MR Perfusion of Human Brain Tumors Demonstrates Increased Blood Volume in Active Tumor before Static Contrast Enhancement or Permeability.

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Purpose: To investigate the relative sensitivity of changes in blood volume and permeability for detecting regions of actively growing tumor, as derived from applying the extended Tofts model to images from dynamic contrast enhanced MR perfusion studies.

Methods: Pre (N=3) and post-surgical (N=4) patients (male = 4) with known brain tumors underwent dynamic contrast enhancement (DCE) perfusion MR imaging (3D fast SPGR sequence EFGRE3D, slices = 28, acq. matrix = 128 x 128, TE = 1.012 ms, TR = 4.46 ms, flip angle = 12 deg, sampling rate = 9.2 s) on a clinical 3T scanner (MR750, GE Healthcare; Waukesha, WI). High-resolution T2-weighted, T2*-weighted and pre- and post-contrast T1-weighted images were performed for anatomical context. T1 mapping was performed using single volume acquisitions at multiple flip angles (1, 4, 8, 12, and 24 deg). Data were fitted voxel-wise using the extended Tofts model to obtain the blood volume (V_b) and permeability (K_{trans}) parameters. Parametric profiles were measured through the lesions to obtain the geographical distribution of each parameter.

Results and Discussion: As a representative example, **Figure 1** shows a T1-weighted contrast enhanced image from a patient who had a biopsy proven WHO grade II non-enhancing oligoastrocytoma in the right parietal lobe that was followed for 6 years without change until MR perfusion detected progressive increasing blood volume without enhancement. The perfusion properties (**Figure 2**) of the lesion were examined using a profile (**Figure 1**, green line). This lesion did not show any contrast enhancement but the K_{trans} profile (**Figure 2a**) shows a small spike within the center of the tumor that exceeded normal variation (**Figure 2a**, dashed lines). In contrast, the V_b profile (**Figure 2b**) shows increases well above normal variation (**Figure 2b**, dashed line) that extend well beyond the margins defined by K_{trans}. In 6 of 7 cases, the profile of significant increases (5-11% over normal tissue values) in V_b was wider than the profile of increased K_{trans}. In fact, three patients showed no increases in permeability profile when there were increases in blood volume. Histology (**Figure 1b**) of resected tumor confirmed increased blood vessels with normal endothelium in the region of increased V_b on the profile in **Figures 1a**.

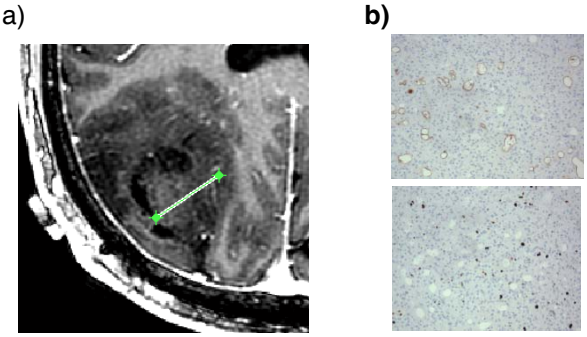

Figure 1: Anatomy (a) of a grade II tumor showing the perfusion profiles used in **Figure 2**. Histological sections (b) showing multiple new blood vessels with normal endothelium (upper) and proliferative cells (lower) within the area of angiogenesis

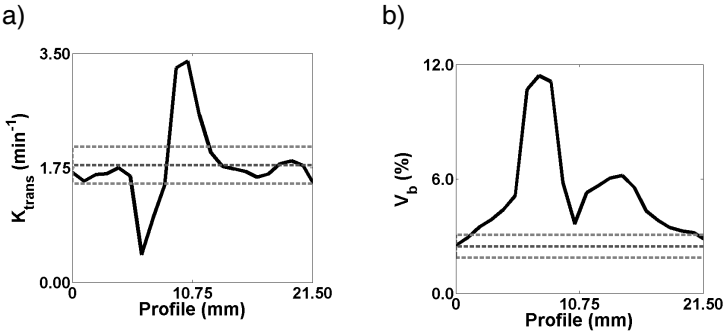

Figure 2: Profile (Figure 1, green line) of permeability (a) and blood volume (b) across a tumor that has been pathologically proved to have progressed from Grade II to Grade III. Grey dashed lines indicate means and standard deviations of K_{trans} and V_b.

Conclusion: This study of brain tumor patients suggests that increased blood volume precedes changes in permeability to better define active tumor margins and progression of tumor grade. Surveillance of tumor growth using perfusion imaging to detect blood volume changes should result in earlier detection of disease progression than conventional contrast enhancement and better define tumor margins.