DSC-MRI Estimates of Perfusion Predict Survival in Brain Tumor Patients

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Introduction: Patient survival is the primary index used to assess whether new treatments or therapeutic strategies are successful in brain tumor and other patients. However, analysis of survival typically requires studying a large cohort of patients and then estimating survival long after the treatment study has ended. Consequently an imaging biomarker, which is predictive of survival, would not only improve the efficiency of treatment trials but also increase the possibility of benefiting more patients in the short term. With this background the goal of this study was to determine the utility of using DSC (dynamic susceptibility contrast)-derived perfusion parameters as indicators of survival for patients with primary brain tumors.

Methods: We analyzed the DSC data performed in 73 patients with a confirmed tissue diagnosis of primary glioma. All MRI studies were performed on either 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) or a 1.5T GE CV system. 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 to seven, 5 mm slices were acquired at TE(GE)/TE(SE) = 30ms/110ms with fat suppression, TR=1s, a FOV=24cm and matrix = 64x64. Finally, conventional post-contrast T1-weighted images were acquired (SE, TE/TR = 11 ms/500 ms, matrix = 256x256). The GE and SE rCBV maps, corrected for agent extravasation, along with mean vessel diameter (mVD) image maps were determined as previously described (1). Data was extracted from ROIs of the whole tumor (avoiding areas of necrosis) and normalized to similar-sized ROIs in contralateral brain.

Statistical Analysis: Statistical analysis was performed using GraphPad Prism version 4.0a for Mac OS X (GraphPad Software, San Diego, CA). ROC curves were generated where the probability of true detection is defined as the probability that a true high grade tumor is correctly classified as a high grade tumor, and the probability of false detection is the probability that a true low grade tumor is falsely classified as a high grade tumor. Based on this analysis a threshold value was chosen, which provides an optimal sensitivity and specificity. Subsequently, Kaplan-Meier survival curves and the log-rank test were used to compare the survival times of the low and high rCBV and mVD groups. At the time of analysis 14 of 73 patients remained alive and no patients were lost to follow-up.

Results: Example GE and SE rCBV, and mVD maps are given in Figure 1 for a patient with a glioblastoma multiforme. Using the results from all patients the area under the ROC curve for GE rCBV, SE rCBV and mVD was 0.91, 0.67 and 0.83 indicating that GE rCBV provides the best test for distinguishing low from high-grade tumors. Based on this ROC analysis the GE rCBV threshold of 1.63 was chosen giving a sensitivity and specificity of 96% and 75%. Likewise a good sensitivity and specificity for mVD of 81% and 79% patients resulted when choosing a threshold of 1.48. A threshhold for SE rCBV could not be found that gave both a sensitivity and specificity near 80%. Consequently, further survival analysis with this SE rCBV was not pursued.

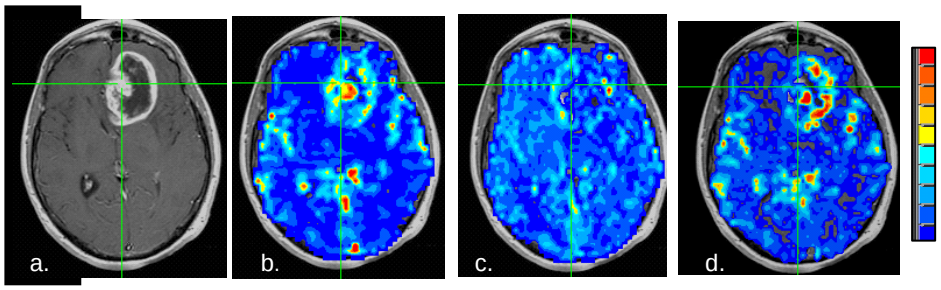

Figure 1. Patient with a glioblastoma mutliforme. Shown are the (a) post-contrast T1w image (b) GE rCBV (c) SE rCBV and (d) mean vessel diameter (mVD) maps.

Using these thresholds the GE rCBV and mVD Kaplan Meier curves were generated as shown in Figure 2. For both parameters the difference in survival was significant (p=0.0008 and p=0.006) giving median survivals of 2297 and 472 days for low and high GErCBV and 1370 and 436 days for low and high mVD.

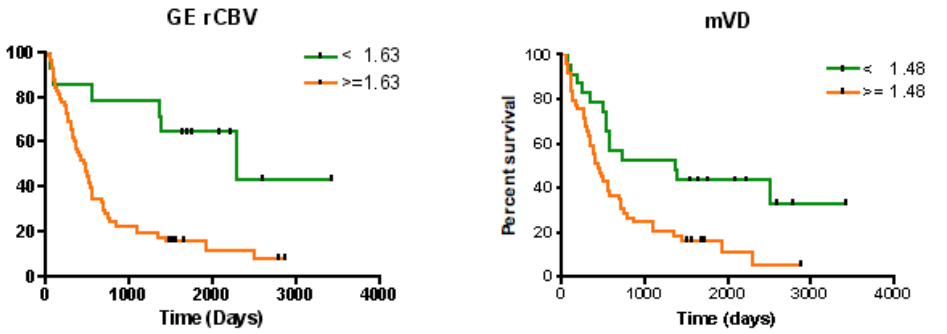

Figure 2. Kaplan-Meier survival curves for GE rCBV and mVD parameters.

Summary: We demonstrated the potential for MRI-derived rCBV information to predict survival, a key criterion used to manage and evaluate treatments for brain tumor patients. The results of this study are consistent with those previously reported by Law et al (2) demonstrating a significant difference in survival when using a rCBV threshold of 1.75. Additional studies and attention to methodological differences are needed to determine a consistent threshold that can be used across sites. Future analyses will investigate whether rCBV in combination with clinical parameters such as age and Karnofsky score (neurologic status) could further improve the prediction of survival and response to treatment.

References: (1) Schmainda et al., AJNR 25:1524 (2004). (2) Law et al., AJNR 58(6):1099-1107 (2006).

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