DSC-MRI perfusion parameters correlate with tumor grade in patients with brain tumors

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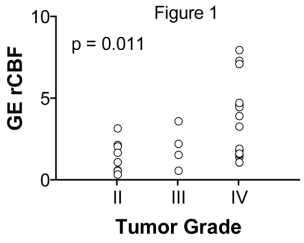
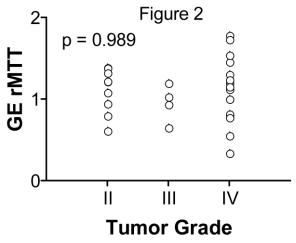
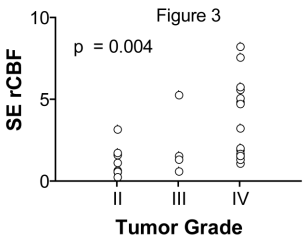
Introduction: Dynamic susceptibility contrast (DSC) MRI methods, which allow the creation of relative cerebral blood volume (rCBV), blood flow (rCBF), and mean transit time (MTT) maps, have the potential to evaluate hemodynamic changes following anti-angiogenic therapy. Using a simultaneous GE/SE EPI DSC method we previously demonstrated that "total" rCBV (GE) and mVD (mean vessel diameter: $\Delta R2^*/\Delta R2$) are predictive of tumor grade, while the "microvascular" rCBV is not unless "hot spots" are exclusively considered (1). Since tumor grade is known to correlate with brain tumor angiogenesis these measurements are reflective of the morphological changes in the tumor vasculature. To better characterize the functional impact of angiogenesis on tumor hemodynamics we now extend the analysis to include measures of GE and SE CBF and MTT. These parameters should provide new insights into tissue perfusion efficiency. In the present study we determine if GE and SE rCBF and MTT measurements also correlate with tumor grade.

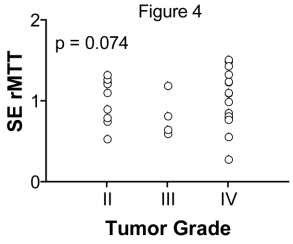
Methods: A total of 250 DSC perfusion studies have been performed to date, with informed written consent, under guidelines approved by the Institutional Review Board at our Institution. Of these 42 patients were used in the previous rCBV study (1). We have completed the perfusion analysis on 28 of these patients. All MRI studies were performed on a 1.5T GE Signa System fitted with a 12" local gradient coil and a quadrature transmit-receive birdcage RF coil (IGC-Medical Advances, Milwaukee, WI). A 0.05-0.10 mmole/kg dose of Gadodiamide (Omniscan; Nycomed Amersham, Princeton, NJ) was administered to diminish T1 effects that might result from agent extravasation. Next, simultaneous GE/SE-EPI images were acquired for 1 minute before and 2 minutes after a 0.15-0.25 mmole/kg bolus injection. Five, 7 mm slices were acquired at TE(GE)/TE(SE) = 30ms/109.1ms with fat suppression, TR=1s, a FOV=24cm and matrix = 64x64. Finally, conventional post-contrast T1-weighted images were acquired (SE, TE/TR = 11ms/500 ms, matrix = 256x256). The GE and SE rCBF and MTT maps, corrected for agent extravasation were determined using the SVD approach (2). Data was extracted from ROIs of the whole tumor (avoiding areas of necrosis) and contralateral brain. All results are normalized to contralateral brain. A correlation between the MRI derived parameters and tumor grade was evaluated with the Spearman rank correlation test.

Results: The results from 28 patients include those with grade II (n = 8), grade III (n =4), and grade IV (n = 16). Mean GE and SE tumor rCBF were mostly higher than normal tissue, while GE and SE MTT values were equally spread above and below normal tissue. There was a significant correlation with grade for GE rCBF ($p = 0.011$) and SE rCBF ($p = 0.004$) but not GE and SE MTT.









Discussion: In this study of 28 patients tumor blood flow was increased relative to contralateral brain, while the tumor MTT values were on average no different than normal tissue. The "total" rCBF and "microvascular" rCBF were unexpectedly predictive of tumor grade, while the MTT for both vascular populations were not. We expected that tumor blood flow heterogeneity would essentially negate its correlation with grade. However, after consideration of the grade IV tumors included in this study it is believed that the majority of the tumor ROIs, which excluded necrotic tissue, consisted of the tumor margins where the earliest stages of angiogenesis are present. The tumor margins are known to have the highest blood flow. Although average tumor MTT across the patients is close to that of normal tissue, a hypothesis currently under study is that the heterogeneity of intravoxel transit times will be more predictive of tumor grade and responsiveness to therapy than the average MTT. Also, the spatial distributions of MTTs may be more revealing of tumor condition on a per-patient basis. Of particular interest are the MTTs that are less than normal contralateral tissue. These are commonly found on the borders of the tumors and indicate an increase in the tumor perfusion efficiency and could be a marker for high metabolic activity. Questions such as these warrant further study and demonstrate the potential of this method to play a key role in the evaluation of brain tumor angiogenesis.

References:

1. Schmainda KM et al., 11th ISMRM, Toronto, Canada, 2003. 2. Ostergaard, L., et al., MRM 36: 715-725, 1996.

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