Assessing Glioma Cell Infiltration Using A Fiber Coherence Index: A DTI Study

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Introduction

Malignant glioma is one of the most lethal tumors that strikes adults in their prime. Despite advances in diagnosis and treatment, prognosis remains dismal largely due to the infiltrating nature of the tumor cells and the inability to detect these cells using conventional imaging techniques. It has been reported that glioma infiltration occurs preferentially along the white-matter fiber tracts *(1)*. A common site of infiltration is the corpus callosum where glioma can extend across the midline to spread to other locations in the brain. With tumor invasion, the organized structure of a fiber tract can lose its structural integrity and directional coherence, leading to changes in the diffusion properties of water molecules.

Diffusion tensor imaging (DTI) is a powerful tool for characterizing tissue diffusion *in vivo (2)*. Recently, several groups employed DTI for the assessment of tumor cell infiltration in glioma patients *(3-5)*. These studies have focused on measuring changes in a scalar diffusion anisotropy index, such as the mean diffusivity, fractional anisotropy (FA), or relative anisotropy (RA). While this approach can be useful in evaluating low-grade gliomas without peritumoral vasogenic edema (PVE), it often fails on patients with high grade gliomas (WHO grade III and IV) due to the presence of PVE, which can also cause a substantial decrease in diffusion anisotropy. Since the edematous regions are not always infiltrated with tumor, a very high false positive rate occurs when using FA or RA to identify tumor infiltration. In this study, we have used an alternative DTI parameter, regional fiber coherence index (r-FCI), for assessing tumor cell infiltration, and compared its performance with that of FA. Our results suggest that r-FCI is advantageous over FA in delineating white-matter fiber tracts infiltrated by tumor cells in the presence of vasogenic edema.

Methods

Unlike the scalar indices such as FA and RA, the r-FCI proposed in this study is based on fiber directional coherence among a cluster of voxels within a region of interest in a fiber tract. The fiber orientation vector ($\boldsymbol{\lambda}_j$) at voxel *j* can be approximated by the principal diffusion direction in that voxel, which can be measured using DTI. After the individual fiber orientations are determined for a cluster of voxels in the fiber, the FCI for voxel *j* can be simply calculated using Eq. [1], where *i* is the index of the voxels in the close proximity of the *j*th voxel, *g(i,j)* is a weighting function that defines the spatial extent over which the summation is performed, and *N* is the total number of voxel pairs used for the vector inner product calculation. To calculate r-FCI within an ROI containing *M* voxels, the individual FCI values can be simply averaged.

$$FCI_j = \frac{1}{N}\left|\sum_{i=1}^{N}\left(\boldsymbol{\lambda}_j \bullet \boldsymbol{\lambda}_i\right) g(i,j)\right| \qquad [1]$$

To investigate r-FCI as an index for detecting tumor infiltration into the white-matter fiber tracts, four patients (2 males and 2 females; age range: 42-65 y.o.) with newly diagnosed glioblastoma multiforme (GBM; WHO grade IV) were enrolled in this study. Prior to surgery, the patients underwent MRI scans performed on a 1.5 T GE Signa NV/*i* scanner. The data acquisition protocol included pre-contrast T1-weighted, T2-weighted, fluid-attenuated inversion recovery (FLAIR), and DTI axial imaging, and post-contrast T1-weighted axial, coronal, and sagittal 2D imaging and 3D gradient echo imaging. Following surgery, MRI scans were repeated approximately at one-month intervals. The DTI studies were carried out using a customized single-shot EPI pulse sequence. The key acquisition parameters were: TR = 4000 ms, TE = 72 ms, NEX = 2, FOV = 22 cm, slice thickness = 5 mm, image matrix = 128^2, b-value = 750 s/mm^2, and number of diffusion gradient directions = 27. The imaging time was ~4 min.

DTI data processing was performed using a custom program developed using Matlab (The MathWorks, Inc., Natick, MA). Regions of interest (ROIs) were drawn in the fiber tracts suspected of tumor infiltration within 2-3 cm zone outside the gadolinium enhancement. This zone typically contained vasogenic edema as seen in the FLAIR images. FCI was evaluated for each pixel in the ROI by computing the inner product only with the nearest neighbors and by setting *g(i,j)* in Eq. [1] to 1.0. The average value of FA and r-FCI were then calculated within the ROI. In order to establish the correlation with follow-up MRI scans, only the ROIs that were not affected by surgical resection were selected.

Results and Discussion

Among the four patients, a total of five ROIs were analyzed. Because biopsies were not taken from these ROIs, we relied on follow-up MRI and/or MRS findings, to which the r-FCI and FA values were correlated (Table 1). Reduction in FA values was observed in all white-matter fiber tracts suspected of tumor infiltration, as compared to the normal fiber tracts in the contralateral side without tumor. Only two out of the five regions with reduced FA, however, developed tumor in the follow-up MRI scans. A possible explanation is that the FA changes were predominately caused by PVE which may or may not contain infiltrating tumor cells. This result suggested that a reduced FA value was not specific to tumor cell infiltration. The reduction in r-FCI, however, correlated well with the follow-up MR results (Table 1). Figure 1 shows two FA maps of patient 3, one day after surgery (left) and approximately three months later (right). Although ROI1 and ROI2 have approximately the same FA values initially (Table 1), ROI1 developed tumor with a drastically decreased FA value 95 days later, whereas ROI2 showed increased fiber intensity, presumably due to the reduced edema. The different fates of the two ROIs correlated well with the initial r-FCI values. Although a larger sample of patients is needed to increase the statistical power of the study, our preliminary results indicate that r-FCI, as a predictive marker for tumor infiltration, can offer advantages over FA in determining whether a vital white-matter fiber tract is invaded.

Table 1. FA, r-FCI, and follow-up MRI Results of 4 Glioma Patients

Patient No.	FA tumor side	FA contra-lateral	r-FCI tumor side	r-FCI contra-lateral	follow-up MRI*
1	0.23 ± 0.06	0.76 ± 0.04	0.45 ± 0.03	0.83 ± 0.01	Y
2	0.35 ± 0.08	0.69 ± 0.06	0.79 ± 0.04	0.76 ± 0.01	N
3a (ROI1)	0.32 ± 0.04	0.74 ± 0.03	0.53 ± 0.02	0.89 ± 0.03	Y
3b (ROI2)	0.36 ± 0.04	0.82 ± 0.04	0.86 ± 0.04	0.91 ± 0.02	N
4	0.22 ± 0.07	0.61 ± 0.04	0.62 ± 0.04	0.74 ± 0.01	N

* Y and N in the last column represent positive and negative tumor detection, respectively.

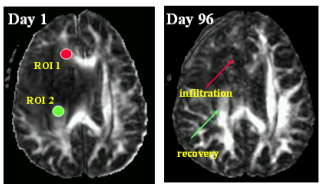

Figure 1

References

1. Enam S, et al., Brain Tumor Invasion: Clinical, Biological and Therapeutic Considerations. New York; 1998; p 133.
2. Basser PJ, Mattiello J, Lebihan D. Biophys J 1994; 66:259-267.
3. Zhou XJ, Leeds NE, Poonawalla AH, Weinberg J. Proc ISMRM 11th Meeting; Toronto, Canada. 2003; p 2238.
4. Price SJ, et al., Clinical Radiology 2003; 58:455-462.
5. Sinha S, Bastin ME, Whittle IR, Wardlaw JM. AJNR 2002; 23:520-527.