rCBV Estimates in Tumor vs. Normal Brain Depend on Acquisition and Analysis Methods

E. S. Paulson[1], D. E. Prah[1], K. M. Schmainda[1,2]

[1]Department of Biophysics, Medical College of Wisconsin, Milwaukee, WI, United States, [2]Department of Radiology, Medical College of Wisconsin, Milwaukee, WI, United States

Introduction

Dynamic susceptibility contrast (DSC) MRI is a noninvasive imaging technique frequently employed to assess intracranial tumor angiogenesis based on estimations of regional cerebral blood volume (rCBV). These rCBV estimates are obtained by finding the area under the concentration-time curve following rapid injection of a paramagnetic contrast agent. Numerical integration over the entire concentration-time curve [1] and fitting a gamma-variate function [2] to the first pass of the concentration-time curve are two commonly used methods for determining rCBV. However, the validity of the results obtained with these methods is based largely upon assumptions regarding the effects of contrast agent extravasation and recirculation as well as the use of optimum imaging acquisition parameters. The goal of this study was to investigate how different acquisition and analysis methods influence rCBV estimate variations in tumor versus normal brain.

Methods

A retrospective study was performed on four patients with intracranial tumors whom underwent rCBV analysis. First, dynamic T2*-weighted images were acquired during the administration of a standard dose of Gadodiamide (0.10 mmol/kg, Omniscan). For this acquisition a low-flip angle pulse sequence was used to diminish T1 leakage effects (GE-EPI: field of view = 24 cm, matrix = 64^2, flip angle = 35 deg, number of slices = 7, echo time = 54 msec, repetition time= 1000 msec). This was followed by acquisition of combined T2 and T2*-weighted images during which a double dose of Gd (0.20 mmol/kg) was administered. Specifically, combined GE/SE-EPI data were collected using the following parameters: field of view = 24 cm, matrix = 64^2, flip angle = 90 deg, number of slices = 7, gradient echo time = 30 msec, spin echo times = 110 msec, repetition time= 1000 msec. Note that administration of the first dose of contrast agent also serves as a "loading" dose or pre-load of contrast agent which acts to diminish T1 leakage effects that may occur during acquisition of the GE/SE-EPI data [1, 3].

Data analysis was performed offline using AFNI. Only the gradient echo data from the second phase of the study were used in the analysis. The MR signal intensity time courses were converted into delta R2* concentration-time curves. Cerebral blood volume was determined by: 1) trapezoidal numerical integration over the entire delta R2* time series, and 2) fitting the concentration-time curves to a gamma-variate function using a nonlinear simplex algorithm. Corrections for agent extravasation and recirculation were not performed. Regions of interest were chosen for white matter, tumor, and contralateral brain. Voxel-wise estimates of rCBV were normalized to their average white matter rCBV. After normalization, mean rCBV values from tumor and contralateral ROIs were obtained. The average percent differences between gamma-variate rCBV and numerical integration rCBV was then determined in tumor and normal brain for each slice of each patient.

Results and Discussion

Figures 1a and 1b display the results of average normalized rCBV values in normal brain and tumor, respectively. The rCBV values in normal brain obtained with gamma-variate and numerical integration were found to be in close agreement, with minimal variations existing during phase 1 and phase 2. In contrast, rCBV values in tumor were found to be highly variable, suggesting that the resulting tumor rCBV is highly dependent on the choice of acquisition and analysis methods. This dependence of tumor on choice of analysis is clearly demonstrated in Figures 2a and 2b where the percent differences between gamma-variate and numerical integration are given for both normal brain and tumor for phase one and two studies. As illustrated in the figures, the percent differences between numeric integration and gamma-variate rCBV in normal brain are small in both phase 1 and phase 2. Conversely, the tumor rCBV was highly dependent on choice of analysis with approximately a 20% difference in normalized rCBV for both phase 1 and phase 2 studies.

These results suggest that gamma-variate and numerical integration derived rCBV values are similar in normal brain, but this agreement diminishes in regions of tumor. These results signify the dependence of rCBV estimates on acquisition and analysis methods. This dependence is most likely a result of assumptions regarding tumor vascular morphology and flow characteristics (implicit to gamma-variate fitting), and the variability in how each method handles T1 leakage effects. Studies are planned to fully characterize the influence of these effects with the goal of defining the most accurate way to determine rCBV in brain tumors.

Figure 1: Normal Brain rCBV (a) and Tumor rCBV (b) normalized to white matter

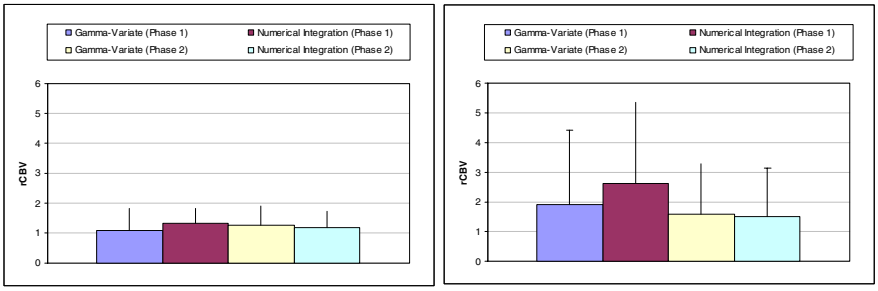
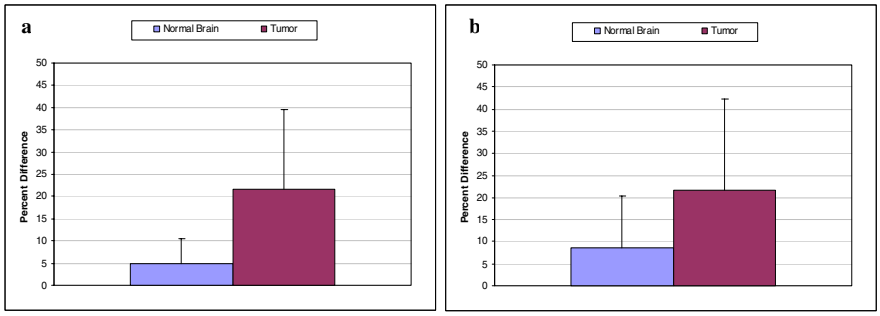


Figure 2: Percent Differences in Numerical Integration vs. Gamma-Variate rCBVs during Phase 1 (a) and Phase 2 (b)



References

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