Detection of abnormal water exchange rate in brain tumor patients

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INTRODUCTION: Detecting invasive brain tumor regions and assessing their response to potential new therapies that target both tumor angiogenesis and tumor invasion is highly important but complicated by the lack of available methods for detecting the early growth. It has been recently shown that transvascular water exchange and the choice of imaging method and parameters can influence the accuracy and precision of blood volume measurements when using an intravascular $T_1$ contrast agent.[1] In this work, using human tumor patients and clinically available contrast agent (i.e., Gd-DTPA), we demonstrated that a novel water exchange sensitive imaging technique can define new tumor border regions in the brain, otherwise undetectable with conventional imaging methods.

MATERIALS & METHODS: Eight brain tumor patients were scanned using 3T Siemens system (Allegra). 3D images were acquired before and after intravenous Gd-DTPA administration using a multi-echo sequence (TE=[2.46, 4.92, 7.38, 9.84 ms]) with Matrix=112x112x88, voxel=2x2x2 mm, TR=12 ms and flip angles=[10, 20, 75°]. As demonstrated previously, water exchange sensitive images can be acquired using low flip angles as compared to relatively high flip angles. Subtraction images (i.e., $SI_{\text{post\_Gd}} - SI_{\text{pre\_Gd}}$) were created for each flip and analyzed.

RESULTS & DISCUSSION: It was recently shown that transvascular water exchange and the choice of imaging method and parameters can influence the accuracy and precision of blood volume measurements when using an intravascular $T_1$ contrast agent. Typically, studies of fractional blood volume ($V_b$) assume that the exchange rate between compartments is either very high (fast exchange) or insignificant (no exchange). Since most living tissues do not exhibit such extreme exchange characteristics, neither of these assumptions accurately describes the biological system. We predicted that the sources of error in the blood volume measurement could be minimized or amplified by carefully selecting the pulse sequence and calculation methods.

In general, elevated vascular permeability is visible in $T_1$-weighted images acquired following the injection of Gd-DTPA where extravasation of Gd-DTPA into the tumor tissue results in shortened $T_1$ relaxation times and hence an increased tumor signal intensity (see Fig 1a). Subtraction map acquired using a small flip angle further revealed a region with significantly elevated water exchange well outside of contrast enhancing tumor regions (yellow ROI) and may represent an invasive tumor border.