Role of diffusion tensor imaging in differentiating subtypes of meningiomas

Place de l'imagerie du tenseur de diffusion pour la différenciation des sous-types de méningiomes


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Summary

Purpose. — Meningiomas are the most common extraaxial intracranial type of tumor, and their management and prognosis depend on their grade and histology. Diffusion-weighted imaging (DWI) and diffusion tensor imaging (DTI) are two new imaging techniques that have proved helpful in elucidating the microarchitecture of brain tumors. The aim of the present study was to assess the role of diffusion and diffusion tensor metrics in the identification and classification of meningioma grades and subtypes.

Methods and materials. — A total of 21 consecutive patients with meningioma were included in this retrospective study, of whom 16 had benign meningiomas (three fibroblastic, 11 transitional/mixed, two meningothelial) and five had atypical meningiomas. Tumor mean diffusivity (Dav), fractional anisotropy (FA), linear anisotropy (CL), planar anisotropy (CP), spherical anisotropy (CS) and eigenvalues (e1, e2, e3) were measured in all cases, and differences in diffusion tensor metrics between atypical, fibroblastic and other benign (transitional, meningothelial) meningiomas were statistically analyzed using the Mann–Whitney test.

Results. — No statistically significant differences were found among the mean Dav values for atypical, fibroblastic and other benign meningiomas. Both atypical and fibroblastic meningiomas showed significantly higher mean FA values and lower mean CS values compared with other meningiomas (P<0.01), but no statistically significant difference in these values between each other. Atypical meningiomas showed higher CL values compared with fibroblastic and other benign meningiomas but, again, the difference was not statistically significant. Both atypical and fibroblastic meningiomas showed statistically significantly higher CP values and lower e3 values compared with transitional meningiomas (P<0.01).
Introduction

Meningioma, the most common type of extraaxial intracranial tumor, accounts for 16–20% of all primary intracranial tumors [1]. According to the World Health Organization (WHO) classification system, these tumors are classified into three grades: grade I = benign, grade II = atypical and grade III = anaplastic or malignant [2]. The histological grade is one of the key determinants of recurrence, with 5-year recurrence rates of 12% for benign meningiomas and 41% for atypical meningiomas [3,4]. Also, with grade I tumors, the surgical outcome is not always favorable, as it will depend on the localization and relationship of the tumor to other structures, and on the tumor histopathological subtype. Another important factor is tumor consistency. A hard consistency, such as encountered in calcified and fibroblastic meningiomas, makes the removal of tumor difficult, especially if located at the base of the skull [5].

Conventional magnetic resonance imaging (MRI) techniques have been used—with limited success—to differentiate between the different grades and subtypes of meningioma [6–10]. Diffusion-weighted imaging (DWI) and diffusion tensor imaging (DTI) are two newer imaging techniques that can provide information on the microarchitecture of brain lesions [11]. These technologies have also been used to study the density and arrangement of cells/fibres in brain tumors [12–23]. The present study aimed to assess the role of DTI in determining meningioma grades and subtypes.

Materials and methods

Patients and meningioma histology

The present retrospective study was approved by the ethics committee of our institute, and included 21 consecutive patients. Of these patients, six were male and 15 were female, with a mean age of 51.28 years (range: 27–69 years). All patients had been treated surgically, and had obtained a pathological diagnosis. The meningiomas were classified according to the WHO 2007 classification [2]: 16 were benign [three fibroblastic, 11 transitional (mixed) and two meningothelial] and five were atypical, defined as having ≥ 4 mitoses/10 high-power fields, or three or more of the following features: increased cellularity; small cells with a high nucleus-to-cytoplasm ratio; prominent nucleioli; uninterrupted patternless or sheetlike growth; foci of ‘spontaneous’ or ‘geographical’ necrosis.

Tumors with large calcifications were excluded.

MRI measurements

A conventional MRI brain examination was performed in each case, using a 1.5-T clinical MRI scanner (Avanto TIM SQ-Engine; Siemens, Erlangen, Germany), and T1-weighted, T2-weighted, fluid-attenuated inversion recovery (FLAIR) and post-contrast T1-weighted sequences. A spin-echo echo-planar DTI sequence was performed with diffusion gradients along 30 non-collinear directions and the following imaging parameters: TR 3500 ms, TE 105 ms, matrix 192 × 192, FOV 230 mm², 5-mm slice thickness with a 1.5-mm gap, averaged twice, and a b factor of 0 and 1000 s/mm².

Post-processing

All analyses and post-processing were performed at a separate workstation (Leonardo, Siemens, Erlangen, Germany) by two neuroradiologists (with experience of 6 and 13 years, respectively). Regions of interest (ROIs) were placed within the solid-looking tumor areas, which were enhanced on post-contrast T1-weighted images. As the ROI had to include almost the entire tumor, it was large for large tumors and small for small tumors. Proper care was taken while placing the ROI to avoid partial-volume effects from the adjacent brain parenchyma and cerebrospinal fluid (CSF). Diffusion tensor metrics, including eigenvalues (e1, e2, e3), mean diffusivity (Dav), fractional anisotropy (FA), and planar (CL) and spherical (CS) anisotropy, were computed using software provided by the vendor; the parameters were calculated using the following standard algorithms:

\[
\mu(D_{av}) = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3}
\]

\[
FA = \sqrt{\frac{3}{2}} \sqrt{\frac{(\lambda_1 - \mu)^2 + (\lambda_2 - \mu)^2 + (\lambda_3 - \mu)^2}{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}}
\]

\[
CL = \frac{\lambda_1 - \lambda_2}{\lambda_1 + \lambda_2 + \lambda_3}
\]

\[
CP = \frac{2(\lambda_2 - \lambda_3)}{\lambda_1 + \lambda_2 + \lambda_3}
\]

\[
CL + CP + CS = 1.
\]

wherein \(\lambda_1, \lambda_2\) and \(\lambda_3\) represent the three eigenvalues (e1, e2, e3) of the diffusion ellipsoid, respectively.

Statistical analysis

Differences in diffusion tensor metrics between atypical, fibroblastic and other benign meningiomas were analyzed using the non-parametric Mann–Whitney test. As the dataset was small, \(P < 0.01\) was considered statistically significant to minimize error.

Results

The different diffusion tensor metrics obtained from the studied meningiomas are summarized in Table 1, and the results of the diffusion tensor metric comparisons among

Conclusion. – These results suggest that diffusion tensor metrics may be helpful in the differentiation of atypical, fibroblastic and other benign meningiomas.
Role of diffusion tensor imaging in differentiating subtypes of meningiomas

Table 1

<table>
<thead>
<tr>
<th></th>
<th>Dav</th>
<th>FA</th>
<th>CL</th>
<th>CP</th>
<th>CS</th>
<th>e1</th>
<th>e2</th>
<th>e3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atypical meningiomas</td>
<td>0.774 ± 0.132</td>
<td>0.498 ± 0.04</td>
<td>0.196 ± 0.067</td>
<td>0.319 ± 0.148</td>
<td>0.486 ± 0.1</td>
<td>1.194 ± 0.172</td>
<td>0.766 ± 0.218</td>
<td>0.369 ± 0.057</td>
</tr>
<tr>
<td>Fibroblastic meningiomas</td>
<td>0.848 ± 0.173</td>
<td>0.471 ± 0.031</td>
<td>0.138 ± 0.026</td>
<td>0.390 ± 0.088</td>
<td>0.472 ± 0.062</td>
<td>1.242 ± 0.23</td>
<td>0.909 ± 0.24</td>
<td>0.394 ± 0.057</td>
</tr>
<tr>
<td>Other benign meningiomas</td>
<td>0.797 ± 0.095</td>
<td>0.285 ± 0.075</td>
<td>0.120 ± 0.048</td>
<td>0.142 ± 0.062</td>
<td>0.390 ± 0.031</td>
<td>1.040 ± 0.1</td>
<td>0.799 ± 0.117</td>
<td>0.593 ± 0.108</td>
</tr>
</tbody>
</table>

Data are expressed as means ± SD.

Discussion

The prognosis and risk of recurrence in cases of meningioma depend on the grade of the tumor [3,4]. Grade I tumors have a good prognosis with a considerably lower incidence of recurrence compared with tumor grades II and III [3,4]. Also, in grade I tumors, their consistency may help in determining a plan of treatment [5]. A hard consistency is thought to be due to a high content of intercellular collagen and reticulin or calcification [24]. Computed tomography (CT) scanning can detect calcification, but cannot differentiate between hard and soft meningiomas or between atypical and benign meningiomas [25]. Conventional MRI techniques also have a limited capacity for differentiating tumor subtypes [6—10].

DWI and DTI are two recent techniques that are widely used to study the microstructure of brain tumors, including their cellularity, arrangement of cells and/or vascularity.
Table 2  Significance (P values, by Mann–Whitney test) of the comparisons of diffusion tensor metrics among atypical, fibroblastic and other benign meningiomas.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Dav</th>
<th>FA</th>
<th>CL</th>
<th>CP</th>
<th>CS</th>
<th>e1</th>
<th>e2</th>
<th>e3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atypical vs fibroblastic meningiomas</td>
<td>0.393</td>
<td>0.393</td>
<td>0.25</td>
<td>0.786</td>
<td>1.0</td>
<td>0.393</td>
<td>0.393</td>
<td>1.0</td>
</tr>
<tr>
<td>Atypical vs other benign meningiomas</td>
<td>1.0</td>
<td>&lt; 0.001</td>
<td>0.046</td>
<td>0.026</td>
<td>0.001</td>
<td>0.075</td>
<td>1.0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Fibroblastic vs other benign meningiomas</td>
<td>0.611</td>
<td>0.004</td>
<td>0.611</td>
<td>0.007</td>
<td>0.004</td>
<td>0.239</td>
<td>0.439</td>
<td>0.007</td>
</tr>
</tbody>
</table>

Dav: mean diffusivity; FA: fractional anisotropy; CL: linear anisotropy; CP: planar anisotropy; CS: spherical anisotropy; e1, e2, e3: eigenvalues.

[12–23]. Both have also been reported to help in differentiating atypical from benign meningiomas and fibroblastic from other benign meningiomas, and in determining meningioma consistency [15–17].

In the present study, atypical meningiomas showed significantly higher FA and lower CS than other benign meningiomas. However, FA and CS did not help to differentiate atypical from fibroblastic meningiomas, which is inconsistent with the findings of Toh et al. [15], who were able to differentiate between atypical and classic meningiomas in their study. However, their series included only two cases of fibroblastic meningioma, and their report did not include a comparison of fibroblastic and atypical meningiomas separately. In the present study, on comparing atypical and benign meningiomas as a group (fibroblastic plus other benign meningiomas), statistically significant differences in FA and CS values between these tumors were obtained ($P = 0.001$ and $P = 0.011$, respectively, by Mann–Whitney test). Dav values showed that diffusion was restricted in all meningiomas, which is consistent with reports in the literature [15,16], and attributable to the compact arrangement of cells observed in meningioma. However, in our present study, this result did not help to differentiate the different types of meningioma [15,16].

Increased anisotropy in both atypical and fibroblastic meningiomas (Figs. 1 and 2) can be attributed to the regular arrangement of cells within these tumors, thus allowing water molecules to move with greater directionality [15,16]. In contrast, in transitional (Fig. 3) and meningothelial meningioma, the cells are haphazardly arranged and so diffusion is more isotropic [15,16].

We also found increased linear anisotropy in atypical meningiomas compared with fibroblastic and other benign meningiomas, although the differences were not statistically significant. Furthermore, we found increased planar anisotropy in atypical and fibroblastic meningiomas compared with other benign meningiomas. Tropine et al. [16], in their series, found increased planar anisotropy in fibroblastic meningiomas compared with other benign meningiomas, which led them to postulate that it might be due to the fascicles being arranged in sheets, the crossing and twisting of fibers and/or partial-volume effects of fascicles sharing borders with more irregular compartments of tumor cells.

Atypical meningiomas showed relative increases in both linear and planar anisotropy, which may be explained by their sheetlike arrangements of cells leading to greater overall anisotropy (FA), with both the linear and planar components contributing to the FA increase. Eigenvalue e3 was significantly lower in atypical and fibroblastic meningiomas compared with other benign meningiomas, which might be attributed to the higher anisotropy in the former two types and the increased isotropy in the latter. Thus, values of FA,

Figure 1  Box plots of diffusion tensor imaging (DTI) parameters according to meningioma subtypes: linear anisotropy (CL); planar anisotropy (CP); spherical anisotropy (CS); fractional anisotropy (FA); mean diffusivity (Dav); eigenvalues (e1, e2, e3). Data are expressed as means and standard deviations (SD).
Figure 2  This atypical meningioma of the right posterior fossa in a 50-year-old woman appears mildly hyperintense on the T2-weighted image (a; 3510/109; flip angle: 140°) and shows homogeneously intense enhancement on the post-contrast T1-weighted fat-suppressed image (b; 847/11; flip angle: 90°). There is restricted diffusion on the Dav (c) and Dexp (d) images, and increased anisotropy on the FA (e) and CS (h) maps. The CL (f) and CP (g) maps show that the increase in anisotropy is mainly due to increased planar diffusion. Histopathology shows increased cellularity and atypical nuclei, which are responsible for the restricted diffusion and increased anisotropy.

Figure 3  This left occipital parasagittal meningioma in a 47-year-old woman appears mildly hyperintense on the T2-weighted image (a; 3510/109; flip angle: 140°), with homogeneously intense enhancement on the post-contrast T1-weighted fat-suppressed image (b; 847/11; flip angle: 90°). The Dav (c) and Dexp (d) images show restricted diffusion; the FA (e) and CS (h) maps show increased anisotropy, mainly due to the increased planar diffusion seen on the CL (f) and CP (g) maps. Histopathology shows regularly arranged fibroblastic cells, which are suggestive of fibroblastic meningioma.

Figure 4  This transitional meningioma of the prepon-tomedullary cistern in a 53-year-old woman appears mildly hyperintense on the T2-weighted image (a; 3510/109; flip angle: 140°), and shows homogeneously intense enhancement on the post-contrast T1-weighted fat-suppressed image (b; 847/11; flip angle: 90°). There is restricted diffusion on the Dav (c) and Dexp (d) images, with decreased fractional, linear and planar anisotropy, and increased isotropy, on the FA (e), CL (f), CP (g) and CS (h) maps, respectively. Histopathology (i) shows a loose arrangement of cells.

Figure 5  This anterior parafalcine transitional meningioma in a 62-year-old man appears mildly hyperintense on the T2-weighted image (a; 3510/109; flip angle: 140°), with heterogeneous enhancement on the post-contrast T1-weighted fat-suppressed image (b; 847/11; flip angle: 90°). There is restricted diffusion on the Dav (c) and Dexp (d) images; the FA (e) and CS (h) maps show increased anisotropy, which can be attributed to the compact arrangement of cells in this particular case (i). The CL (f) and CP (g) maps show low linear and planar anisotropy, respectively.
CS and e3 can help to differentiate atypical and fibroblastic meningiomas from other benign meningiomas, whereas CL and CP values can help to differentiate atypical from fibroblastic meningiomas.

In one particular case of transitional meningioma, the FA was extremely high (Fig. 4), and the tumor histopathology showed a well-formed whorl pattern that was more compactly arranged than are other cases of transitional meningioma. However, the CP value was significantly lower than in either atypical or fibroblastic meningioma. This suggests that, on occasion, transitional meningiomas can show high FA and, in such cases, the CP values may help to differentiate them from atypical and fibroblastic meningiomas.

The present study has several limitations. First, the study population was small, and further studies of larger numbers of patients are required. Second, the diffusion findings and histopathology were not quantified so, although we can hypothesize that a high FA is related to a regular sheetlike arrangement of cells, we cannot make a direct pathological correlation. Therefore, it cannot be definitively stated that differences in diffusion metrics are solely due to tumor architecture and/or cellularity. Third, we did not study other subtypes of WHO grade-I tumors, such as angiomatous, microcystic, secretory and metaplastic meningiomas, nor other WHO grade-II tumors, such as chordoid and clear-cell meningiomas, which may have different patterns of diffusion. Finally, DTI did not cancel out perfusion effects, so tumor vascularity and microcirculation may be affecting FA values.

**Conclusion**

Diffusion tensor metrics may help to differentiate among atypical, fibroblastic and other benign meningiomas. Although all will show decreased diffusivity (Dav), atypical meningiomas will have increased FA with increased linear and planar anisotropy, and lower e3 values, while fibroblastic meningiomas will have increased FA and planar anisotropy, decreased linear anisotropy and lower e3 values, and other benign meningiomas will show decreased FA, decreased linear and planar anisotropy, and higher e3 values.

**Conflict of interest statement**

None.

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