The utility of preoperative diffusion tensor imaging in the surgical management of brainstem cavernous malformations

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OBJECT Resection of brainstem cavernous malformations (BSCMs) may reduce the risk of stepwise neurological deterioration secondary to hemorrhage, but the morbidity of surgery remains high. Diffusion tensor imaging (DTI) and diffusion tensor tractography (DTT) are neuroimaging techniques that may assist in the complex surgical planning necessary for these lesions. The authors evaluate the utility of preoperative DTI and DTT in the surgical management of BSCMs and their correlation with functional outcome.

METHODS A retrospective review was conducted to identify patients who underwent resection of a BSCM between 2007 and 2012. All patients had preoperative DTI/DTT studies and a minimum of 6 months of clinical and radiographic follow-up. Five major fiber tracts were evaluated preoperatively using the DTI/DTT protocol: 1) corticospinal tract, 2) medial lemniscus and medial longitudinal fasciculus, 3) inferior cerebellar peduncle, 4) middle cerebellar peduncle, and 5) superior cerebellar peduncle. Scores were applied according to the degree of distortion seen, and the sum of scores was used for analysis. Functional outcomes were measured at hospital admission, discharge, and last clinic visit using modified Rankin Scale (mRS) scores.

RESULTS Eleven patients who underwent resection of a BSCM and preoperative DTI were identified. The mean age at presentation was 49 years, with a male-to-female ratio of 1.75:1. Cranial nerve deficit was the most common presenting symptom (81.8%), followed by cerebellar signs or gait/balance difficulties (54.5%) and hemibody anesthesia (27.2%). The majority of the lesions were located within the pons (54.5%). The mean diameter and estimated volume of lesions were 1.21 cm and 1.93 cm³, respectively. Using DTI and DTT, 9 patients (82%) were found to have involvement of 2 or more major fiber tracts; the corticospinal tract and medial lemniscus/medial longitudinal fasciculus were the most commonly affected. In 2 patients with BSCMs without pial presentation, DTI/DTT findings were important in the selection of the surgical approach. In 2 other patients, the results from preoperative DTI/DTT were important for selection of brainstem entry zones. All 11 patients underwent gross-total resection of their BSCMs. After a mean postoperative follow-up duration of 32.04 months, all 11 patients had excellent or good outcome (mRS Score 0–3) at the time of last outpatient clinic evaluation. DTI score did not correlate with long-term outcome.

CONCLUSIONS Preoperative DTI and DTT should be considered in the resection of symptomatic BSCMs. These imaging studies may influence the selection of surgical approach or brainstem entry zones, especially in deep-seated lesions without pial or ependymal presentation. DTI/DTT findings may allow for more aggressive management of lesions previously considered surgically inaccessible. Preoperative DTI/DTT changes do not appear to correlate with functional postoperative outcome in long-term follow-up.

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KEY WORDS cavernous malformations; brainstem; diffusion tensor imaging; diffusion tensor tractography; resection; outcome; vascular disorders

ABBREVIATIONS BSCM = brainstem CM; CM = cavernous malformation; CST = corticospinal tract; DTI = diffusion tensor imaging; DTT = diffusion tensor tractography; FA = fractional anisotropy; ICP = inferior cerebral peduncle; ML = medial lemniscus; MLF = medial longitudinal fasciculus; mRS = modified Rankin Scale.

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DISCLOSURE The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.
Cavernous malformations (CMs) are uncommon lesions, with an estimated prevalence of 0.4%–0.8%. They represent 10%–20% of all CNS vascular malformations, with the majority of cases involving supratentorial structures. Approximately 10%–35% of CMs arise in the brainstem and may be associated with initial hemorrhage and rebleeding rates higher than those occurring with supratentorial and spinal cord lesions. Resection may reduce the risk of a stepwise neurological deterioration, but the complexity of brainstem anatomy makes this task technically demanding and is associated with the risk of additional brainstem injury.

Several adjuvant techniques have been implemented in the surgical management of brainstem lesions, such as functional MRI, intraoperative frameless stereotactic navigation, and intraoperative MRI. None of those methods can precisely visualize white matter tracts or define essential aspects of tract location or displacement. Diffusion tensor imaging (DTI) and diffusion tensor tractography (DTT) are promising neuroimaging techniques that help overcome some of those limitations. They have become useful clinical tools that can delineate functionally important white matter tracts for surgical planning.

Tractography based on diffusion MRI explores the correlation between water diffusion and brain structure to delineate the course of white matter pathways. Diffusion tensor tractography (DTT) follows a white matter tract from voxel to voxel in 3 dimensions by assuming that the direction of least restricted diffusion corresponds to the orientation of axons. As a result of this predictable pattern of diffusion, which is orientation dependent (or anisotropic), location and orientation of white matter tracts can be determined.

Several articles have described the implementation of DTI for a multitude of neurological diseases and neuroanatomical studies; however, none has addressed its specific application in the management of brainstem cavernous malformations (BSCMs).

The goals of the present study were to determine if preoperative DTI and DTT can clearly identify relevant fiber tracts adjacent to BSCMs and to evaluate their roles in surgical planning. We analyze the correlation of DTI and DTT findings with known microsurgical anatomy of the brainstem safe entry zones, and their implications for the selection of surgical approaches. Finally, we attempt to correlate preoperative changes in DTI and DTT and functional outcome after resection of these lesions.

Methods

Patients

All patients who were evaluated for a BSCM at the University of Texas Southwestern Medical Center between July 2007 and July 2012 were screened for inclusion into the study. Eleven patients who underwent resection of a symptomatic BSCM and had a preoperative DTI scan were identified. Retrospective chart review was used to identify patients with a minimum of 6 months of clinical and radiographic follow-up. Surgical intervention was considered in cases of 1) BSCMs with pial presentation, independent of the number of hemorrhages preoperatively; or 2) history of BSCMs and progressive neurological deficits, with or without radiographic evidence of rehemorrhage. Detailed neurological examination and brain MRI gradient echo and gadolinium contrast-enhanced sequences were obtained. All patients were reassessed daily during hospital admission, then routinely during outpatient clinic visits for a minimum of 6 months postoperatively. Retrospective analysis and data collection were approved by the institutional review board at our institution.

Conventional MR and DTI

All patients underwent initial brain MRI with and without gadolinium contrast as part of their diagnostic workup. Once the patients were selected for surgical intervention, additional brain MRI with fast imaging employing steady state acquisition (FIESTA) and DTI protocol were performed (Signa HDxt 3.0T, GE Medical Systems; FOV 16.0 cm, matrix size 320 × 256, slice thickness 2.00 mm). DTI was performed using single-shot spin-echo planar imaging (TR 8,500–12,000 msec, TE 75–85 msec, matrix 128 × 128, slice thickness 2.4 mm, gap 0 mm). Nineteen diffusion directions at b = 1000 sec/mm² were acquired in addition to b = 0 images. All images were reviewed by one of the senior authors (A.R.W.). A default fractional anisotropy (FA) threshold of 0.20 and minimum fiber length of 50 mm were used for construction of DTT, as validated by Kunimatsu et al.

Patterns of fiber tract alterations (based on morphological appearance on color map FA threshold and reconstructed 3D tractography) were classified into 4 groups, as described by Lazar et al. (Table 1). Areas of interest were limited to the neuroanatomical region of the brainstem correlating to the BSCM site and its hemorrhage. The following major fiber tracts were selected for evaluation: 1) corticospinal tract (CST), 2) medial lemniscus (ML) and medial longitudinal fasciculus (MLF), 3) inferior cerebellar peduncle (ICP), 4) middle cerebellar peduncle, and 5) superior cerebellar peduncle (Fig. 1). Scores of 0–4 were applied according to the degree of distortion seen in each of the involved tracts, and the sum of individual fiber tract scores was used for univariate analysis.

Initial postoperative imaging follow-up consisted of noncontrast head CT scanning, completed up to 24 hours after resection. Postoperative brain MRI with gadolinium contrast was obtained during the hospital stay or

<table>
<thead>
<tr>
<th>Description</th>
<th>Score</th>
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<tbody>
<tr>
<td>Normal</td>
<td>0</td>
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<tr>
<td>Deviated</td>
<td>2</td>
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<tr>
<td>Deformed</td>
<td>3</td>
</tr>
<tr>
<td>Interrupted</td>
<td>4</td>
</tr>
</tbody>
</table>

* As described in the study by Kovanlikaya et al. Modified from Lazar et al.
after discharge, but no longer than 6 months postoperatively. If no evidence of a recurrent or residual lesion was identified on initial brain MRI, this study was repeated at 6-month intervals for the first 2 postoperative years and at 2-year intervals thereafter.

Anatomical Location and Hemorrhage Status

Cavernous malformation location was stratified into 5 categories: mesencephalic, pontomesencephalic, pontine, pontomedullary, and medullary. Sizes were measured on thin-slice T1- or T2-weighted sequences, including the extralesional hematoma cavity (if present). The volume (including BSCM and surrounding hematoma) was calculated assuming an approximate ellipsoid lesional shape: 

$$V = \frac{4}{3} \pi \times r_1 \times r_2 \times r_3$$

Clinical criteria to determine evidence of hemorrhage were 1) acute onset of neurological deficit that persisted for more than 24 hours and 2) deterioration of preexisting symptoms or development of new neurological deficits in patients with previously ruptured BSCMs.

Surgical Principles and Technique

Several surgical approaches were used (Fig. 2). To minimize local tissue trauma, the hemosiderin-stained surrounding parenchyma is not routinely resected in our practice. Developmental venous anomaly was preserved in all identified cases. The 2-point method was used when feasible to guide the surgical decision-making process, as described elsewhere. The selected surgical approach was correlated with the results from preoperative DTI/DTT and the initial surgical plan adjusted if the findings showed discrepant results or potential risk to the integrity of major long fiber tracts. Somatosensory, motor, and brainstem auditory evoked potential monitoring, as well as electromyographic recordings of specific cranial nerves, were performed selectively based on CM location. A perioperative lumbar drain was used only once for adequate brain relaxation (subtemporal approach for a mesencephalic CM). Histopathological confirmation was obtained for all surgical specimens.
Clinical and/or radiographic follow-up was obtained at the first postoperative clinic evaluation and subsequent clinic visits. Neurological examination findings at the time of discharge and the first and most recent postoperative visits were reviewed. Functional outcomes were measured independently by 2 separate observers at the time of admission, discharge date, and last clinic visit using the modified Rankin Scale (mRS) score. Excellent (mRS Score 0–1), good (mRS Score 2–3), or bad (mRS Score 4–6) outcome was determined preoperatively and at the time of the last clinic visit. No patients were lost to follow-up.

Statistical Analysis

Patient data including age, sex, medical and neurosurgical history, number of hemorrhages before surgical intervention, and length of hospital and inpatient rehabilitation stays were collected. Mean, standard deviation, and range were determined for all the demographic data analyzed. Fisher’s exact test, independent samples t-test, or Mann-Whitney U-test was performed as indicated for categorical and continuous variables, using available commercial software (version 20.0, IBM SPSS Statistics, IBM Corp.). The Spearman correlation coefficient test ($r_s$) was used for analysis of nonparametric data, with bivariate correlations obtained to quantify the degree of association between independent continuous variables. A test probability value < 5% was considered significant.

Results

Patient Characteristics and Presentation

Between November 2007 and March 2012, 11 patients with surgically treated BSCMs were identified and fulfilled the enrollment criteria (Tables 2 and 3). The mean age at presentation was 49 years, with a male-to-female ratio of 1.75:1. Cranial nerve deficits were the most common presenting symptoms (81.8%), followed by cerebellar signs and gait/balance difficulties (54.5%) and hemi-body numbness/hemianesthesia (27.2%). Headaches were infrequent complaints at initial presentation (9%); only 1 patient (with a left posterior pontine tegmental lesion) presented with hemiparesis.

Lesion Characteristics and Location

The majority of the lesions were located within the pons (72.7%). The remaining lesions were mesencephalic ($n = 2$) and medullary ($n = 1$). Seven patients (63.6%) underwent resection of the CM after a single symptomatic event; 3 patients (27.3%) were submitted to resection after a second symptomatic event. One patient with a CM located on the posterolateral aspect of the midbrain (epicenter on lateral mesencephalic sulcus) had 3 hemorrhages before surgical intervention (including a remote episode 10 years before his presentation to our institution). The mean size of symptomatic lesions was 1.21 cm, and the mean estimated volume was 1.93 cm³. No statistical difference was seen for mean size and volume between patients with 1 or 2 or more hemorrhagic episodes ($p = 0.842$ and $p = 0.963$, respectively). The mean elapsed times from symptom onset to surgical intervention were 103.86 days and 120.50 days for patients with 1 or more than 1 hemorrhagic episode, respectively.

Diffusion Tensor Imaging and Diffusion Tensor Tractography

The mean time from DTI data acquisition to operative intervention was 24.45 days. All patients had changes in DTI and DTT involving at least 1 major fiber tract; 82% showed involvement of 2 or more fiber tracts. Overall, a total of 32 fiber tracts in all 11 patients were found to have some degree of disturbance caused by a BSCM and associated hemorrhage. CST and ML/MLF were the most commonly affected ($n = 8$ and $n = 9$, respectively). The majority of changes were displacement ($n = 14$) or partial interruption and distortion ($n = 14$). Complete interruption was seen in 4 cases (2 pontine, 1 pontomedullary, and 1 medullary lesion), 3 of those involving the CST (Table 4). The results obtained from DTI and DTT were cross-referenced with the planned surgical approach. Four cases with radiographic evidence of pial presentation on preoperative MRI underwent surgery through the originally selected surgical approach. This paramount principle of resection of brainstem lesions is associated with a better postoperative neurological outcome and lower incidence of new neurological deficits, in part because it minimizes normal brainstem tissue retraction, avoids ex-
tensive parenchymal surgical corridors, and utilizes the local surface changes caused by the underlying lesion and hemorrhage as a reliable marker for entry zone selection.\(^1,2,7,9,21,27,28,45,52,60\) The pial presentation on MRI correlated with DTI/DTT findings (fiber tract deviation or interruption at the selected brainstem entry point) as well as the intraoperative findings during initial microscopic dissection. In 4 patients with no clear evidence of pial presentation on preoperative MRI studies, the decision-making process was influenced by the results of DTI/DTT. A 50-year-old patient presenting after second hemorrhage from a known right pontine cavernous malformation diagnosed after new onset of left facial weakness and hemifacial numbness (Fig. 4A) underwent a far-lateral transcondylar transpeduncular approach instead of a transventricular/posterior approach after DTI/DTT showed the cavernous malformation to displace the ML, ICP, and the facial colliculus posteromedially (Fig. 4B and C). Postoperative MRI showed gross-total resection. The patient underwent gross-total resection of her CM with a peritrigeminal area brainstem entry point (Fig. 3D). In a similar situation, a 15-year-old boy with a posteriorly located left pontomedullary junction cavernous malformation diagnosed after new onset of left facial weakness and hemifacial numbness (Fig. 4A) underwent a far-lateral transcondylar transpeduncular approach instead of a transventricular/posterior approach after DTI/DTT showed the cavernous malformation to displace the ML, ICP, and the facial colliculus posteromedially (Fig. 4B and C). Postoperative MRI showed gross-total resection. The patient had no new postoperative neurological symptoms. Two other patients (a 48-year-old woman with a right rostral anterior pons and a 59-year-old man with a right upper pyramidal/medullary CM) harbored lesions without pial presentation in which the results from preoperative DTI/DTT were important for selection of brainstem entry zones.

### Surgical Approaches

Four patients (36.3%) underwent a far-lateral approach and its variations for resection of lesions located at the pons or pontomedullary junction. Three patients (27.4%) had large CMs abutting the floor of the fourth ventricle, with intraventricular pial presentation, and underwent a midline suboccipital craniotomy. Table 5 summarizes the remaining surgical approaches used for the resection of the BSCMs.

### Outcomes

All 11 patients had gross-total resection of their BSCMs. The mean overall hospital length of stay was 13.09 days. Six patients (54.5%) were discharged home after recovering from the surgical procedure; 5 patients (45.5%) required admission to an inpatient rehabilitation facility, with a mean length of stay of 28.60 days; all 5 patients

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**TABLE 2. Brainstem cavernous malformations: general patient demographic data**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>No. of Preop Hemorrhages</th>
<th>Location</th>
<th>Anteroposterior Size (mm)</th>
<th>Volume (cm³)</th>
<th>LOS (days)</th>
<th>LOS Rehab (days)</th>
<th>Surgical Approach</th>
<th>Follow-Up (mos)</th>
<th>Initial mRS Score</th>
<th>Last mRS Score</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>40, F</td>
<td>1</td>
<td>1</td>
<td>Pons</td>
<td>12</td>
<td>1.04</td>
<td>5</td>
<td>—</td>
<td>Far lateral</td>
<td>59.00</td>
<td>1</td>
<td>0</td>
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<tr>
<td>2</td>
<td>44, F</td>
<td>1</td>
<td>1</td>
<td>Pons</td>
<td>5</td>
<td>0.07</td>
<td>7</td>
<td>—</td>
<td>Transvermian</td>
<td>53.60</td>
<td>2</td>
<td>1</td>
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<tr>
<td>3</td>
<td>48, F</td>
<td>2</td>
<td>2</td>
<td>Pons</td>
<td>6</td>
<td>0.20</td>
<td>7</td>
<td>—</td>
<td>Transpetrosal presigmoid</td>
<td>45.93</td>
<td>1</td>
<td>1</td>
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<tr>
<td>4</td>
<td>15, M</td>
<td>1</td>
<td>1</td>
<td>Pons</td>
<td>12</td>
<td>0.97</td>
<td>6</td>
<td>—</td>
<td>Far lateral transcondylar</td>
<td>39.83</td>
<td>1</td>
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<tr>
<td>5</td>
<td>70, M</td>
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<td>1</td>
<td>Pons</td>
<td>9</td>
<td>0.62</td>
<td>21</td>
<td>22</td>
<td>Telovelar</td>
<td>35.90</td>
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<tr>
<td>6</td>
<td>29, M</td>
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<td>2</td>
<td>Pons</td>
<td>19</td>
<td>5.69</td>
<td>8</td>
<td>—</td>
<td>Telovelar</td>
<td>32.37</td>
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<tr>
<td>7</td>
<td>67, F</td>
<td>1</td>
<td>M</td>
<td>Midbrain</td>
<td>12</td>
<td>1.04</td>
<td>38</td>
<td>23</td>
<td>Subtemporal</td>
<td>22.20</td>
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<td>2</td>
</tr>
<tr>
<td>8</td>
<td>62, M</td>
<td>3</td>
<td>M</td>
<td>Midbrain</td>
<td>10</td>
<td>0.58</td>
<td>17</td>
<td>57</td>
<td>Subtemporal</td>
<td>28.17</td>
<td>0</td>
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<tr>
<td>9</td>
<td>55, M</td>
<td>1</td>
<td>1</td>
<td>Pons</td>
<td>6</td>
<td>0.53</td>
<td>8</td>
<td>29</td>
<td>Far lateral</td>
<td>20.47</td>
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<td>2</td>
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<tr>
<td>10</td>
<td>50, M</td>
<td>2</td>
<td>1</td>
<td>Pons</td>
<td>29</td>
<td>9.84</td>
<td>6</td>
<td>12</td>
<td>Transpetrosal presigmoid</td>
<td>16.30</td>
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<td>2</td>
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<tr>
<td>11</td>
<td>59, M</td>
<td>1</td>
<td>M</td>
<td>Medulla</td>
<td>13</td>
<td>0.67</td>
<td>21</td>
<td>—</td>
<td>Far lateral transcondylar</td>
<td>6.00</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

LOS = length of stay; — = not applicable.

**TABLE 3. Descriptive analysis of 11 patients who underwent resection of symptomatic BSCMs**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>SD</th>
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</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>15</td>
<td>70</td>
<td>49.00</td>
<td>16.535</td>
</tr>
<tr>
<td>Time b/w diagnosis/ presentation and surgery in days</td>
<td>39</td>
<td>224</td>
<td>109.91</td>
<td>56.749</td>
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<tr>
<td>Bleeding episodes until surgery</td>
<td>1</td>
<td>3</td>
<td>1.45</td>
<td>0.688</td>
</tr>
<tr>
<td>Anteroposterior size (mm)</td>
<td>5</td>
<td>29</td>
<td>12.09</td>
<td>6.877</td>
</tr>
<tr>
<td>Volume (cm³)</td>
<td>0.07</td>
<td>9.84</td>
<td>1.932</td>
<td>3.045</td>
</tr>
<tr>
<td>Time b/w DTI acquisition and surgery in days</td>
<td>1</td>
<td>69</td>
<td>24.45</td>
<td>21.135</td>
</tr>
<tr>
<td>Hospital LOS (days)</td>
<td>5</td>
<td>38</td>
<td>13.09</td>
<td>10.261</td>
</tr>
<tr>
<td>Rehab LOS (days)</td>
<td>12</td>
<td>57</td>
<td>28.06</td>
<td>17.009</td>
</tr>
<tr>
<td>Follow-up (mos)</td>
<td>6</td>
<td>58</td>
<td>32.04</td>
<td>16.209</td>
</tr>
<tr>
<td>Initial mRS score</td>
<td>0</td>
<td>3</td>
<td>1.45</td>
<td>0.820</td>
</tr>
<tr>
<td>Last mRS score</td>
<td>0</td>
<td>2</td>
<td>1.45</td>
<td>0.688</td>
</tr>
</tbody>
</table>
were eventually discharged home. Need for inpatient rehabilitation admission postoperatively did not predict worse outcome (p = 0.137). As observed in various other studies, most patients had transient worsening of preoperative neurological deficits or development of new neurological symptoms; nonetheless, all 11 patients had improvement in neurological function by the first postoperative outpatient visit; the improvement continued over the first 24 months. The mean length of postoperative follow-up was 32.04 months. There were no deaths during long-term follow-up.

Two patients developed postoperative CSF leak. One of the cases resolved after lumbar drain placement and temporary CSF diversion; the second patient required reoperation for an enlarging pseudomeningocele and wound infection with early meningitis. One patient required temporary tracheostomy/gastrostomy tube placement that was discontinued 3 months postoperatively (Table 6).

Five patients (45.5%) had excellent outcomes (mRS

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Medulla Oblongata</th>
<th>Pons</th>
<th>Midbrain</th>
<th>DTI Score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ICP</td>
<td>CST</td>
<td>ML/MLF</td>
<td>ICP</td>
</tr>
<tr>
<td>1</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
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<tr>
<td>11</td>
<td>—</td>
<td>3</td>
<td>4</td>
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</tbody>
</table>

ICP = inferior cerebellar peduncle; MCP = middle cerebellar peduncle; SCP = superior cerebellar peduncle.
Score 0–1 at the time of their last outpatient clinic evaluation. Six patients (54.5%) had good outcomes (mRS Scores 2–3). No patients had an mRS score of 4 or 5 at last follow-up. Compared with preoperative assessment, 5 patients (45.5%) had improvement of neurological function; 2 patients (18.2%) remained stable, and 4 patients (36.3%) had some degree of neurological decline postoperatively. Except for the number of preoperative bleeding episodes ($p = 0.047, 95\% \text{CI 0.015–1.413}$) and initial mRS score ($p = 0.021, 95\% \text{CI 10.210–2.005}$), no other independent variable was associated with long-term outcome.

The mean DTI scores for patients with a stable/improved or worse mRS score postoperatively were 8.00 and 7.50, respectively ($p = 0.724$). The results were similar after stratification by brainstem location for pontine lesions ($p = 0.687$); small sample size prevented statistical analysis of mesencephalic lesions. The only patient with a medullary BSCM had overall improvement and mRS Score 1 preoperatively, despite significant changes seen on DTI.

Discussion

Cavernous malformations are discrete, lobulated, well-circumscribed lesions consisting of dilated and thin-walled capillaries with simple endothelial lining and variably thin fibrous adventitia. The typical CM has no interwalled capillaries with simple endothelial lining and variably thin fibrous adventitia. The typical CM has no interwalled capillaries with simple endothelial lining and variably thin fibrous adventitia. The typical CM has no interwalled capillaries with simple endothelial lining and variably thin fibrous adventitia. The typical CM has no interwalled capillaries with simple endothelial lining and variably thin fibrous adventitia. The typical CM has no interwalled capillaries with simple endothelial lining and variably thin fibrous adventitia. The typical CM has no interwalled capillaries with simple endothelial lining and variably thin fibrous adventitia. The typical CM has no interwalled capillaries with simple endothelial lining and variably thin fibrous adventitia. The typical CM has no interwalled capillaries with simple endothelial lining and variably thin fibrous adventitia. The typical CM has no interwalled capillaries with simple endothelial lining and variably thin fibrous adventitia. The typical CM has no interwalled capillaries with simple endothelial lining and variably thin fibrous adventitia. The typical CM has no interwalled capillaries with simple endothelial lining and variably thin fibrous adventitia. The typical CM has no interwalled capillaries with simple endothelial lining and variably thin fibrous adventitia. The typical CM has no interwalled capillaries with simple endothelial lining and variably thin fibrous adventitia. The typical CM has no interwalled capillaries with simple endothelial lining and variably thin fibrous adventitia. The typical CM has no interwalled capillaries with simple endothelial lining and variably thin fibrous adventitia. The typical CM has no interwalled capillaries with simple endothelial lining and variably thin fibrous adventitia. The typical CM has no interwalled capillaries with simple endothelial lining and variably thin fibrous adventitia. The typical CM has no interwalled capillaries with simple endothelial lining and variably thin fibrous adventitia. The typical CM has no interwalled capillaries with simple endothelial lining and variably thin fibrous adventitia. The typical CM has no interwalled capillaries with simple endothelial lining and variably thin fibrous adventitia. The typical CM has no interwalled capillaries with simple endothelial lining and variably thin fibrous adventitia. The typical CM has no interwalled capillaries with simple endothelial lining and variably thin fibrous adventitia. The typical CM has no interwalled capillaries with simple endothelial lining and variably thin fibrous adventitia. The typical CM has no interwalled capillaries with simple endothelial lining and variably thin fibrous adventitia. The typical CM has no interwalled capillaries with simple endothelial lining and variably thin fibrous adventitia. The typical CM has no interwalled capillaries with simple endothelial lining and variably thin fibrous adventitia.

Natural History

There is variable risk of hemorrhage reported in the literature, partially due to preselection of patients in retrospec-

NATURAL HISTORY

Since the advent of DTI 2 decades ago, there has been significant interest in its potential clinical applications. The physical principles and rationale of this technique have been extensively debated, and a more profound discussion is beyond the scope of the current study.
underwent surgery with DTI-integrated neuronavigation. Median survival rates were reported in 118 patients who underwent surgery with standard techniques. Others have shown good concordance between tractography results and intraoperative direct electric stimulations.

Despite good data on DTI use for supratentorial lesions, there have been only a limited number of studies regarding its application in brainstem pathologies, partially because of known technical difficulties intrinsic to this location. Kovanič et al. investigated the role of DTI and DTT on the CST alterations caused by space-occupying lesions in the brainstem before and after resection in 14 patients. All of the patients with normal CST on DTT presented without motor deficit on neurological examination. DTT was shown to have high sensitivity (100%) and negative predictive value (100%), but high false-positive results (positive predictive value of 42.9%) in preoperative evaluation, related to lesion artifact. In 2 separate articles, Chen et al. acknowledged that, compared with conventional MRI, DTI and DTT provided superior quantification and visualization of lesion involvement in eloquent fiber tracts of the brainstem. Moreover, DTI and DTT were found to be beneficial for white matter recognition in the neurosurgical planning and postoperative assessment of brainstem lesions.

In our study, 82% of the patients presented with DTI changes involving 2 or more major fiber tracts. Most disturbances were displacements or partial interruptions and involved the CST and ML/MLF complex. Sensitivity and negative predictive value were excellent and similar to the ones presented by Kovanič et al. Positive predictive values as low as 37.5% were also observed in our study. Preoperative DTI was not shown to correlate with postoperative outcome, as determined by the mRS score. These findings suggest that preoperative DTI/DTT may not be a useful tool for prediction of neurological deficits or long-term outcome after resection of BSCMs. Part of the explanation could reside in the fact that the majority of preoperative symptoms in our population were cranial nerve deficits (81.8%), which are not well delineated by DTI/DTT. Another explanation derives from limitations in the technique itself. The hemosiderin rim is well known to cause local modifications in tissue anisotropy and to falsely disrupt tractography maps. Additionally, echo planar imaging–based DTI is hindered by susceptibility distortions at the proximity of the skull base air-filled spaces, partially secondary to pulsatile cardiac and respiratory motion artifacts.

DTI could represent, however, a valuable tool in preoperative and intraoperative planning for resection of specific subtypes of lesions. Cavernous malformations are thought to displace rather than infiltrate surrounding structures. Some neurological deficits observed preoperatively could be attributed to tissue expansion and displacement caused by blood contained in the hemorrhagic cavity; resorption of blood products correlates positively with neurological improvement and is one of the reasons why some authors recommend resection in a delayed fashion. This delay allows for partial liquefaction of the hematoma, which facilitates resection and minimizes surgery-related trauma. In cases in which the BSCM has pial or ependymal presentation, the lesion itself provides the surgical access route. In our series, 4 patients with preoperative imaging studies suggesting pial presentation had concordant intraoperative findings; more importantly, DTI and DTT in these cases confirmed displacement of major fiber tracts by the lesion, and no overlying tract was identified on the planned brainstem entry zone. In 2 patients with pontine lesions without pial presentation, DTI information was important for approach selection. On 2 other occasions, deep-seated lesions were removed through safety entry zones selected based on preoperative DTI/DTT data.

To our knowledge, this is the largest study published to date involving brainstem cavernous malformations and DTI. Our results confirm the feasibility of DTI and DTT on preoperative assessment of patients with brainstem space-occupying lesions such as BSCMs. In selected cases, DTI/DTT could provide useful information preoperatively that may influence surgical results in deep-seated brainstem lesions without pial or ependymal presentation. In this subtype of BSCMs, DTI/DTT may assist in the selection of the surgical approach and brainstem entry zone. In the future, intraoperative DTT visualization for neurosurgical planning can be integrated with the neurosurgical microscope and real-time querying tractography obtained, maximizing resection while preserving structure and, subsequently, function. DTI/DTT could be a potential tool for preoperative counseling of patients with critically located lesions, anticipating neurological deficits that—even transiently—can impact negatively on quality of life. The long follow-up demonstrated well the remarkable functional recovery those patients can attain after an initial expected postoperative neurological decline. Dukatz et al., in a study published in 2011, emphasized the importance of the quality-of-life assessment after resection of BSCMs. In that study, 87% of the individuals who underwent surgical treatment for BSCMs pursued the same professional activity as before surgery at last follow-up. Of all 71 patients, 58 (82%) felt good or better after surgery and 63 (89%) stated that they had experienced emotional relief postoperatively.

Several factors need to be taken into account when evaluating the results of this study. The small sample size and the retrospective nature of our data collection incur a strong selection bias. The absence of a control group is an important limiting factor for the analysis of our surgical results. We did not routinely obtain postoperative DTI in our patients; different authors have shown improved DTI signal or correction of distortion on major fiber tracts postoperatively, with possible correlation of those findings with final neurological symptoms. Finally, there are limitations of the technique itself. DTI is still highly operator dependent and subject to interobserver variability. Its information is limited to long fiber tract alterations, and the technique does not provide information on brainstem substructures such as nuclei, their interconnecting fibers, and cranial nerve trajectories. Artifacts caused by...
the BSCM itself, hemorrhage, and hemosiderin deposits as well as surrounding blood vessel pulsations can limit adequate imaging acquisition. Some of these obstacles can be overcome with ongoing improvements in the technique, such as high angular resolution diffusion imaging and q-ball reconstruction of high angular resolution diffusion imaging information.\textsuperscript{6,37} Tract-based spatial statistics is a promising approach that can improve the sensitivity, objectivity, and interpretability of the analysis of multisubject diffusion imaging studies.\textsuperscript{54,35} However, its use for large space-occupying lesions on the brainstem is still limited.

Conclusions

Diffusion tensor imaging and DTT are potentially useful preoperative tools that could be considered when evaluating patients with deep-seated, symptomatic BSCMs. In patients in whom no clear radiographic evidence of pial or ependymal presentation is seen, DTI and DTT could influence the selection of surgical approach or brainstem entry zone. In our series, preoperative DTI/DTT changes did not appear to correlate with patients’ functional postoperative outcome on long-term follow-up.

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References


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