Brain white matter anatomy of tumor patients evaluated with diffusion tensor imaging
We applied multislice, whole-brain diffusion tensor imaging DTI to two patients with anaplastic astrocytoma. Data were analyzed using DTI-based, color-coded images and a 3-D tract reconstruction technique for the study of altered white matter anatomy. Each tumor was near two major white matter tracts, namely, the superior longitudinal fasciculus and the corona radiata. Those tracts were identified using the color-coded maps, and spatial relationships with the tumors were characterized. In one patient the tumor displaced adjacent white matter tracts, whereas in the other it infiltrated the superior longitudinal fasciculus without displacement of white matter. DTI provides new information regarding the detailed relationship between tumor growth and nearby white matter tracts, which may be useful for preoperative planning.

Introduction

Approximately 18,000 brain tumors are diagnosed annually in the United States.1 Advancing faster than effective new brain tumor therapies are new magnetic resonance–based techniques for characterizing these malignancies. A significant problem in brain tumor imaging and therapy is the accurate depiction of white matter involvement. Are there effects of tumor on white matter pathways that are not seen on conventional T₁- or T₂-weighted images? That question has important implications for the accurate localization of radiation ports and for determining whether and how extensive surgery should proceed. Diffusion tensor imaging (DTI) is a technique that can characterize the properties of water diffusion in the brain by providing three types of information, namely, the extent (apparent diffusion constant, or ADC) and directionality (anisotropy) of diffusion and its predominant orientation.2 The ADC and anisotropy are believed to be related predominantly to the integrity of axonal tracts3,4 and depict contrast that is different from conventional T₁- and T₂-weighted images. Abnormalities on diffusion-weighted images due to brain tumors have been reported,5 including an increase in ADC within malignant tissue,6–11 detection of changes in white matter fiber angles,12 and ADC and anisotropy changes seen with therapy.12–13 In contrast to the aforementioned studies, in which DTI provided a method of characterizing the tumor itself, we focused on the capability of DTI to reveal the effect of tumor on white matter pathways. We found that DTI is an effective tool for delineating the effect of tumor on nearby white matter tracts, information that may facilitate preoperative planning.

Patients and Methods

MRI Data Acquisition

Studies were performed using a 1.5T Philips GyroscanNT (Best, The Netherlands) system. DTI was accomplished using multislice, segmented echo-planar imaging (EPI) with cardiac triggering (repetition time [TR] = 5 heartbeats; echo time [TE] = 92ms) and
navigator echo phase correction. A data matrix of $128 \times 95$ over a field of view of $230 \times 173$ mm was obtained, acquiring 17 echoes per excitation. Slice thickness was 3 mm (coronal, 40–60 slices) without gaps. Diffusion weighting was performed along 6 axes, using a $b$-value of 600 s/mm$^2$. A reference image with low diffusion weighting ($b=33$ s/mm$^2$) was recorded. Measurements were repeated 6 times to increase signal/noise. Double-echo $T_2$-weighted imaging (TEs of 22 and 100ms; image resolution equal to DTI) was performed for anatomic guidance. Total examination time was 1 hour. Diffusion tensors at each pixel were calculated using multivariate linear least square fitting$^2$ and diagonalized. The eigenvector ($v_1$) associated with the largest eigenvalue ($\lambda_1$) was assumed to represent the local fiber direction. Anisotropy maps were obtained using the orientation-independent fractional anisotropy (FA)$^{14}$ DTI-based color maps were created from FA values (image intensity) and the three vector elements of $v_1$,$^{15,16}$ red indicated fibers running along the right to left direction, green represented anterior to posterior, and blue was superior to inferior. The average diffusion constant, $ADC_{av}$, was calculated from the trace of the diffusion tensor. Axial and sagittal images were obtained by reslicing the 3-D volume data. For 3-D reconstruction of tracts of interest, the Fiber Assignment by Continuous Tracking method was employed.$^{17-19}$ Tract reconstruction required 20 minutes using an 833 MHZ Pentium III Workstation (Dell, Austin, TX).

Patients

Patient 1 was a male age 36 years with a right frontal anaplastic astrocytoma. Originally he presented with two partial seizures in 1 week due to a left-sided, low-grade glioma that eventually dedifferentiated to an anaplastic astrocytoma, necessitating resection. Contralateral extension of the left frontal mass was found in follow-up imaging. Patient 2 was a male age 45 years with a posterior left frontal anaplastic astrocytoma. He presented with aphasia, hemiparesis, and simple partial seizures involving the right face. DTI data on healthy volunteers were obtained from our normative DTI database (19 subjects, ages 19–43 years; 10 male).
Results

Figures 1a-c show the $T_2$-weighted image, FA map, and ADCav map for Patient 1. The $T_2$-bright lesion in the left hemisphere was due to a surgical cavity. High ADCav values (see figure 1c) were found within the tumor, in keeping with previous reports.6-11,13 The $T_2$-abnormal portion of the tumor (see figure 1a) had low FA (0.05 to 0.15; see figure 1b). The boundary of the tumor identified in the FA maps was not as clear as that on the $T_2$-weighted images, because the anisotropy of the tumor was similar to that of gray matter. To clarify white matter anatomy, the DTI-based color map was compared with that of a healthy volunteer (figures 1d-g). When the 2 subjects were compared, several major anatomical changes become evident. First, the corona radiata of the right hemisphere of the patient was dislocated medially (white arrowheads). Second, the corpus callosum genu was severely affected in the patient. This was in contrast to the cingulum, which was adjacent to the corpus callosum but structurally preserved. The superior longitudinal fasciculus (SLF) is a prominent white matter tract that projects through regions occupied by the tumor. In figure 1e, only the posterior SLF can be appreciated (yellow arrowheads) in the patient brain. Figures 1f and g depict the right SLF of the patient dislocated superiorly as it courses anteriorly. Figure 2 shows color maps (figures 2a-d) and $T_2$-weighted images (figure 2e) of Patient 2. Tumor could be identified by $T_2$ hyperintensity and low anisotropy. Although this tumor displayed similar histology to that of Patient 1, the color maps indicate that the low anisotropy regions were not accompanied by deformation of adjacent white matter structures. As with Patient 1, the SLF of Patient 2 lay within the path of the tumor. The SLF can be appreciated in the contralateral hemisphere (yellow arrowheads) but not near the tumor. The SLF was apparently within the area of lowest anisotropy. To confirm that, we reconstructed the trajectory of the SLF in the contralateral hemisphere. For the reconstruction, the SLF was identified at the slice level shown in figure 2c, and tracking results that penetrated the identified SLF were searched. The result is shown in figure 2e (red), superimposed on $T_2$-weighted images. The $T_2$-hyperintense regions correlated spatially with the brain regions occupied by the SLF.

A 3-D reconstruction of the corona radiata was performed for both patients and is shown in figure 3. The 3-D relationship of the corona radiata with the tumor can be clearly appreciated. The corona radiata of Patient 1 surrounds the surface of the tumor because of mechanical compression. On the other hand, the tumor in Patient 2 did not change the trajectory of the corona radiata, and it projected into the core of the $T_2$-hyperintense regions, where the tracking terminated due to the low anisotropy.
Discussion

We report the application of 3-D DTI-based white matter anatomic studies for 2 patients with brain tumors. We found that FA alone might not provide contrast superior to that of conventional T2-weighted images to define tumors. However, the DTI-based color-coded maps could provide unique information about white matter architecture and its alteration due to the tumors. This finding is in line with previous reports on altered fiber angles due to tumor mass. In this study, we also employed 3-D tract reconstruction techniques, which greatly aided the slice-by-slice interpretation of the color maps, especially in cases of deformed anatomy.

Both patients had anaplastic astrocytomas. However, the effects of their tumors on the 3-D white matter disposition were different. In Patient 1, the tumor grew discretely, compressing the corona radiata and slf, which were dislocated medially and superiorly, respectively (see figure 1). The corpus callosum genu was severely affected, likely due to Wallerian degeneration after surgery in the left hemisphere. Although the T2-weighted image of Patient 1 (see figure 1a) also showed that the tumor compressed adjacent white matter, information regarding the specific white matter tracts dislocated, and in which directions, could be obtained only by 3-D DTI. Unlike the tumor of Patient 1, the tumor of Patient 2 did not induce significant anatomic deformation. That difference is best illustrated by examining the corona radiata (see figures 2 and 3). Patient 2 (see figure 2) illustrates the fact that significant decreases in anisotropy may be evident even without marked anatomic deformity. Figure 2e shows that the high T2 signal and low FA regions spread and follow regions occupied by the slf, consistent with the proposed theory that tumors might spread along white matter tracts. However, we could not conclude whether the T2 hyperintensity along the slf indicates infiltrating tumor or Wallerian degeneration. Comprehensive, longitudinal studies with histological correlation are needed. While 3-D tract reconstruction provides a new way to evaluate white matter architecture, its limitations should also be recognized. DTI is of limited resolution (2 x 2 x 3 mm interpolated to 1 x 1 x 3 mm in the presented work), leading to substantial partial volume effects, including multiple populations of fibers with different orientations within a pixel. Consequently, it cannot provide information about connectivity of the brain at the cellular level. The reconstructed tract trajectories reflect only the macroscopic configuration of prominent fiber bundles. Another problem is the motion susceptibility of the high-resolution segmented EPI approach, which presently limits its utility for pediatric or uncooperative patients.

In conclusion, we have demonstrated the application of 3-D DTI to the study of white matter trajectory using data from patients with anaplastic astrocytomas. The DTI-based color maps and 3-D tract reconstructions provided detailed anatomic information on
relationships between tumors and nearby white matter tracts, which may be important in therapeutic planning.

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