Estimation of white matter and gray matter cerebral blood volume using a partial-volume model

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1. Introduction

Measurements of blood volume in the brain can be obtained from magnetic resonance imaging using dynamic-susceptibility bolus-tracking perfusion imaging. However, as a consequence of the larger volume of the acquired voxels, significant partial voluming of gray matter (GM) and white matter (WM) may occur. Gray matter has been shown to exhibit relative cerebral blood volume (rCBV) values approximately two times that of white matter. Thus, most analyses of perfusion data have relied upon manual delineation of regions of interest in order to limit the confounding effects of partial voluming. This study aims to address this limitation by explicitly modeling the rCBV of healthy tissue as a function of partial volumes of WM and GM. We apply rigid and non-rigid image registration techniques to improve the correspondence between rCBV and tissue type. The partial volume model is also used to verify the consistency of perfusion quantification algorithms. The resulting "pure" WM and GM rCBV values obtained with these methods may be useful in normalizing perfusion data in the absence of an arterial input function.

2. Materials and Methods

Twenty patients (8 female, 12 male, 23–73 yrs) with a diagnosis of grade III (n = 5) or IV (n = 15) gliomas received MRI exams on a 1.5 T GE Signa Echospeed scanner within two weeks following surgery but before initiation of radiation therapy. At minimum, T2-FLAIR and T1-weighted SPGR images (TR/TE = 27 / 6 msec, $1 \times 1 \times 1.5$ mm^3 voxels) with and without gadopentetate dimeglumine (Gd-DTPA) contrast and proton spectroscopic imaging data were acquired. Voxels in the T2-FLAIR or T1-Gd lesion or exhibiting an abnormal ratio of choline to N-acetylaspartate were excluded from further analysis. The perfusion imaging consisted of the injection of a bolus of 0.1 mmol/kg body weight of Gd-DTPA contrast agent at a rate of 5 mL/s. A series of 60 T2*-weighted echo-planar gradient-echo images were acquired with a TR/TE of 1000 / 54 msec, 35° flip angle, a FOV of 26×26 cm^2 with a 128×128 acquisition matrix, and a 3–6 mm nominal slice thickness. The perfusion data series for each voxel was converted into relative $\Delta R2^*$ which was then modeled with a modified gamma-variate function including a recirculation parameter, adapted here to model recirculation and leakage in gradient echo experiments.[1] The $\Delta R2^*$ for each voxel was subjected to a nonlinear fit calculated with a Nelder-Mead simplex algorithm. An example of this fitting is shown as figure 1. A second fit was derived for each voxel using the same model, but computed using an simplified iterative linear algorithm.[2] The first time point of the perfusion series was aligned to the pre-contrast T1-weighted by a rigid body transformation with a normalized mutual information cost function, followed by a nonrigid registration through optimization of control point positions for a grid of B-splines.[3] The rigid and nonrigid transformations were applied to all 60 time points and the fitting algorithms reapplied to the aligned dynamic data. Example results are shown in figure 2. The T1-SPGR images were then segmented into GM, WM, and CSF using a hidden Markov random field model. The resulting maps were regridded to yield the fraction of each perfusion voxel that was WM, f_{WM}, or GM, f_{GM}. All voxels in which $f_{GM} + f_{WM} < 0.95$ were excluded from further analysis. The observed rCBV was then modeled as $rCBV_o \approx (rCBV_{WM} - rCBV_{GM}) \cdot f_{WM} + rCBV_{GM}$, where $rCBV_{WM}$ and $rCBV_{GM}$ represent the rCBV values for an idealized voxel of pure WM or GM. This is similar to models utilized for spectroscopy and blood flow.[4,5] This model was fit to the voxels from each patient using a robust linear regression with bisquares weighting.

3. Results and Discussion

The rigid and nonrigid registrations were shown to produce improvements in the correlation between voxel content and computed rCBV. This is shown for an example subject in figure 3. For all twenty patients, the rigid registration improved the fit to the partial-volume model, while the nonrigid registration resulted in further improvements for all but two patients. The improvements in the correlation are shown in figure 4. Following either rigid or nonrigid registration, the nonlinear rCBV calculation algorithm resulted in rCBV values with a higher correlation to underlying tissue content than the simplified linear fit in all but two patients. The $rCBV_{WM}$ and $rCBV_{GM}$ for each patient was extrapolated using the partial-volume model and used to estimate the GM / WM ratio of CBV values for the entire population. While there is no widely accepted gold standard value for the CBV ratio, a value of 2 is consistent with recent ^{15}O-PET studies as well as MRI studies, and is often quoted as a standard value. The results for the nonlinear algorithm with nonrigid registration are shown in figure 5. For the nonlinear fitting, this ratio was found to be 2.11 ± 0.47 before alignment, falling to 2.00 ± 0.32 and 2.03 ± 0.31 following rigid and nonrigid registration. Using the linear fitting algorithm, these values were found to be 1.68 ± 0.25, 1.71 ± 0.25, and 1.87 ± 0.28. The improved accuracy of the nonlinear fitting was achieved at the expense of computation time: the algorithm was implemented in a voxel-wise parallel manner on an array of 24 Pentium 4 Xeon processors (2.8 GHz), requiring 5 min per examination, compared with a single-processor computation time of 10 min for the linear algorithm. Similarly, the improved correlations resulting from nonrigid registration required 6-8 hours, compared with < 3 minutes for the rigid registration.

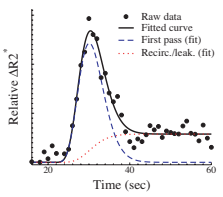

Figure 1. Example of a nonlinear fitting result.

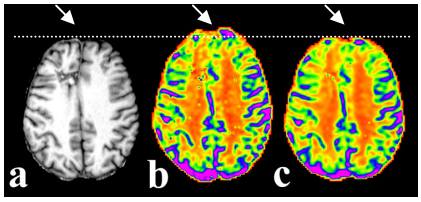

Figure 2. Example (a) T1-SPGR and rCBV map after (b) rigid and (c) nonrigid alignment.

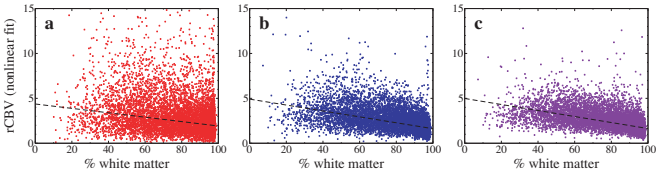

Figure 3. rCBV versus voxel WM tissue content for the nonlinear fitting: (a) unaligned, ρ = –0.431; (b) rigid, ρ = –0.668; (c) nonrigid, ρ = –0.716.

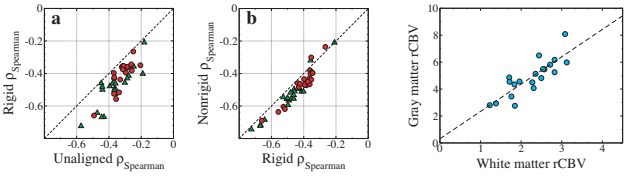

Figure 4. The correlation between the WM content of a voxel and the computed rCBV after (a) rigid and (b) nonrigid registration. Each point is a single patient, assessed by linear (●) or nonlinear (▲) fitting.

Figure 5. The pure GM and WM rCBV for all patients, derived from nonlinear fitting and nonrigid registration. The line represents a linear fit.

4. Conclusions

The use of a nonlinear fitting algorithm to estimate the rCBV yields results that are more strongly correlated with the underlying physiology than a faster but less accurate linear fitting algorithm. The GM/WM ratios estimated with the nonlinear algorithm also appear to be closer to published values. We suggest that the partial-volume model may be used to compare the accuracy of perfusion analysis algorithms in the absence of absolute quantification or a gold standard. The application of nonrigid registration techniques further improves the consistency of the calculations over rigid registrations, but the difference in the computed GM/WM ratios are very small and may not justify the computational expense. However, when studying very small structures or at higher field strengths, nonrigid registration may become critical.

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