

Quantification of microvascular leakage in malignant glioma and solitary brain metastasis using dynamic bolus tracking susceptibility perfusion MR imaging

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Introduction

Differentiation between malignant glioma and solitary metastatic brain tumor is important clinically but remains a challenge due to the nonspecificity of standard contrast-enhanced MR imaging techniques. Both types of tumors tend to exhibit avid tumor enhancement surrounded by peritumoral edema. It has been shown histopathologically that the capillaries of metastatic neoplasms resemble those from the site of the original systemic cancer in that they lack blood-brain barrier (BBB) components and therefore have increased vascular permeability [1]. Glioma microvasculature exhibits variable degrees of BBB disruption due to the formation of new brain capillaries and damage to existing ones, suggesting higher vascular permeability in metastatic brain tumors than in high grade gliomas [2]. Dynamic bolus tracking susceptibility perfusion MR imaging allows the noninvasive measurement of relative cerebral blood volume (rCBV), however, in regions of microvascular leakage this estimation makes use of corrections that assume an intact BBB. For contrast-enhancing brain tumors this assumption is clearly invalid. This study investigated non-parametric parameters corresponding to the peak height and percent recovery of the T2* relaxivity curve to characterize the difference in microvascular leakage in regions of T2 abnormality and contrast enhancement in order to differentiate between malignant glioma (glioblastoma multiforme; GBM) and metastatic brain tumor types.

Methods

Forty patients with a diagnosis of GBM (23 patients) or metastatic brain tumor (17 patients) were recruited for this study prior to receiving treatment. MRI exams were performed on a 1.5 T Signa Echosped scanner (GE Medical Systems, Milwaukee, WI). Axial fluid-attenuated inversion recovery (FLAIR) or fast spin echo (FSE) T2-weighted and post-contrast T1-weighted spoiled gradient recalled (SPGR) images were acquired and used to define regions of T2 or T1 contrast enhancing abnormality. The perfusion imaging consisted of the injection of a bolus of 0.1 mmol/kg body weight of gadopentetate dimeglumine (Gd-DTPA) contrast agent at a rate of 5 mL/s. A series of 60 T2*-weighted gradient-echo, echo-planar images were acquired during the first pass of the bolus injection, with a TR/TE of 1000-1250/54 ms, 35° flip angle, FOV of 26 × 26 cm², 128 × 128 acquisition matrix, and 3-6 mm slice thickness. The perfusion series was resampled to a 32 × 32 grid in-plane with a 16 × 16 cm² FOV so that the observed signal changes had sufficient signal to noise ratio to be analyzed reliably on a voxel by voxel basis. The T2* signal intensity time curve, S(t), was converted to relative concentration using the relationship C(t) ~ -ln(S(t)/S₀), where S₀ is the average pre-contrast signal intensity baseline. Peak height and percent recovery of the post bolus signal from the peak were calculated for each voxel within the entire T2 lesion (T2L), contrast enhancing lesion (CEL), and nonenhancing peri-tumoral lesion (T2L-CEL). Peak height values were normalized to the peak of a model curve function derived from normal appearing brain based on histogram analysis of the pre-contrast echo planar images. Voxels with peak height values greater than twice the model curve were classified as having abnormal peak height (aPH). Regions with no signal drop (NSD), as defined by a flat signal on the time series data, were excluded from the calculations.

Results

All tumors exhibited contrast enhancement on post-contrast T1-weighted SPGR images and variable degree of peri-tumoral edema on FLAIR and FSE images. Figure 1 shows the heterogeneity in the dynamic concentration curve shapes overlaid on a post-contrast T1-weighted SPGR image in GBM and metastatic tumors. The statistical significance of all the group comparisons, as denoted by an asterisk in Figures 2 and 3, was determined through the use of a Wilcoxon ranked sum test. Figure 2 compares the normalized mean volumes within regions of NSD, CEL, aPH, and less than 50% recovery for GBM and metastatic groups. The volume of less than 50% recovery was significantly greater for metastasis than for GBMs. The volumes of aPH and region of greater than 75% recovery were significantly greater for GBMs compared to metastatic tumors. There was no significant difference in mean and maximum peak height values within the contrast enhancing regions between the two groups. The mean and max peak height within the peri-tumoral region appeared higher for GBM compared to metastatic tumors, but this difference was only significant for mean peak height values. The minimum and mean recovery values are shown in Figure 3 for both the CEL and the T2L-CEL. The mean and minimum recovery of the T2* signal within the entire CEL was greater in GBM patients. No significant difference in mean or minimum recovery was observed in the T2L-CEL lesion, although a trend towards greater recovery appeared in GBM tumors.

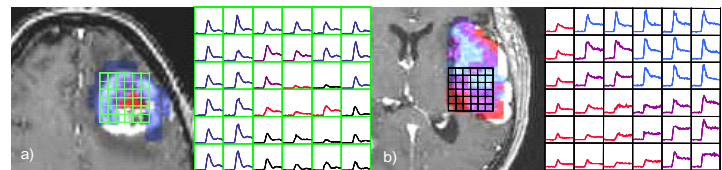


Figure 1: Abnormal peak height (blue) and recovery (red) maps overlaid on a post-contrast T1 image and corresponding concentration curves for a) a GBM tumor and b) a metastatic brain tumor

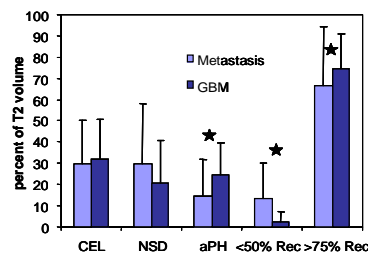


Figure 2: Normalized mean volumes for regions of contrast enhancement lesion (CEL), no signal drop (NSD), abnormal peak height (aPH), <50% recovery, and >75% recovery in GBM and metastatic tumors

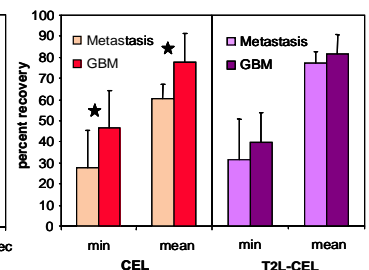


Figure 3: Minimum and mean percent recovery of T2* signal within the CEL (left) and T2L-CEL (right) for GBM and metastatic tumors

Discussion

Capillary permeability of tumor vasculature provides important information about the nature of neovascularization and the integrity of the blood-brain barrier. Alteration of microvascular permeability in brain tumors may be captured and quantified noninvasively by using dynamic bolus tracking susceptibility perfusion MR imaging. The results of our study suggest that quantitative analysis of the T2* relaxivity curve provides information on microvascular leakage that adds specificity to differentiating between malignant glioma and solitary metastasis. We found that within the contrast enhancement, metastatic brain tumors exhibited larger degrees of microvascular leakage during the bolus passage of Gd-DTPA when compared to GBMs, which can be attributed to the absence of a blood-brain barrier within the microvasculature of metastatic brain tumors. The degree of vascularity, as determined by abnormal peak height, was similar for both tumor types, correlating with histologic evidence of neovascularization in both. The microvascular leakage within the nonenhancing peritumoral edema of metastatic tumors tended to be greater than that of GBMs, suggesting a greater compromise in capillary permeability within the vasogenic edema associated with metastatic brain tumors. However, the vascularity within the peritumoral region was higher in GBMs, suggestive of a more complex biology of edema associated with GBMs. Further investigations to directly correlate imaging with histologic standards may strengthen the validity of the T2* signal peak height and recovery measurements during bolus tracking perfusion MR imaging as a noninvasive marker of vascularity and microvascular permeability.

References

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