Cellular-level investigation of a diffusion time dependent contrast enhancement technique for oncological imaging

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INTRODUCTION

Diffusion weighted (DW) MRI is uniquely sensitive to tissue microstructure. DW imaging has been proposed as an enhancement technique for tumors[1], and recently a diffusion-time dependent contrast enhancement technique was used as a means to improve tumor visibility in MRI[2]. The mechanism described is a mixture of effects caused by heterogeneous intracellular T_2—the cell nucleus is assumed to have long T_2 compared to cytoplasm—and where the contributions of contrast enhancement resulting from restricted and hindered water diffusion are separated by subtraction of data acquired at short and long diffusion times. The effects are assumed to be pronounced in tumor tissue because of its high cellularity. Here, we report contrast enhancement in cell-dense areas using high resolution DW MR microscopy data from fixed rat hippocampus.

METHODS

Data were acquired using micro surface coils (res = 12.5 x 12.5 x 50μm). The CA1 pyramidal cell layer was identified under a dissecting microscope and positioned so that its cell-body dense tissue transected the coil's center. This ensured sufficient portions of the adjacent lamina—strata radiatum and oriens—were present for comparison. Slice data was acquired using Pulsed Gradient Spin Echo techniques at multiple diffusion weightings (b = 0.4 – 3.2 ms/μm^2) and diffusion time differences (ΔT_{diff} = 0.25 – 13.0 ms) [3]. Cellularity contrast was achieved as described in [2] by subtraction of the MR signal generated at the shortest possible diffusion time (i.e. the hindered pool) from signal generated at progressively longer diffusion times. This analysis is purported to isolate diffusion signal contrast produced by the restricted water pool.

RESULTS

The cellularity contrast enhancement effect is strongest in the cell-dense CA1 pyramidal cell layer but less evident in the adjacent laminae (Str. Or. and Str. Rad.) (Figs. 1 and 2). Subtracting data sets obtained with the most disparate diffusion times yielded the greatest contrast enhancement. Notably, this effect is stronger than b-value dependency (Fig. 2). In the cases of strata radiatum and oriens, the effect is less pronounced.

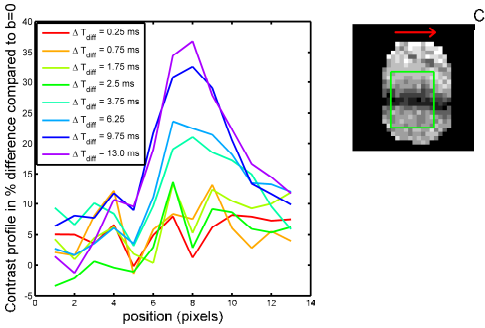

Fig 1. Cellularity contrast observed in hippocampal CA1 lamellae generated using restriction spectrum imaging and the S(Δ)-S(Δmin) method described in [2]. Signal from multiple pixels within the same tissue layer were averaged along the direction of the red arrow. Contrast enhancement is denoted by increasing profile height. The pyramidal cell layer (darkest band, pixels 7-10) clearly generates the most cellularity contrast. Str. Or. = pixels 1-6, Str. Rad. = pixels 11-13

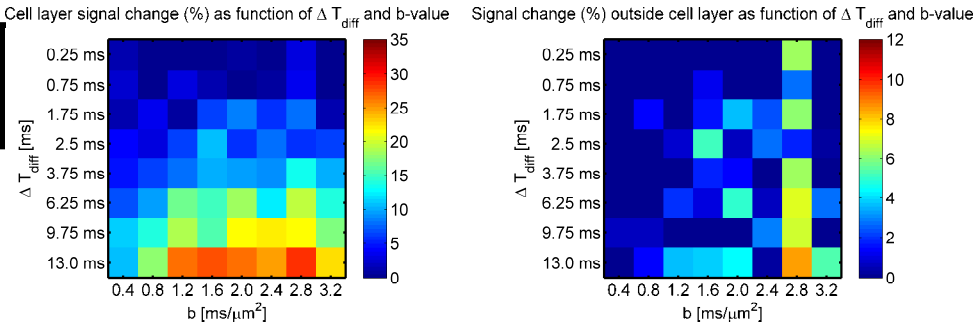

Fig 2. Evaluation of the total signal change observed using the $S(\Delta_1)$-$S(\Delta_2)$ method in the pyramidal cell layer (left map) and the laminae adjacent to the cell layer (stratum oriens + stratum radiatum; right map) as a function of the differences in Δs (y axes) and b-value (x axes). Datasets with the largest difference in Δs yielded the greatest signal enhancement, and this effect was stronger than the b-value dependency. Contrast enhancement was observed to be far greater in the cell-dense stratum pyramidale than in the surrounding, cell-body poor laminae of the strata oriens and radiatum.

DISCUSSION and CONCLUSIONS

The rat hippocampus has a lamellar composition which makes it ideal for applications comparing cell-body dense regions—in this case, stratum pyramidale— to comparatively perikarya poor tissues: the adjacent layers of stratum radiatum and stratum oriens. Its diverse tissue types which lie in close proximity and are delineated by sharp, clearly defined boundaries are well suited to studying tissue heterogeneity in micro-imaging studies limited to small sample volumes. In the present study, the tissue region with the highest cellularity contrast correlates to the hippocampal lamina with the highest density of cell bodies tested: the stratum pyramidale. Our data supports that the contrast enhancement technique presented in [2] for aiding in tumor visualization is highly specific to cell-dense areas.

REFERENCES and ACKNOWLEDGEMENTS

[1] White et al., (2013) AJNR 34:958-64. [2] Hope et al., (2014) Proc. Intl. Soc. Mag. Reson. Med. 22 [3] Portnoy et al., (2013) MRM 69(4):1131-45 Project funded by the NIH (1R01EB012874) and the NSF through the National High Magnetic Field Laboratory.