Comparison of Perfusion- and Diffusion-weighted Imaging Parameters in Brain Tumor Studies Processed Using Different Software Platforms

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Rationale and Objectives: To compare quantitative imaging parameter measures from diffusion- and perfusion-weighted imaging magnetic resonance imaging (MRI) sequences in subjects with brain tumors that have been processed with different software platforms.

Materials and Methods: Scans from 20 subjects with primary brain tumors were selected from the Comprehensive Neuro-oncology Data Repository at Washington University School of Medicine (WUSM) and the Swedish Neuroscience Institute. MR images were coregistered, and each subject's data set was processed by three software packages: 1) vendor-specific scanner software, 2) research software developed at WUSM, and 3) a commercially available, Food and Drug Administration–approved, processing platform (Nordic Ice). Regions of interest (ROIs) were chosen within the brain tumor and normal nontumor tissue. The results obtained using these methods were compared.

Results: For diffusion parameters, including mean diffusivity and fractional anisotropy, concordance was high when comparing different processing methods. For perfusion-imaging parameters, a significant variance in cerebral blood volume, cerebral blood flow, and mean transit time (MTT) values was seen when comparing the same raw data processed using different software platforms. Correlation was better with larger ROIs (radii $\geq$ 5 mm). Greatest variance was observed in MTT.

Conclusions: Diffusion parameter values were consistent across different software processing platforms. Perfusion parameter values were more variable and were influenced by the software used. Variation in the MTT was especially large suggesting that MTT estimation may be unreliable in tumor tissues using current MRI perfusion methods.

Key Words: Tumor imaging; cerebral perfusion; cerebral diffusion; MRI.

Diffusion tensor imaging (DTI) measures the microscopic diffusion properties of water and is often altered in pathologic conditions. Mean diffusivity (MD) represents the average mobility of free water molecules within tissue. Fractional anisotropy (FA) measures the asymmetry of water diffusion due to the microstructure of the underlying tissue and is a predictor of the architecture and integrity of the brain white matter (WM) (1). MD has been shown to be decreased in dense cellular tumors such as primitive neuroectodermal tumors and lymphomas (2,3).

Dynamic susceptibility contrast (DSC) magnetic resonance imaging (MRI) is an imaging method that measures the passage of a bolus of contrast through the brain tissue and estimates cerebral perfusion parameters, such as cerebral blood volume (CBV), cerebral blood flow (CBF), and mean transit time (MTT).

DSC MRI has been applied to the study of brain tumors. Specifically, CBV has been shown to be helpful in characterization of brain tumors (4–8). In particular, the CBV of glial tumors, typically normalized to contralateral WM, has been established as a predictor of glioma grade (9–11). Many studies have investigated the use of diffusion and perfusion

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parameters to monitor the response to therapy and differentiate radiation necrosis from tumor recurrence (4,8,12–16). Perfusion imaging appears to have a significant impact on clinical decision making and physicians' confidence in management plans for patients with brain tumor (17). Thus, an incorrect estimation of tumor grade, response, or recurrence resulting from a misestimation of the CBV value could lead to incorrect treatment and patient morbidity.

With increasing use of quantitative and semiquantitative measurements for diagnosis and treatment decisions, it is important for measurements to be accurate and precise across different software platforms. The effect of scanner type and acquisition methods has been discussed with respect to MD in a phantom study (18), and the effect of software platform has been investigated with respect to DSC computed tomography (CT) in stroke (19). With regard to brain tumors, Paulson and Schmainda (20) investigated the effect of acquisition and postprocessing methods on the value of the relative CBV. However, in subjects with brain tumors, the impact of variations in image processing methodology has not been considered in multiple DTI and DSC parameters.

MATERIALS AND METHODS

MRI Acquisition and Preprocessing

Preoperative MRI scans from 20 subjects with malignant primary brain tumors were selected for comparison from the Comprehensive Neuro-oncology Data Repository (CONDR) at Washington University School of Medicine (WUSM) and Swedish Neuroscience Institute (SNI). For each subject, the following structural images were obtained: T_1-weighted (T_1W), fluid attenuation inversion recovery, susceptibility-weighted imaging, and magnetization prepared rapidly acquired gradient echo. Physiological imaging data included DTI and DSC imaging. The image acquisition was relatively standardized across both institutions, although some differences exist between the two sites. Specifically, diffusion-weighted imaging scans at WUSM were acquired using 12-direction gradient scheme and b = 1000 s/mm^2, and SNI diffusion sequences were obtained using 25-direction gradient encoding with b = 1000 s/mm^2. In the DSC sequence, the only difference was the repetition time of 2000 milliseconds at WUSM and of 1500 milliseconds at SNI. Raw data from each individual subject's MRI sequences were coregistered to a target postcontrast T_1W image. Spatial registration was performed using affine registration using WU developed software. Each subjects T_1W image was registered to a T_1W atlas template image, and other T_1W and T_2W sequences were coregistered with the subject's T_1W target image. $T_1W \rightarrow T_1W$ registration used maximization of spatial correlation (21), whereas cross-modality registration (eg, $T_2W \rightarrow T_1W$) used alignment of intensity gradients (22). Perfusion and diffusion parameter maps were transformed to the T_1W target space using a transformation matrix obtained from coregistering respective anatomy sequences.

Diffusion and Perfusion Processing Packages

Following these acquisition and registration steps, each subject's raw diffusion and perfusion data were processed. Multiple parameter maps were created for each subject. The parameter maps included measures of CBV, CBF, MTT, FA, and MD. The processing was performed for each subject using three different software platforms:

1. An in-house software developed at WUSM, Saint Louis, MO (based on Lee et al.(23) for perfusion processing and Basser et al. (24) for diffusion processing).
2. An Food and Drug Administration (FDA)-approved commercial stand-alone package NordicNeuroLab (NNL; Bergen, Norway)
3. The FDA-approved Siemens (Erlangen, Germany) Leonardo workstation v. 8 (SL).

In all cases, the perfusion processing was done using a selection for the arterial input function (AIF) and a convolution/deconvolution method. In the case of method 1, the local AIF was computed automatically, and in the case of methods 2 and 3, the AIF was selected by an experienced operator. For subjects whose data were acquired at WUSM, where Siemens MR scanners are used, raw data were processed using all three software platforms. For subjects whose data were acquired at SNI, where GE scanners are used, data were processed and compared using the NNL and WUSM software platforms. All parametric maps were obtained in native space and transformed to the target space using the transform for echo planar imaging scans computed at the registration step.

Region of Interest (ROI) Analysis

ROIs were chosen by a neuroradiology fellow (the same individual chose all of the ROIs) within three types of tissue, using T_1 post-Gd contrast image as a reference. The regions of the first type were selected from abnormal tissue regions (labeled as "tumor") and were drawn within areas of tumor enhancement rim on T_1 post-Gd and in the center of surrounding edema. A half of ROIs labeled as tumor contained a single tissue, and another half had several tissue types mixed (this was validated by comparing respective histograms from T_1 post-Gd ROIs). The second tissue type was selected in ipsilateral normal tissue regions. The third tissue type was chosen within each patient's contralateral normal WM for normalization of perfusion metrics. The ROI selection was validated by an experienced member of the neuroradiology faculty. CBV, MTT, and CBF maps were converted to dimensionless units by dividing each voxel's value by the average signal of a spherical region within contralateral WM of the same radius as the original region. Of note, we designate these normalized values as "relative", which is different than the convention