Repeatability of the Perfusion MRI Brain Tumor Vasculature Sensitive Biomarker, Arterio-Venous Overlap (AVOL) in Recurrent Brain Tumor Patients with Two Baseline Imaging Scans

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TARGET AUDIENCE: Scientists and clinicians interested in brain tumor perfusion modeling.

INTRODUCTION A recent report describes a novel perfusion imaging biomarker, arterio-venous overlap (AVOL), which appears to be sensitive to brain tumor vasculature, as well as patient survival following treatment with bevacizumab[1]. The biomarker is generated with independent component analysis (ICA) of dynamic susceptibility contrast (DSC) MRI data. The ICA algorithm separates arterial and venous vasculature into separate components[2-4]. The overlap of these components occurs in greater proportions within contrast enhancing tumor, suggesting that the perfusion characteristics of neoplastic vasculature differ from normal brain. The initial report modeled 3 components for the analysis: arterial, venous, and one additional component. Because the AVOL biomarker is in its early developmental stages, it is necessary to determine the proper number of components modeled that results in a highly repeatable AVOL maps. This study addresses two questions with a unique dataset where two baseline DSC acquisitions took place days apart. We first determine what number of components optimizes repeatability of the AVOL biomarker, and second compare results from spin-echo and gradient-echo acquisitions.

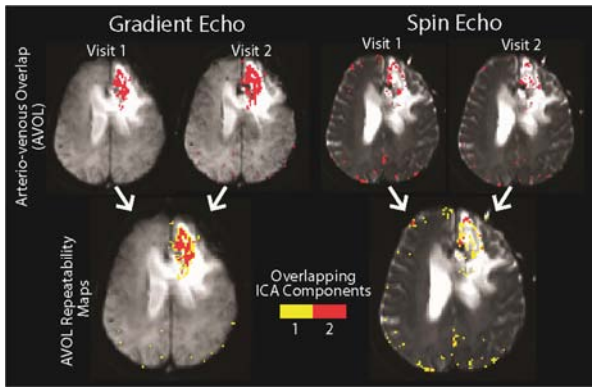

Figure 1. Demonstration of the creation of AVOL repeatability maps for SE and GE acquisitions, combining each visit.

METHODS *Patient Population* 27 patients with recurrent glioblastoma multiforme (GBM) were recruited prior to the onset of cediranib treatment. *Imaging* Each patient was scanned twice, generally 3-4 days apart, using an identical imaging protocol on a 3T MRI system (TimTrio, Siemens, Malvern, PA). DSC-MRI was acquired using a dual-echo, combined GE and SE echo planar imaging sequence. To minimize T1-leakage effects, a preload of Gd was administered[5-7]. *Independent Component Analysis* SE and GE acquisitions were processed separately for each visit. Pre-processing of each DSC acquisition consisted of removing the first 4 time points and motion correction using MCFLIRT (FMRIB tool library). Data was then processed using probabilistic independent component analysis[8] as implemented in MELODIC (FMRIB tool library). For each patient, each visit and for both SE and GE acquisitions, 2-10 components were modeled. The resulting components were then visually sorted to determine which best represented the arterial and venous phase of Gd perfusion. The statistically thresholded[3] arterial and venous maps were then binarized and the overlap of the two was found (AVOL)[1]. These AVOL maps were then brought from visit 2 into the same space as visit 1 by co-registering the mean SE-DSC images. Repeatability maps were created to visualize the overlap of each session's arterial and venous components (Figure 1). Voxel values in these maps represent the number of overlapping sessions (of 2) with components present. An overall repeatability index (RI) was calculated for GE and SE and each number of components modeled using the equation shown, where N=2, and n_i is the number of voxels overlapping "i" times. The range of RI is between 0 and 1, where 1 indicates perfect repeatability[2] Enhancing tumor regions of interest were manually drawn on T1+C images collected in the same slice prescription as the DSC data. The AVOL repeatability maps were then masked by the tumor ROI, and the RIs were compared across component numbers with a repeated-measures ANOVA.

$$RI = \frac{1}{(N-1)}\left(\frac{\sum_{i=1}^{N} in_i}{\sum_{i=1}^{N} n_i} - 1\right)$$

RESULTS Figure 1 shows a demonstration of the creation of AVOL repeatability maps, from which the RI was calculated. Figure 2 shows the results from the RI analysis. GE-derived AVOL within enhancement were significantly more repeatable than SE-derived AVOL for 3,4,5,6,7,and 9 components modeled. The RI for GE AVOL was maximized at 4 and 5 components modeled.

DISCUSSION This study shows that the AVOL biomarker is highly repeatable with GE acquisitions and maximally repeatable when 4 or 5 components are modeled. SE acquisitions are not ideal for deriving the AVOL biomarker, as repeatability is minimal.

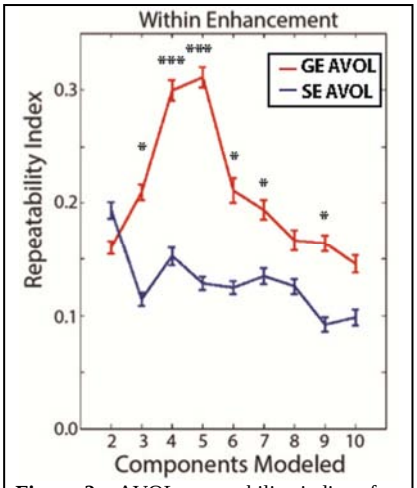

Figure 2. AVOL repeatability indices for GE and SE acquisitions versus # of components modeled.

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