Standardization decreases interpatient differences in rCBV measurements as a function of brain tumor grade

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Introduction Dynamic susceptibility contrast (DSC) magnetic resonance imaging (MRI), has demonstrated the potential to evaluate functional changes in cerebral blood volume (CBV) caused by brain tumor angiogenesis. One of the main limitations faced in using (non-quantitative) relative CBV (rCBV) measurements to assess intracranial tumor, is that the rCBV values for the same tissue type such as white matter (WM) or tumor can vary significantly across studies due to slight differences in system stability or contrast agent dose administered. As a result, most studies report rCBV values as normalized to WM or contralateral brain. Outlining regions of interest (ROI) for normalizing rCBV values is very user dependent and subjective in nature and thus introduces variability. As a solution we recently proposed a standardization method for blood volume maps that translates all maps to a similar scale [1]. This approach enables easy and accurate visual comparison, which is quite important for clinical longitudinal evaluation of this type of qualitative data.

In this study we address the hypothesis that standardization of rCBV maps will have the added advantage of decreasing variability of the rCBV values within each tumor grade group. Though many have reported an overall correlation between normalized tumor rCBV and grade, there remains much overlap between the groups, making it difficult to rely on rCBV to distinguish grades on an individualized basis. To address this hypothesis we compared the standardized (STD) rCBV values with normalized (NRM) rCBV values obtained from patients with gliomas.

Data Acquisition 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 Scanner. A 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 0.2 mmole/kg bolus injection. Five, 7 mm slices were acquired at TE (GE)/TE(SE) = 30ms/109.1ms with fat suppression, TR = 1s, a FOV = 24cm and matrix = 64x64. Finally, post-contrast T1-weighted images were acquired (SE, TE/TR = 11ms/500 ms, matrix = 256x256).

Data analysis Forty nine subjects with confirmed diagnosis of glioma tumor grade were analyzed. Our dataset included 2 subjects with grade I tumor, 10 with grade II tumor, 10 with grade III tumor and 27 with grade IV tumor. The rCBV maps were corrected for contrast agent leakage effecs as previously described [2]. Data was extracted from ROIs of the whole tumor (avoiding areas of necrosis), contralateral brain and normal-appearing white matter, which were used to obtain NRM rCBV values. We used 25% of subjects from each tumor grade group to train the standardization scheme and these training parameters were applied to standardize rCBV maps for all 49 subjects [1]. The Spearman's rank correlation test was performed to determine the significance of the correlation between NRM and STD rCBV measurements and tumor grade. Also, the coefficient of variation was determined for each tumor grade group.

Results and Discussion Figures 1 and 2 show normalized (a) and standardized (b) maps for GE rCBV and SE rCBV respectively. The Spearman Rank correlation results are shown in Figures 3 and 4 for normalized and standardized SE and GE rCBV data respectively. Standardization results in an improved correlation for both GE and SE data with correlation coefficients, r, increasing from 0.029 to 0.125 for SE and from 0.45 to 0.49 for GE. In addition though significance did not change the p-values improved from 0.84 to 0.19 for SE and from 0.006 to 0.0001 for GE. This suggests that standardization not only performs as well as the more labor-intensive normalization methods, but in fact performs better. From Table 1, we observe that the variability in the rCBV values, as indicated by the reported coefficient of variations, decreases in all but one case (grade II GE data). Thus, from this study we can conclude that when standardization is performed there is a tendency towards reduction in variance of rCBV values within each tumor grade i.e. tighter range of rCBV values within each grade group is obtained, which enables improved discrimination between tumor grades. We also conclude that standardization of rCBV maps, an objective method translating all rCBV values to a consistent scale, enables easy visual comparison between studies.

Figure 1. GE CBV maps.

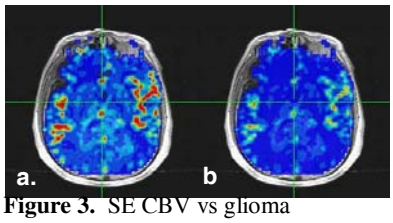
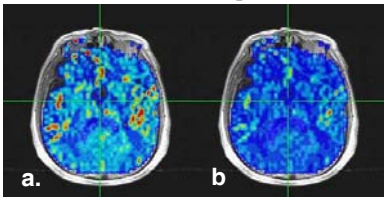


Figure 2. SE CBV maps.



Grade	NRM GE (%)	STD GE (%)	NRM SE (%)	STD SE (%)
II	89.23	103.34	52.06	54.62
III	42.07	40.51	39.80	33.49
IV	61.15	45.66	54.25	46.22

TABLE I. Coefficient of variation for NRM and STD rCBV values for each glioma grade category.

Figure 3. SE CBV vs glioma grade.

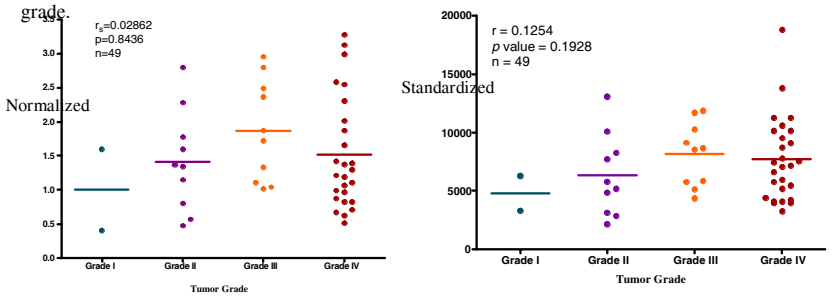
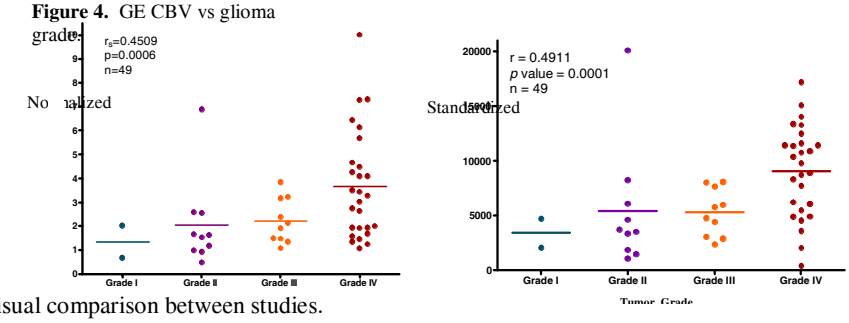


Figure 4. GE CBV vs glioma grade.



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References

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