Diffusion tensor tractography in patients with cerebral tumors: A helpful technique for neurosurgical planning and postoperative assessment

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Abstract

Objective: To demonstrate the role of diffusion tensor tractography (DTT) in preoperative mapping of eloquent tracts in relation to cerebral tumors and to determine whether it is helpful for neurosurgical planning and postoperative assessment.

Methods and materials: Sixteen patients with brain tumors underwent diffusion tensor imaging (DTI). The pyramidal tract, corpus callosum and optic radiation were reconstructed and the exact location of a lesion with respect to these tracts was observed to design a reasonable surgical plan for preserving vital tracts while maximizing tumor resection. After surgery, DTI was performed again and these tracts were evaluated to investigate the surgical outcomes. Twenty-four patients with suspicion of pyramidal tract involvement were also evaluated as a control group.

Results: The relationship between tracts and tumors was classified as three types: type I is simple displacement, type II is displacement with disruption and type III is simple disruption. Twelve cases involved in pyramidal tract (DTT group), one was type I with reduction of displacement after surgery, nine were type II with reduction of displacement and other two were type III without any improvement. The extent of tumor resection (p = 0.045) and postoperative improvement of locomotive function (p = 0.015) of DTT group were significantly higher than those of control group. Corpus callosum was involved in seven cases, three were type II with reduction of displacement and four were type III without any improvement. Optic radiation was involved in three cases, all were type I with reduction of displacement.

Conclusion: DTT allowed for visualization of the exact location of tumors relevant to eloquent tracts and was found to be beneficial in the neurosurgical planning and postoperative assessment.

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Keywords: Tractography; Diffusion tensor imaging; Magnetic resonance imaging; Brain tumor

1. Introduction

Preservation of vital white matter tracts while maximizing tumor resection is a principal goal in neurosurgery. Many brain tumors originate within and involve in the white matter of the brain. In most situations, the eloquent white matter tracts are intact or only displaced. So it is essential to distinguish intact from disrupted white matter tracts during excision of brain tumors.

Conventional MR techniques (include T2-weighted, T1-weighted and FLAIR imaging) have widely used for radiological assessment and localization of brain tumors. But these MR methods could not give any precise information about the integrity and location of white matter tracts in the immediate region surrounding tumors. Functional MRI can be used to localize important cortical areas near brain tumors [1,2]. However, this imaging modality can not show the exact location of a possibly displaced tract.
Recently, diffusion tensor imaging (DTI) has been used to assess white matter tracts in the brain [3–5]. It is sensitive to the diffusion of water molecules and can measure the displacement of diffusion which revealing the orientation of white matter tracts in brain. This orientation information can then be used to delineate white matter tracts of the brain by employing tractography (also called fiber tracking) algorithms [6–8].

Currently, diffusion tensor tractography (DTT) is the only imaging modality with the potential to generate realistic fiber-tract trajectories in white matter of the brain in vivo. This technique has hitherto been largely restricted to studies of the healthy human brain and has provided demonstrations of white matter tracts that have coherence with known anatomy [9,10]. Previous investigations in patients with brain tumors have employed DTT to demonstrate local abnormalities in tract orientation and surrounding edema [11–13], and used DTT to illustrate displacement of some vital white matter tracts [14,15], but they were all restricted to preoperative assessment. In this study, we have applied DTT to investigate clinically eloquent white matter tracts in 16 patients with cerebral tumors, and to investigate the potential of DTT for neurosurgical planning and postoperative assessment. Current limitations of this technique are also discussed.

2. Materials and methods

2.1. Patient selection

From August 2003 to June 2004, diffusion-tensor MR images were obtained in 16 consecutive patients (12 men, 4 women; age range: 20–72 years; mean age: 51.7 years) who were undergone preoperative and postoperative evaluation of brain tumors. Patients whose pyramidal tract was affected by tumors on the DTT images were regarded as DTT group (12 patients). A control group of 24 patients (17 men, 7 women; age range: 25–68 years; mean age: 52.5 years) with suspicion of pyramidal tract being involved were also retrospectively investigated. These patients had enough clinical and MRI data before and after surgery for comparison. Institutional review board approval was obtained for the study. All examinations were performed after written informed consent was obtained from the patients or their next of kin. Patient data are summarized in Table 1.

2.2. MRI acquisition

MR imaging was performed by using a 1.5-T MR system (Sonata; Siemens, Erlangen, Germany) with a single-shot echo-planar sequence and the following parameters: 6100/106 (repetition time ms/echo time ms), 30 contiguous sections, a 4.0-mm section thickness, ten signals acquired, a 128 × 128 matrix, a 230 mm × 230 mm field of view, and a total imaging time of 7 min 15 s. A total seven image sets were acquired: six with noncolinear diffusion weighting gradients with ab value of 1000 s/mm² and one without diffusion weighting. The diffusion gradients in the x, y, and z directions were, respectively, (1, 0, and 1); (−1, 0, and 1); (0, 1, and 1); (0, 0, and −1); (1, 1, and 0); and (−1, 1, and 0). Homodyne reconstruction with zero-filled interpolation was used in the axial planes to obtain 256 × 256 matrix images, the size of a voxel was 0.9 mm × 0.9 mm × 4.0 mm. Diffusion tensor MR images were acquired at the end of the routine examination (which included T1-, T2-, and FLAIR) for the evaluation of brain tumors, but before contrast-enhanced (gadopentate dimeglumine, Magnevist; Schering, Guangzhou, China) T1-weighted MR imaging in three orthogonal directions. All diffusion tensor imaging were performed successfully, and no obvious image distortions that can interfere with visualization of white matter tracts were observed.

<table>
<thead>
<tr>
<th>Patient no./age (year)/sex</th>
<th>Pathological diagnosis (WHO grading)</th>
<th>Pyramidal tract Type</th>
<th>Corpus callosum Type</th>
<th>Optic radiation Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/61/M</td>
<td>Astrocytoma (2)</td>
<td>III N</td>
<td>–</td>
<td>– I CRN</td>
</tr>
<tr>
<td>2/41/W</td>
<td>Oligodendroglioma (2)</td>
<td>–</td>
<td>– III N</td>
<td>–</td>
</tr>
<tr>
<td>3/46/M</td>
<td>Astrocytoma (3)</td>
<td>II – RD</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>4/30/M</td>
<td>Astrocytoma (3)</td>
<td>– – –</td>
<td>– – –</td>
<td>– I CRN</td>
</tr>
<tr>
<td>5/20/M</td>
<td>Oligoastrocytoma (3)</td>
<td>II CRN</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>6/59/W</td>
<td>Oligoastrocytoma (3)</td>
<td>–</td>
<td>– CRN</td>
<td>–</td>
</tr>
<tr>
<td>7/62/M</td>
<td>Oligoastrocytoma (3)</td>
<td>II RD</td>
<td>II RD</td>
<td>–</td>
</tr>
<tr>
<td>8/56/M</td>
<td>Oligoastrocytoma (3)</td>
<td>II RD</td>
<td>II RD</td>
<td>–</td>
</tr>
<tr>
<td>9/72/M</td>
<td>Glioblastoma (4)</td>
<td>I RD</td>
<td>III N</td>
<td>–</td>
</tr>
<tr>
<td>10/80/M</td>
<td>Glioblastoma (4)</td>
<td>II – RD</td>
<td>– III N</td>
<td>–</td>
</tr>
<tr>
<td>11/29/M</td>
<td>Glioblastoma (4)</td>
<td>–</td>
<td>– III N</td>
<td>–</td>
</tr>
<tr>
<td>12/45/W</td>
<td>Glioblastoma (4)</td>
<td>II – RD</td>
<td>II RD</td>
<td>–</td>
</tr>
<tr>
<td>13/38/M</td>
<td>Metastatic adenocarcinoma</td>
<td>III N</td>
<td>III N</td>
<td>–</td>
</tr>
<tr>
<td>14/46/M</td>
<td>Metastatic adenocarcinoma</td>
<td>II RD</td>
<td>–</td>
<td>– CRN</td>
</tr>
<tr>
<td>15/55/M</td>
<td>Metastatic adenocarcinoma</td>
<td>II CRN</td>
<td>–</td>
<td>– I CRN</td>
</tr>
<tr>
<td>16/50/W</td>
<td>Malignant lymphoma</td>
<td>II CRN</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

APC: assessment of postoperative changes; N: no improvement; RD: recovery of displacement; CRN: completely returned to normal; ‘–’: not measurably involved.
The tractography method employed was so-called stream-line fiber tracking [6,7]. Subvoxel fiber tracking was performed by interpolation of the principal direction field with a specified vector step length. The tracking algorithm was initiated from a user-defined region of interest. Tracking was performed in both anterograde and retrograde directions according to the direction of the principal eigenvector in the ROI. Diffusion tensors, eigenvalues and eigenvectors were computed from linearly interpolated diffusion tensor images at each iteration. Tracks were terminated for reaching given threshold values of FA and angle between consecutive vector lines as described previously [19,20]. Two schemes were used to localize the structures of interest. One was to define a single seed ROI and to display all the trajectories that passed through both of these regions. The location of ROI and reconstruction parameters of pyramidal tract, corpus callosum and optic radiation were shown in Table 2.

2.5. Assessment and treatment

The 3D structures of interest were superimposed on T2-weighted images and then the exact location of brain tumors relevant to these white matter tracts of ill side was carefully investigated by comparing with those of the healthy side. The relationships of lesions and clinical eloquent white matter tracts were divided into three types: type I is simple displacement, type II is displacement with disruption and type III is simple disruption. Type I indicated displacement of the location of a white matter tract without disruption of its integrity. Type II showed reduced fibers of a tract and the residual part of the tract was displaced from its normal location. Type III denoted fibers’ reduction without any displacement of the residual part of it.

Based on the results of DTT and contrast-enhanced T1-weighted MR images, the margin of tumors and eloquent white matter tracts were carefully determined. Then some basic measurements (i.e. tumor size, the least distance from a tumor to the adjacent tracts, the distance from a tumor to some stable markers of surface of brain) were obtained. According to results of above measurements, appropriate neurosurgical plan was carefully designed for each patient to maximize tumor resection while preservation of vital white matter tracts. The extent of resection is about 5 mm from the eloquent tract. In type I, optimal approach was chosen to preserve displaced white matter tract while maximizing tumor resection. In type II, optimal approach was chosen to resect tumors while preservation of the displaced part of the tract. In type III, appropriate approach was designed to resect the tumor while preservation of the residual part of the tract.

One to three months later after surgery, DTT and contrast-enhanced T1-weighted MR imaging were performed again in all patients. The locomotive function status was evaluated before and after surgery (1–3 month after surgery) both in the DTT group and control group, and the integrity of these eloquent tracts and the extent of resection in the two groups of patients were also investigated.

Rank sum test was used for comparison of surgical outcomes between the two groups. Statistical difference was examined when p-value less than 0.05.

3. Results

The exact location of tumor relevant to eloquent white matter tracts could be displayed with the aid of DTT in each case. The relationships between tumor and tracts could be divided into three types: simple displacement (type I), displacement with disruption (type II) and simple disruption (type III). The location of brain tumors relevant to the eloquent tracts and the surgical outcomes were also shown in Table 1.

### Table 2

<table>
<thead>
<tr>
<th>Fiber tract</th>
<th>Location of ROI</th>
<th>FAT</th>
<th>AT° ( )</th>
<th>SL (mm)</th>
<th>NSVL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyramidal tract</td>
<td>Cerebral peduncle of midbrain in the axial plane</td>
<td>0.20</td>
<td>45</td>
<td>0.30</td>
<td>2</td>
</tr>
<tr>
<td>Optic radiation</td>
<td>The first ROI at the occipital lobe and the second ROI near the lateral geniculate body in sagittal plane</td>
<td>0.20</td>
<td>45</td>
<td>0.30</td>
<td>2</td>
</tr>
<tr>
<td>Corpus callosum</td>
<td>Commisures of corpus callosum in the mid-sagittal plane</td>
<td>0.20</td>
<td>45</td>
<td>0.30</td>
<td>2</td>
</tr>
</tbody>
</table>

FAT: fractional anisotropy threshold; AT: angle threshold; SL: step length; NSVL: number of sampling in a voxel length.
In sixteen patients, pyramidal tract was involved in 12 cases (DTT group), only 1 case was type I with reduction of displacement after surgery and the anterior part of the left-side pyramidal tract being clearly injured (Fig. 1), nine cases were type II with reduction of displacement (Fig. 2) and other two cases were type III with no improvement (Fig. 3). Corpus callosum was involved in seven cases, three of them were type II with reduction of displacement of the displaced fibers after surgery (Fig. 4) and other four cases were type III with no improvement after surgery (Fig. 5). Optic radiation was involved in three cases, all of them belonged to type I with reducing of displacement after surgery (Fig. 6).

The extent of tumor resection of the DTT group was clearly higher \( (p = 0.045) \) than that of the control group, and postoperative improvement of locomotive function of DTT group was also significantly higher \( (p = 0.015) \) than that of the control group (Table 3).

### Table 3

<table>
<thead>
<tr>
<th>Tumor resection of DTT group and control group</th>
<th>Number</th>
<th>Ratio of total resection</th>
<th>Functional status of movement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Partial resection</td>
</tr>
<tr>
<td>DTT group</td>
<td>12</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Control group</td>
<td>24</td>
<td>12</td>
<td>7</td>
</tr>
<tr>
<td>Sum</td>
<td>32</td>
<td>20</td>
<td>19</td>
</tr>
</tbody>
</table>

The mean rank of DTT group and control group is 13.50 and 21.00, \( p = 0.045 \). The mean rank of DTT group and control group is 12.50 and 21.50, \( p = 0.015 \).
Fig. 3. Patient 13. Metastatic adenocarcinoma in a 68-year-old man in the left frontal lobe. The preoperative coronal image (top left) showed the location of two-side of vertical fibers of the internal capsule containing the pyramidal tract was symmetrical which indicated there was no displacement of the left-side vertical fibers and the size of the left-side vertical fibers (red fibers) was clearly smaller than that of the right-side in the sagittal image (view from right, top right) which indicated disruption of the left-side vertical fibers. The postoperative coronal (bottom left) and sagittal (bottom right) images showed there was no improvement of those left vertical fibers.

of vital cerebral function, and the quality of life of these patients will be largely improved. Simultaneously maximizing tumor resection can reduce the chance of recurrence of tumors and improve longer patient survival and long-term functional status [19,20]. For realizing these two goals, many imaging modalities were used to assess brain tumors, which include conventional MRI, positron emission tomography, magnetoencephalography, and functional MRI [21–23]. These tools were used to determine the relationship of tumors with surrounding cortical function areas but provide no information concerning the status of the eloquent white matter tracts. Knowledge of the structural integrity and location of eloquent white matter tracts relevant to cerebral tumors is crucial in neurosurgical planning, because damage to these clinically eloquent pathways can result in postoperatively neurological deficits as damage of functional cortical areas. Consequently,

Fig. 4. Patient 2. Grade 2 oligodendrogloma in a 41-year-old woman in right frontal lobe. The preoperative image (left) showed the anterior part of the right-side corpus callosum (yellow fibers) was clearly disrupted by the mass. Since before surgery the tracts were already identified as disrupted, improvement or return to normal was not expected in this case after surgery, which could also be clearly demonstrated by DTI (right).
it is very important for designing appropriate neurosurgical plan that determining the exact location of tumors relevant to eloquent white matter tracts.

DTT is an important progress in the field of MR imaging. Currently, it is the only imaging method that can visualize the 3D structures of white matter tracts in the brain in vivo. Recently some researchers have reported that DTT can be used to illustrate the relationship of clinical eloquent white matter tracts with brain tumors [14,15], and they were all restricted to preoperative studies.

Our study demonstrated that DTT could be used to reveal the exact location of tumors relevant to eloquent white matter tracts in patients with cerebral tumors. It is not only a beneficial tool for neurosurgical planning but also for postoperative assessment. In the present study we categorized the relationship of lesions and clinical eloquent white matter tracts into three types: simple displacement (type I), displacement with infiltration (type II) and simple disruption (type III). In our study, four cases were type I (one pyramidal tract and three optic radiations) that caused by the occupying effect of tu-
mors and peritumoral edema. Displacement of these structures was significantly reduced after surgery. Fourteen cases were type II (10 pyramidal tracts and 4 corpus callosums) that resulted from direct involvement, compression of tumors and peritumoral edema. It was the most common type of pyramidal tract and maybe resulted from the pyramidal tract having longer fibers and larger range of movement. The results of significantly reducing of displacement of pyramidal tract after surgery also confirmed our hypothesis. On the contrary, we supposed that the fact of corpus callosum being apt to disrupt by tumors maybe related with it having relatively short fibers and small range of movement. Seven cases were simple disruption (two pyramidal tracts and five corpus callosums) that all resulted from direct involvement of tumors and have no improvement after surgery.

As for surgical approaches for different types, we propose to try one’s best to preserve displaced white matter tract while maximizing tumor resection in type I, to enlarge the extent of tumor resection while preservation of the displaced part of the tract in type II, and to maximize tumor while preservation of the residual part of the tract in type III.

The main question we address in this article is whether DTT is suitable for neurosurgical planning. On the basis of the comparison of clinical outcomes between the DTT group and control group, we can conclude that DTT is helpful for neurosurgical planning and can produce better surgical outcomes. Several limitations, however, need to be considered before it can be integrated into a neurosurgical planning system.

Firstly, there is no “gold standard” for in vivo tractography. In fact, DTT is the only method that permits the calculation and visualization of fiber tract trajectories in vivo. None of the existed method could accurately validate the reliability of DTT. In vitro validation of DTT had obtained histologically [24,25], however, sample registration, dissection, freezing, dehydration, fixation, microtoming, thawing, etc., each can alter tissue microstructure and microanatomy and introduce geometric distortion in the histological sample. Therefore, great care must be used to compare fiber directions in living tissue and a fixed specimen.

Secondly, the diffusion tensor used to measure the fiber tract direction is a voxel-averaged quantity. If voxels containing anisotropic fibrous tissue with a uniform fiber direction, the eigenvector associated with the largest eigenvalue of the effective diffusion tensor can provide an unbiased estimate of microscopic fiber field direction vector. But if there is a non-uniform distribution of fiber directions, the MR signal we measure depends on the complicated way on structure and architecture of the tissue [26]. Then the eigenvector associated with the largest eigenvalue of the effective diffusion tensor only corresponds to a consensus average fiber direction within this voxel. If voxels contains curved fiber tracts, then using smaller voxels can ameliorate this problem. If the voxel contains two or more distinct populations, then reducing voxel size does not remedy the problem. This problem becomes even more severe when fiber tracts cross or “kiss”, or branch or merge. In these situations, DTT could not follow the true fiber tract trajectory.

Thirdly, DTT is a user-defined process. In particular, the tracking results were found to vary according to FA threshold, angular threshold, step length and numbers of sampling in a voxel length. Choosing different parameters can produce different fibers. And tracked volumes are also dependent on the size and locations of the seed ROIs. Thus, one might envisage the use of standard regions that after transformation to the patient’s image space might be applied.

Finally, we can not determine the effect of peritumoral edema on tractography. In the present study, sometimes fibers could not pass through the area of peritumoral edema. Whether this phenomenon results from tumor infiltration or simple edema needs to be determined. Because edema may present a possible confound in fiber tracking studies. Vasogenic edema induced in cats by cortical cold lesioning resulted in an increase in diffusion [27] and a swelling of neuronal fibers of 2.3% in the longitudinal direction and 91.1% in the transverse direction [28]. These changes would be expected to reduce anisotropy. If the anisotropy reduction was sufficiently great, it may no longer be possible to detect sufficient diffusion directionality to reconstruct a fiber pathway despite the presence of intact axonal structures in this region. Further investigations are required to determine the effect of edema on tractography.

Despite existing some limitations, new approaches such as models of diffusion that incorporate multiple principal directions [29,30], the use of appropriate registration techniques, and the development and optimization of fiber tracking algorithms may lead to the use of fiber tracking as a neurosurgical planning tool.

5. Conclusion

Our study showed diffusion tensor tractography allowed for assessment of the exact location of tumors relevant to eloquent white matter tracts and it was a beneficial technique not only in neurosurgical planning but also in postoperative assessment.

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References


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