MRI-derived rCBV Can Guide Intraoperative Diagnosis of Brain Tumors

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Introduction: An intraoperative (IOP) diagnosis based on tissue frozen sections are fundamental to the strategy of neurosurgeons when removing brain tumor tissue. This information can be used to guide the approach and extent of surgery as well as the choice of intraoperative therapies. However, in practice the intraoperative diagnosis is not reliable with regard to accurately predicting the final diagnosis. This inaccuracy is due in large part to the inherent soft nature of the central nervous system (CNS), which renders poor-quality frozen sections thereby making these sections difficult to interpret (1). Given the many studies showing the potential of rCBV methods to distinguish brain tumor grades, we hypothesize that rCBV will be more accurate than frozen sections in predicting both the presence of tumor and its grade, and may therefore play a role in guiding the intraoperative diagnosis. To address this hypothesis the current study was undertaken to compare the ability of MRI-derived relative cerebral blood volume (rCBV) maps to intra-operative frozen section pathology to predict brain tumor grade. This comparison is a first step in examining the utility of rCBV maps, obtained before surgery, to guide intra-operative pathologic diagnosis.

Methods: A retrospective study was performed in 41 patients with a final diagnosis of glial tumor. 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 system. A 0.05-0.10 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 0.15-0.25 mmole/kg bolus injection. Five, 5 mm slices were acquired at TE(GE)/TE(SE) = 30ms/110ms with fat suppression, TR=1s, a FOV=24cm and matrix = 64x64. Finally, conventional post-contrast T1-weighted images were acquired (SE, TE/TR = 11 ms/500 ms, matrix = 256x256). The GE and SE rCBV maps, corrected for agent extravasation were determined as previously described (21.). Data was extracted from ROIs of the whole tumor (avoiding areas of necrosis) and normalized to similar-sized ROIs in contralateral brain. From this data ROC curves were generated where the probability of true detection is defined as the probability that a true high grade tumor is correctly classified as a high grade tumor, and the probability of false detection is the probability that a true low grade tumor is falsely classified as a high grade tumor. For each patient, an intraoperative diagnosis, based on tissue frozen sections, was made by an experienced pathologist. Following surgery, a final pathologic diagnosis was made according to the WHO grading system for brain tumors, again by an experienced pathologist.

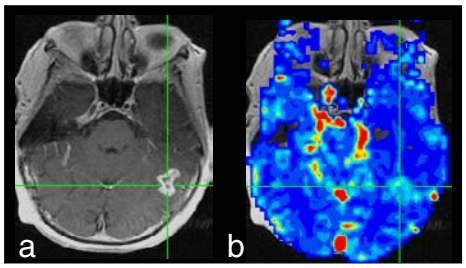

Figure 1. Post-contrast T1w image (a) and (b) GE rCBV map from a patient with an intraoperative diagnosis of "gliosis, rule out tumor" and final diagnosis of GBM.

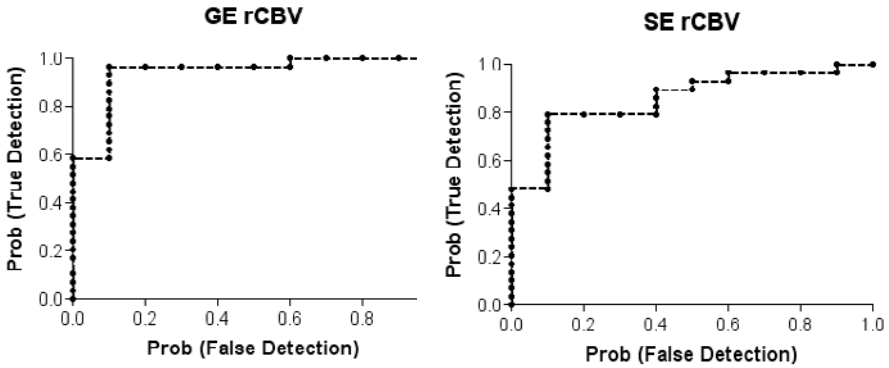

Figure 2. ROC curves for GE rCBV data and SE rCBV data. Probability of true detection is the probability that a true high-grade tumor is correctly classified.

Results: The IOP frozen-section diagnosis agreed with the final diagnosis, in distinguishing low-grade (I, II) from high-grade (III, IV), in only 49% of the cases. For the remaining 51% of the cases for which there was disagreement, in 7 of 21 cases (33%), the IOP diagnosis said no tumor while the final diagnosis was tumor. In 11 of 21 (52%) cases the IOP diagnosis wrongly diagnosed a low-grade tumor when it was a high-grade tumor and in 3 of 21 (14%) of cases an IOP high-grade tumor diagnosis disagreed with the final low-grade diagnosis. An example is shown in Figure 1 where the IOP diagnosis was "gliosis, rule out tumor" while the final diagnosis was high-grade tumor. In this case, the increased blood volume noted in the GE rCBV map (Fig 1b) would have provided supplemental information in favor of a higher-grade tumor diagnosis. Contrast the lack of concordance between IOP and final diagnosis to the predictability of tumor grade using GE and SE rCBV data, as illustrated by the ROC curves in Figure 2. For a normalized GE rCBV value of 2.0, the probability of false detection is 10% and the probability of true detection is 90%. For a normalized SE rCBV value of 2.0 the probability of false detection is 20% while the probability for true detection is 79%.

Summary: In order for advanced functional imaging techniques, such as rCBV (relative cerebral blood volume) imaging, to be accepted into routine clinical practice, their impact on clinical decision making must be soundly demonstrated. Here we demonstrate the potential for MRI-derived rCBV information to guide the neuropathologist in evaluating tissue received at the time of operating room consultation with the neurosurgeon.

References: (1) Savargaonkar P et al., Annals of Clin Lab Sci 31(2):133 (2001) (2) Schmainda et al., AJNR 25:1524 (2004).
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