. *In vivo* DESPOT1 data were acquired of the same individual with increasing spatial resolution, from 1.2mm to 0.5mm isotropic voxel dimensions. A common FOV of $22cm^2$ x 12.5cm was used with matrix sizes of 184x184x108, 220x220x128, 320x320x184 and 440x440x256. TE/TR/α combinations used for each were: 1.6ms/6.6ms/4°,18°, 1.7ms/6.8ms/4°,18°, 1.7ms/7ms/4°,18°, and 3.2ms/9.7ms/4°,20°, respectively. Multiple averages were acquired of each flip angle to yield imaging times of 12mins,, 27mins, 1hr, and 1.5hrs for each dataset. For the 0.5mm isotropic data, 3 scan session were performed and the results linearly co-registered and averaged. DESPOT1-HIFI IR-SPGR data were acquired with half the spatial resolution in Y and Z as the SPGR data and with an inversion time of 450ms. From the acquired data, voxel-wise T_1 maps were calculated and slices through the thalamus, cerebellum and visual cortex examined and compared with corresponding slices through the T_1-weighted SPGR data,

Results / Discussion: Figures 1, 2, 3 and 4 show representative slices through the *in vivo* ρ and T_1 maps acquired at each resolution through the cerebellum, visual cortex and deep brain. As anticipated, visualization of subtle structures obviously improves as spatial resolution increases. With the cerebellum, for example, (Fig. 1) while the dentate nucleus is visible at the 1.2mm level, partial volume effects make it impossible to fully appreciate the convoluted geometry of the structure, important since, like the thalamus, the dentate is topologically arranged with discrete areas responsible for relaying information to and from different areas of the cerebral cortex. Appreciation of the intricate cerebellum cortex is also improved with increased spatial resolution. Partial volume effects also make it difficult to discriminate the Line of Gennari within the visual cortex (Fig.2), as well as the separation between the internal and external globus pallidus (Fig. 3), which require an in-plane resolution of at least 0.7mm to appreciate. The higher content of myelin in these areas, compared with the surrounding cortex and pallidum results in a significant decrease in T_1, making them readily visible on a T_1 map. Within the thalamus (Fog. 4), additional contrast and structure is noted despite the higher resolution images having reduced signal-to-noise ratio compared with the 1.2mm map.

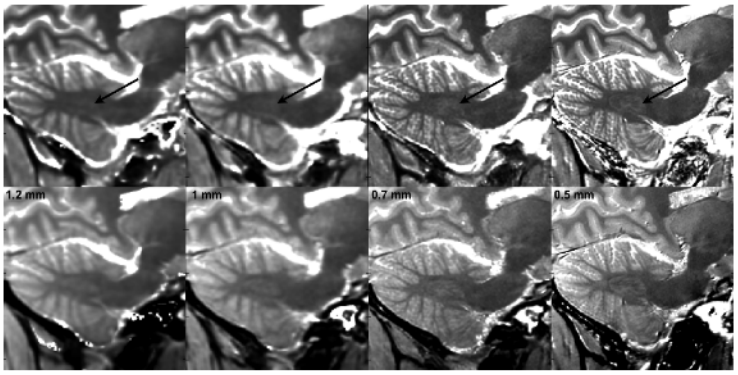

Figure 1: Corresponding slices through the cerebellum T_1 (*top*) and ρ (*bottom*) maps across the different spatial resolutions. Arrows indicate the dentate nucleus.

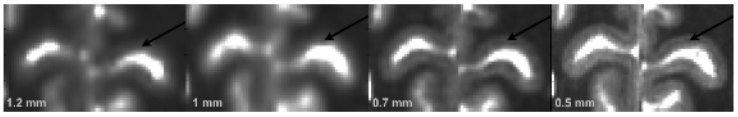

Figure 2: Corresponding slices through the T_1 maps of the visual cortex. Arrows indicate the Line of Gennari which becomes visible at the 0.7mm level.

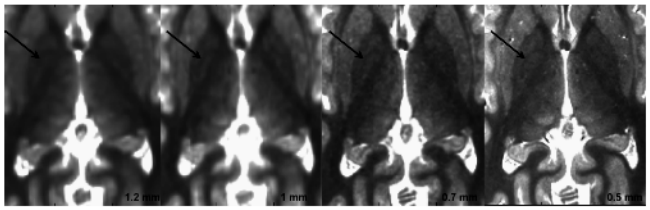

Figure 3: Matching slices through T_1 maps of the deep brain. Arrows indicate a separation between the internal and external globus pallidus, which becomes visible at the 0.7mm level and clearly appreciated at 0.5mm.

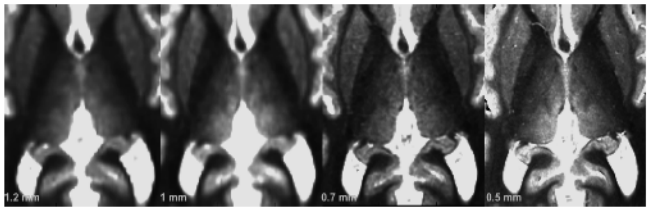

Figure 4: Matching slices through T_1 maps of the deep brain. Despite the reduced signal-to-noise ratio at high resolution, improved contrast and structure are evident within the thalamus.

Conclusions: The utility of quantitative T_1 (as well as T_2 and proton density) mapping in delineating structurally similar neighboring regions has been previously demonstrated within the thalamus[2]. Here we have expanded upon this result, demonstrating its utility in additional brain regions, which, despite having known histological and functional differences have proved difficult to visualize. While the scan time used for the 0.5mm images shown here is clinically infeasible (4.5hrs), we have emphasized the use of isotropic voxel dimensions. Significant reductions in scan times can therefore be realized by decreasing the through-plane resolution whilst still permitting the appreciation of subtle structure, such as the Line of Gennari.

References: [1] Bridge H. Clare S. Philos. Trans. R. Soc. Lond. Bio. Sci. 2006;361:137-146, [2] Deoni SCL. et al. HBM. 2005;25:353-359, [3] Christensen KA. et al. J. Phys. Chem. 1974;78:1971-1977, [4] Deoni SCL. submitted 2007 ISMRM abstract #306.