Quantitative T1sat : Tool for Diagnosis and Characterization of Spheroid Tumors and Detection of Blood-Brain Barrier Disrupted Regions

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INTRODUCTION: In early stages, primary brain tumors are protected by the blood-brain-barrier (BBB); tumor cells infiltrate into surrounding brain tissue, with the BBB blocking delivery of contrast agents for diagnostic imaging and therapeutic agents for treatment. Thus, an MRI modality capable of locating tumorous tissue absent the administration of an MR contrast agent is of potential value. Quantitative magnetization transfer imaging (MTI) offers a probe of the water-to-macromolecular interfaces, the dynamics of which are radically altered in pathology, and provide insight into the biophysical state of water and protein integrity.

METHODS: Athymic rats injected with primary explant fragments from human glioblastomas were studied ~2 months after tumor implantation (n=10). MRI measurements were performed in a 7 Tesla, 20-cm bore magnet. MTC images were acquired from a single 2-mm thick slice (FOV=32 mm, 128x128 matrix). Rapid estimates of T_1, T_{1sat} (T_1 under an off-resonance saturation of the macromolecular pool), K_{for} (apparent forward rate constant) and MTR (magnetization transfer ratio) maps were obtained from composite images using TOMROPS (T1 by multiple read of pulses) [1]. The integrity of the BBB was evaluated by injection of a gadolinium-chelate (Gd-DTPA) contrast media (0.1 mmol/Kg, i.v. bolus) followed by serial T1 measurements at 2.5 minute intervals, again using TOMROPS (TR=50 ms, TE=2.18 ms, 128x64, 24 echoes, 3 slices, 2-mm thick) for 25 minutes. Blood-to-brain transfer constant (K_i) maps of Gd-DTPA and distribution space of Gd-affected protons (V_p) were also constructed from the MRI data using the Patlak plot method [2,3]. MT-defined areas were compared with area of injury from histology.

RESULTS: The spheroid tumors were distinctly manifested as an increased signal on the T_{1sat} map, but **not visible on any of the standard MR imaging modalities**, namely, T2WI, T1WI, DWI, CBF, or in several cases T1 measurements with Gd-DTPA contrast. Tumors were identified in only five of the ten animals studied, as confirmed by histology. Multiple regions of heterogeneous tissue damage indicated by the white, red and yellow regions on the theme map were observed in all tumor-positive animals. The green and blue regions correspond to gray and white matter respectively (Fig. 1). The composite of white, red, and yellow signatures is congruent with the dark area of the in-situ hybridization section. The white and red regions of the theme map had T_{1sat} greater than 1.25 with respect to contralateral normal tissue. These regions corresponded with BBB leakage areas noted on Patlak plot maps. Estimates of K_i and V_p were well correlated with T_{1sat} ($r = 0.91$, $p = 0.03$ for K_i and $r = 0.94$, $p = 0.017$ for V_p).

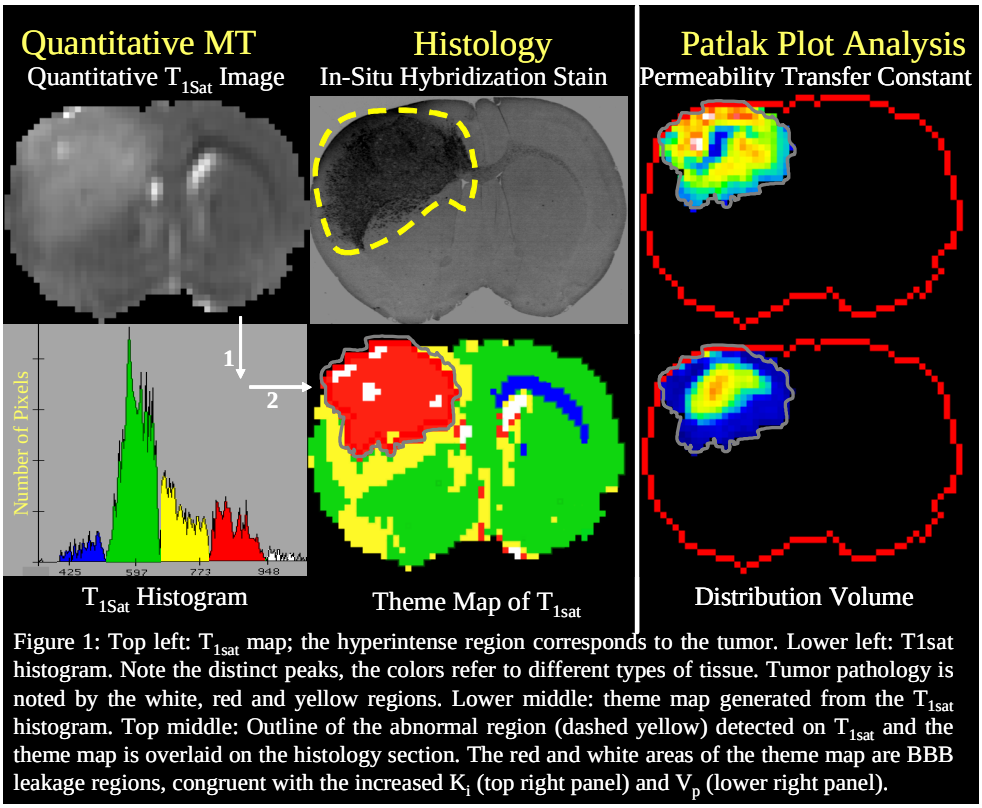

Figure 1: Top left: T_{1sat} map; the hyperintense region corresponds to the tumor. Lower left: T1sat histogram. Note the distinct peaks, the colors refer to different types of tissue. Tumor pathology is noted by the white, red and yellow regions. Lower middle: theme map generated from the T_{1sat} histogram. Top middle: Outline of the abnormal region (dashed yellow) detected on T_{1sat} and the theme map is overlaid on the histology section. The red and white areas of the theme map are BBB leakage regions, congruent with the increased K_i (top right panel) and V_p (lower right panel).

CONCLUSIONS: These results establish the unique and versatile features of quantitative T_{1sat} and MT tissue signatures in early characterization of cerebral tumor pathology. A significant correlation between T_{1sat} and K_i validates T_{1sat} as a surrogate for characterizing tumor vasculature. Further detailed studies are needed to attribute tissue histopathology to individual MT tissue signatures. A single MTI sequence offers the possibility of a "truly" noninvasive, repeatable imaging modality to identify, localize and characterize BBB opening in tumors.

References:

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