

Correlation of DSC parameters with histopathological complex microvasculature in GBM patients

E. Essock-Burns^{1,2}, J. J. Phillips^{3,4}, J. M. Lupo², S. Cha^{2,5}, S. M. Chang⁵, and S. J. Nelson^{1,6}

¹UCSF/UCB Joint Graduate Group in Bioengineering, University of California San Francisco, San Francisco, California, United States, ²Department of Radiology and Biomedical Imaging, University of California San Francisco, San Francisco, California, United States, ³Department of Pathology, University of California San Francisco, ⁴Department of Laboratory Medicine, University of California San Francisco, San Francisco, California, United States, ⁵Department of Neurological Surgery, University of California San Francisco, San Francisco, California, United States, ⁶Department of Bioengineering and Therapeutic Sciences, University of California San Francisco, San Francisco, California, United States

Introduction: One of the hallmarks of glioblastoma multiforme (GBM) is the presence of glomeruloid vascular structures, which is characterized by hyperplasia and tortuous lamina, and is associated with breakdown of the blood-brain barrier (BBB) [1,2]. Obtaining accurate T2*-weighted dynamic susceptibility contrast (DSC) MRI data in regions with BBB disruption is a challenge due to the extravasation of contrast agent, which results in competing signal enhancement. Multiple methods exist to address this concern [3]. Small-flip angle DSC is one acquisition strategy to limit the competing T1 enhancement, without necessitating additional gadolinium exposure to the patient. This study aims to compare how perfusion parameters calculated from DSC imaging data acquired with either a 35° or 60° flip angle correlate to histopathological evidence of complex microvasculature from biopsies of treatment naïve GBM patients.

Methods: 10 patients newly diagnosed with GBM received preoperative anatomic and physiologic imaging with a 3T GE scanner and image-guided stereotactic biopsy specimens were collected. Patients received T2* DSC gradient-echo echo-planar imaging (TE=54-56ms, TR=1.5-2s, 4 mm slice thickness) with either a 35° flip angle (5 patients) or 60° flip angle (5 patients). 22 total biopsies were taken (35° acquisition: n=12 samples, 60° acquisition: n=10 samples). Density of complex microvascular hyperplasia was measured qualitatively using Factor VIII staining of the biopsies blinded to DSC data. The relative contribution of complex vascular morphology to total vascular density was scored on a four-tier scale (0, no contribution; 1, minor; 2, moderate; 3, extensive). MR imaging coordinates obtained during the stereotactic biopsy procedure (Brainlab) were used to identify the biopsy location and an average DSC relaxivity curve was generated within this region. Peak signal height (PH) and percent of signal recovery (%REC) were calculated from the average curve for each biopsy. The degree of association between the perfusion parameters and complex vasculature rating was assessed using Pearson correlation for the total population as well as separately for each flip angle paradigm.

Results: Across the total biopsy population, %REC was inversely correlated with the presence of complex vasculature ($R=-.6336$, $p=.002$). %REC calculated from DSC data acquired with 35° flip angle was inversely correlated with complex vasculature ($R=-.6274$, $p<.03$), while %REC from the 60° DSC data was not significantly correlated with complex vasculature (Figure 1). PH was not found to significantly correlate with extent of complex vasculature. %REC and PH of the normal-appearing white matter were not significantly different between the 35° and 60° angle acquisition (mean %REC_{wm60°} = 86.3%, mean %REC_{wm35°} = 84.1%; Wilcoxon rank sum $p=1$, mean PH_{wm60°} = 672.2, mean PH_{wm35°} = 526.9; Wilcoxon rank sum $p=.42$). Within the subset of biopsies that had histological evidence of either delicate or complex vasculature (n=18 biopsy samples), DSC data acquired with 60° flip angle had significantly greater %REC than data acquired with 35° flip angle (mean PR_{60°} = 80%, mean PR_{35°} = 73%; Wilcoxon rank sum $p<.0005$) (Figure 2).

Conclusions: This study identified that %REC derived from DSC data correlated to histopathological evidence of complex vasculature observed in image-guided biopsy samples from treatment naïve GBM patients. Furthermore, the strength of association between DSC data and complex vasculature differed between the 35° and 60° flip angle acquisitions. While this initial study is limited by sample size, these results support that %REC calculated from DSC data acquired with 35° flip angle is reflective of complex, glomeruloid vasculature. Furthermore, where there is complex microvascular hyperplasia with associated BBB breakdown and contrast agent extravasation, acquiring DSC data with 35° flip may indeed reduce confounding T1-effects, while data acquired with 60° flip may overestimate %REC thereby underestimating the biological abnormality (Figure 2). Continued studies will include greater number of samples to further investigate this difference in association of histopathology and perfusion parameters between 35° and 60° flip angle DSC data acquisition.

References: [1] Rojiani, et al. (1996) *J Neurosurg* 85(6):1078-84, [2] Barajas, et al. (2010) *Rad* 254(2):564-76, [3] Paulson, et al. (2008) *Rad* 249(2):601-13

Acknowledgments: This research was supported by NIH Grant R01 CA127612-01A1 and NIH Grant P01 CA11816-01A2.

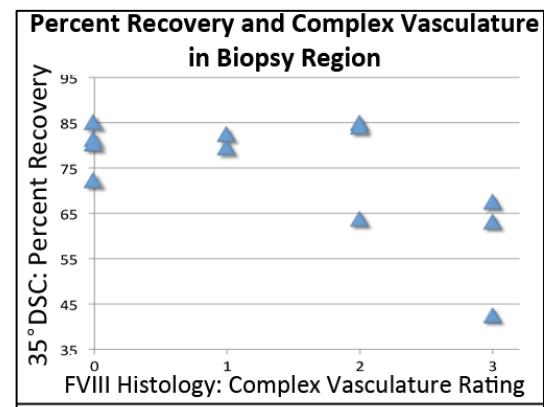


Figure 1. 35° percent recovery correlates with complex vasculature.

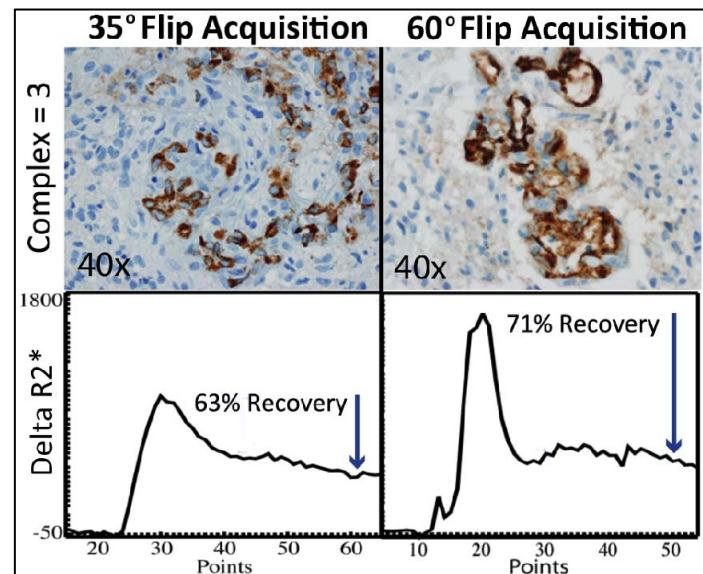


Figure 2: Factor VIII staining of 2 biopsies with equivalent complex vasculature (top) and the corresponding DSC data (bottom). Percent recovery from 35° acquisition correlates well with complex vasculature, while 60° acquisition may overestimate percent recovery in the presence of complex vasculature.