

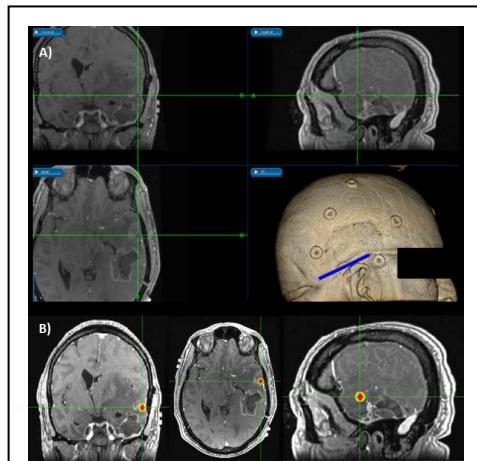
## Comparison of standardized and normalized rCBV to differentiate astrocytic brain tumors

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**Target Audience:** Neuro-oncologists, neuroradiologists, neurosurgeons, brain tumor imaging scientists.



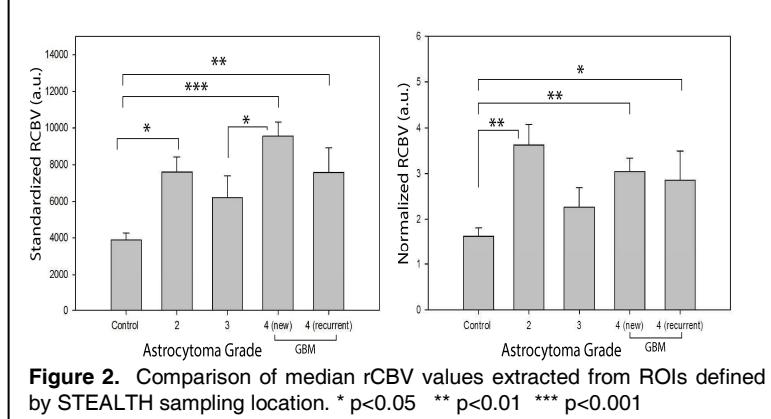
**Figure 1.** A) Intraoperative screenshot of tissue sampling site. B) ROIs (in red) drawn on matched MR slices of co-registered preoperative MR imaging.

**Introduction:** Preoperative advanced MR imaging techniques, like DWI/DTI and DSC, provide significant structural and functional information about the tumor biology.<sup>1,2</sup> Still, the histopathological evaluation of biopsy samples remains the gold standard for the diagnosis of brain tumors. Standardized, opposed to normalized, RCBV (relative cerebral blood volume) maps provide an objectively quantifiable means to reduce interpatient and interstudy variability for the same tissue type.<sup>3</sup> Here we present a comparison of standardized vs. normalized RCBV, used in conjunction with intraoperative navigation, for astrocytoma grading. To our knowledge, such a comparison between techniques or with direct spatial correlation with tissue diagnosis has not been previously undertaken.

**Methods:** The histopathological findings of 81 tissue specimens from 25 adult patients who underwent brain tumor biopsy or resection were used for this study: normal control brain tissue (n=28), Grade 2 Astrocytoma (n=7), Grade 3 Astrocytoma (n=7), newly diagnosed Grade 4 Astrocytoma/GBM (n=22), and recurrent Grade 4 Astrocytoma/GBM (n=17). Preoperative MR imaging included a T1-weighted reference scan, as well as dynamic susceptibility contrast (DSC) for calculation of RCBV. Using a StealthStation® S7™ surgical navigation unit (Medtronic, Minneapolis, MN), screenshots were taken intraoperatively of each distinct tissue sampling site (Figure 1A). Preoperative imaging was co-registered to the MRI uploaded for surgical navigation, and a 3 mm spherical region of interest (ROI) was drawn manually with AFNI software<sup>4</sup> on a case-by-case basis for data extraction and comparison across sampling sites (Figure 1B). Calculation of both standardized and normalized leakage-corrected RCBV (sRCBV and nRCBV, respectively) from raw DSC data

was processed with IB Neuro™ Software (Imaging Biometrics LLC, Elm Grove, WI).<sup>5</sup> The nRCBV generation utilized manually drawn ROIs in normal appearing white matter. Only positive non-zero RCBV values were used for analysis. Histopathological diagnosis for each tissue specimen was obtained from the neurosurgical pathology report and according to the WHO brain tumor grading system. Statistical analysis included One-Way ANOVA with pairwise multiple comparison procedures and Receiver Operator Curves (ROC).

**Results:** Both sRCBV and nRCBV significantly distinguished Grade 4 GBMs (new and recurrent), as well as Grade 2 Astrocytomas, from control tissue (Figure 2). Additionally, the sRCBV differed significantly between Grade 3 and new Grade 4 GBMs. There was a trend of recurrent GBMs to have lower sRCBV than new ones, but it was not significant (p=0.071). However, ROC analysis revealed that while sRCBV and nRCBV were equally sensitive when differentiating new and recurrent GBM tumors, sRCBV was more specific than nRCBV (sRCBV Sensitivity%/Specificity% of 70.59/76.19 vs. nRCBV Sensitivity%/Specificity% of 70.59/63.64). Grade 2 tumors had unusually high sRCBV and nRCBV values, which may be due to misregistration because of brain decompression<sup>6</sup>, high regional microvessel density<sup>7</sup>, or a mix of new and recurrent tumor samples.



**Figure 2.** Comparison of median rCBV values extracted from ROIs defined by STEALTH sampling location. \* p<0.05 \*\* p<0.01 \*\*\* p<0.001

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**Discussion:** This study represents the first comparison of sRCBV and nRCBV combined with spatial tissue correlation for astrocytoma grading. nRCBV is commonly used in characterization of brain lesions, as well as MRI-tissue correlation studies.<sup>1,2,8,9</sup> While both techniques exhibit similar sensitivity in distinguishing between the different tumor grades, sRCBV may have greater potential, particularly in differentiating between high grade astrocytomas, possibly due to its lower variability.<sup>3</sup> This study reinforces the importance of perfusion imaging in brain tumor characterization.

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