

# Initial Experience With Vessel Size Imaging in Recurrent Glioblastoma Multiforme using a Multiple Spin and Gradient Echo (SAGE) Perfusion Bolus Contrast Sequence

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**INTRODUCTION** – 17,000 newly diagnosed cases of Glioblastoma Multiforme (GBM) are identified per year. Multimodality treatment options have resulted in difficulty distinguishing tumor growth/recurrence from radiation necrosis in many patients. Dynamic susceptibility-contrast gradient echo (GE) perfusion imaging measurements of relative CBV can distinguish tumor recurrence from radiation necrosis (1). Spin echo (SE) and GE images have varying sensitivities to vessel diameter based on differential sensitivity to the size scale of the field inhomogeneity and static or dynamic dephasing regimes (2,3). For typical scan parameters, SE images are most sensitive to vessel diameters in the microvascular range (~25  $\mu$ m). GE are roughly twice as sensitive, specifically to larger vessel size (i.e. more reflective of total blood volume vs. capillary CBV) (3). Animal tumor models and human MR experience have suggested that the ratio of GE and SE relaxation rates ( $\Delta R_2^*/\Delta R_2$ ) correlates with vessel diameter (4-6). In this retrospective, IRB-approved pilot study, a combined dynamic multiecho SE and GE (SAGE) EPI sequence acquired during bolus contrast (7) allows direct evaluation of  $R_2$  changes to  $R_2^*$  changes for relative vessel size imaging (VSI) (5,8,9). Our goal was to evaluate parameters derived from this SAGE EPI technique with respect to GBM recurrence versus radiation necrosis, and identify a more sensitive method to detect tumor recurrence enabling more timely modification of therapy and ultimately improve patient prognosis.

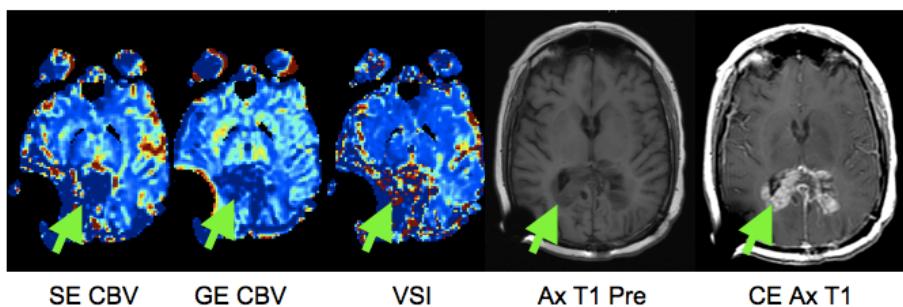
**METHODS** – Routine tumor imaging was performed in 8 post-chemoradiation GBM patients at 1.5T and 3T, following informed patient consent. Additional VSI images were acquired using 3 or 5-echo SAGE-EPI acquisition with echo times of TE = 17-101 ms. 15 5-mm slices with in-plane resolution of 84x84 (96x96 in 3-echo cases) were acquired with 24 cm FOV. A 90° spectral-spatial RF excitation pulse was followed by a 180° spin-echo pulse. PWI was based on the acquisition of 60 EPI volumes with TR = 1800 ms. Single-dose bolus Gd-based contrast agent was administered via power-injector. Perfusion parameters were obtained using the RAPID post-processing toolbox (11). Relative VSI maps were determined from the ratio of  $R_2$ - and  $R_2^*$ -weighted CBV values (9). VSI maps were correlated with abnormal enhancement and  $T_2$  signal abnormality.

**RESULTS** – 3 of 8 patient scans demonstrated findings on VSI to suggest tumor involvement at the time of imaging. Figure 1 illustrates a case of GBM infiltration of the splenium, in a patient previously treated with chemoradiation, with evidence of large vessel neovascularity. Figure 2 highlights a case that initially demonstrated no conventional MR imaging findings of tumor recurrence, but shows subtle findings on VSI anterior to the resection cavity. Interestingly, this same region later demonstrates marked pathologic enhancement on conventional MR sequences 6 and 9 months later. Similar findings are noted about the resection cavity in a third case (data not shown). Of the 5 cases with no VSI findings of recurrent or residual tumor, none demonstrated positive findings up to one year, suggesting that VSI may have a strong negative predictive value.

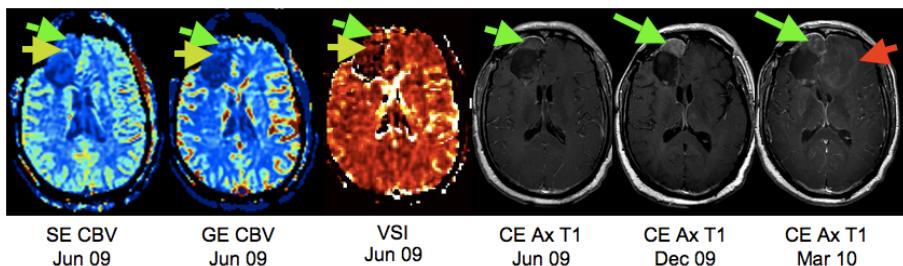
**DISCUSSION** – Initial results demonstrate feasibility of the SAGE EPI method in imaging GBM in recurrent and/or treated tumor, and suggest that detection of both microvasculature (in recurrence, possibly as a consequence of novel therapeutic agents targeted at inhibiting neoangiogenesis) and large vessel detection in recurrent and treated primary neoplasm, may be a sensitive method for tumor detection. The observation that VSI can detect subtle tumor recurrence, in light of apparently “negative” GE-based PWI suggests that this method may provide earlier modification in therapy. Of note, the SAGE technique permits a straightforward approach to leakage correction, compared with traditional GE-based PWI, by using the multi-echo data to eliminate  $T_1$ -shortening effects. In summary, the use of VSI calculated from simultaneously acquired GE and SE-based EPI images using SAGE-EPI is easily incorporated into a conventional tumor imaging protocol and may hold promise in the evaluation of brain neoplasms.

**REFERENCES** – [1] Hu *et al*, AJNR, Mar 2009; 30: 552-558, [2] Fisel *et al*, MRM 17:336-347, [3] Boxerman *et al*, MRM 34:555-566, [4] Dennie *et al*, MRM 40:793-799, [5] Tropres, *et al*, MRM 45:397-408, [6] Schmainda *et al*, AJNR 25:1524-1532, [7] Newbould *et al*, Proc ISMRM 2007, p1451, [8] Kiselev *et al*, MRM 53:553-563, [9] Schmiedeskamp, *et al*. Proc ISMRM 2010, p 1785, [10] Straka *et al*, JMRI 32:1024-1037.

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**Fig. 1** – SAGE PWI maps acquired at 3T with 3 echoes, including SE and GE CBV, and VSI in a 58-year-old patient 1 yr following diagnosis of GBM. Images demonstrate extensive enhancement and necrosis of the splenium of the corpus callosum, with corresponding VSI maps suggesting primarily large vessel neovascularity (green arrows). Large susceptibility artifact results from patient's VP shunt. The patient was deceased 1 month following scan.



**Fig. 2** – SAGE PWI maps acquired at 3T in a 68-year-old patient post gross-total resection of right frontal GBM, with follow-up imaging 6/09, initially interpreted as “no recurrent tumor” (based on GE CBV and absence of enhancement on axial T1 post-Gd images above). Retrospective evaluation with combined SAGE EPI maps reveals a subtle region of microvasculature (yellow arrow) on SE CBV and VSI, not seen on GE CBV. Follow-up imaging 6 and 9 months later (12/09, and 3/10, respectively) demonstrates more obvious enhancing tumor, which later involves the left frontal lobe (red arrow). Area of large vessel abnormality on SAGE EPI maps (green arrows) later becomes area of avid enhancement anterior to the resection cavity on follow-up imaging.