Distinct displacements of the optic radiation based on tumor location revealed using preoperative diffusion tensor imaging

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OBJECTIVE Visual field defects (VFDs) due to optic radiation (OR) injury are a common complication of temporal lobe surgery. The authors analyzed whether preoperative visualization of the optic tract would reduce this complication by influencing the surgeon’s decisions about surgical approaches. The authors also determined whether white matter shifts caused by temporal lobe tumors would follow predetermined patterns based on the tumor’s topography.

METHODS One hundred thirteen patients with intraaxial tumors of the temporal lobe underwent preoperative diffusion tensor imaging (DTI) fiber tracking. In 54 of those patients, both pre- and postoperative VFDs were documented using computerized perimetry. Brainlab’s iPlan 2.5 navigation software was used for tumor reconstruction and fiber visualization after the fusion of DTI studies with their respective magnetization-prepared rapid gradient-echo (MP-RAGE) images. The tracking algorithm was as follows: minimum fiber length 100 mm, fractional anisotropy threshold 0.1. The lateral geniculate body and the calcarine cortex were employed as tract seeding points. Shifts of the OR caused by tumor were visualized in comparison with the fiber tracking of the patient’s healthy hemisphere.

RESULTS Temporal tumors produced a dislocation of the OR but no apparent fiber destruction. The shift of white matter tracts followed fixed patterns dependent on tumor location: Temporal tumors resulted in a medial fiber shift, and thus a lateral transcortical approach is recommended. Temporopolar tumors led to a posterior shift, always including Meyer’s loop; therefore, a pterional transcortical approach is recommended. Temporomesial tumors also induced a lateral fiber shift. For those tumors, a transsylvian-transcisternal approach is recommended. Temporocentral tumors produced a lateral and superior shift; thus, a transsylvian-transcisternal approach will result in maximum sparing of the fibers. Temporocentral tumors also induced a lateral fiber shift. For those tumors, a transsylvian-transopercular approach is recommended. Tumors of the fusiform gyrus generated a superior (and lateral) shift; consequently, a subtemporal approach is recommended to avoid white matter injury. In applying the approaches recommended above, new or worsened VFDs occurred in 4% of the patient cohort. Total neurological and surgical morbidity were less than 10%. In 90% of patients, gross-total resection was accomplished.

CONCLUSIONS Preoperative visualization of the OR may help in avoiding postoperative VFDs.

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KEY WORDS DTI; fiber tracking; temporal lobe; tumor surgery; visual field defect; optic radiation; oncology

NEW visual field defects (VFDs) through optic radiation (OR) injury constitute the most common complication following temporal lobe surgery. The frequency of VFDs after temporal lobe surgery is reported to be as high as 20%–100% in previous studies. Postoperative VFDs after anterior temporal lobe resection, as conducted in epilepsy surgery, for example, have been estimated around 70%, depending on the extent of resection. This enormous visual morbidity is easily explained by the anatomy of the human OR, which traverses a major expanse of the temporal lobe. Of all the white matter tracts within the temporal lobe network, the OR is the largest.

Recent technical progress has enabled the visualization of fiber tracts in the living subject through diffusion tensor imaging (DTI). Before that, knowledge of the visual pathway was based mainly on fiber dissection studies in deceased subjects and partly on the analysis of postoperative visual field deficits. The underlying physics of the DTI technique have been described well and extensively, as have the technique’s physical limitations.

ABBREVIATIONS CP = computerized perimetry; DTI = diffusion tensor imaging; GBM = glioblastoma multiforme; LGB = lateral geniculate body; MP-RAGE = magnetization-prepared rapid gradient-echo; OR = optic radiation; VFD = visual field defect; VOI = volume of interest.


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A variety of different tracking algorithms have been employed.\textsuperscript{20} Clearly, the visualization of the anterior visual pathway using DTI is difficult, with the proximity of air-filled spaces in the bony structures of the anterior and middle cranial fossae, as well as the many crossing fibers and small fiber diameters, leading to artifacts.\textsuperscript{22} However, the posterior portion of the visual tracts from the lateral geniculate body (LGB) onward have been clearly and reproducibly illustrated, despite varying tracking algorithms.\textsuperscript{20,23,31}

To date, the majority of tractography studies of the visual pathway have been undertaken in healthy subjects, mainly in the context of anatomical investigations.\textsuperscript{9,21,23,34} Here, we aimed to analyze whether DTI would prove feasible in the diseased brain of patients with space-occupying lesions. After all, it can be assumed that infiltrative tumors growing in the direction of the OR can lead to destruction of the fibers or at least interference with their visualization by DTI. Alternatively, it is conceivable that fibers stay largely intact and are merely shifted in another direction by the tumor's mass effect. This finding would substantiate the suitability of fiber tracking for neurosurgical planning in temporal lobe tumor surgery. We then tested the hypothesis that the supposed fiber shifts follow predetermined patterns based on the tumor's topography.

Recently, we established a classification of temporal lobe tumors and suggested the respective surgical approaches,\textsuperscript{9} however, these approaches were based solely on anatomical considerations. In that tumor series we found a considerably low incidence of new postoperative VFDs. We, therefore, hypothesized that the suggested surgical approaches largely respect the fiber integrity of the OR. This prompted us to further investigate this finding by expanding our series of temporal lobe tumors and incorporating preoperative DTI fiber tracking to visualize the relation of these tumors to the OR.

Hence the second aim of our study was to determine whether preoperative visualization of the optic tract would reduce the complication of postoperative VFDs by influencing a surgeon's decisions about surgical approaches.

Methods

Patients

One hundred thirteen patients with intraaxial tumors of the temporal lobe, who had undergone preoperative DTI fiber tracking, were included in this study. Thirty patients from our previously published cohort,\textsuperscript{7} who had adequate DTI data sets with their preoperative imaging, were also included in this study cohort. The inclusion criteria were as follows: 1) tumor confined to the temporal lobe with anatomical vicinity to the OR; 2) intraaxial, infiltrative growing tumor; and 3) preoperative DTI sequence, as well as pre- and postoperative evaluations of visual fields. The exclusion criteria were as follows: 1) tumor transgressing the frontal, parietal, or occipital lobe; 2) extraxial tumor (for example, meningioma) or vascular lesion; 3) previous temporal lobe injury (for example, recurrent tumor) or occipital lobe injury; 4) pacemaker or other circumstance precluding MRI; and 5) relevant preexisting visual impairment due to disease of the anterior optic pathway (for example, ocular blindness).

All patients had received high-dose glucocorticoids to reduce peritumoral edema for several days preoperatively and before perimetry.

Magnetic Resonance Imaging Data Acquisition

Diffusion tensor imaging data sets were acquired using an 8-channel head coil and a 1.5-T MRI unit (GE Healthcare). The tensors were averaged by repeating a diffusion-weighted single-shot echo planar sequence along 23 different geometric directions with a slice thickness of 3 mm, b-value of 1000 sec/mm\textsuperscript{2}, TR of 11,000 msec, TE of 83 msec, matrix size of 128 × 128, and FOV of 240 × 240 mm. A total of 1008 images were generated. Data acquisition time was approximately 8 minutes.

In addition, conventional MRI was performed in the same session, including a 1-mm slice thickness TI inversion-recovery 3D gradient-echo (magnetization-prepared rapid gradient-echo [MP-RAGE]) sequence among other conventional sequences commonly employed for tumor imaging.

Diffusion Tensor Imaging Processing and Fiber Tracking

Brainlab's iPlan 2.5 navigation software was used for tumor reconstruction and fiber visualization after fusion of the DT images with their respective MP-RAGE images. The MP-RAGE and DTI files were converted into a single multivolume file and then corrected for eddy currents and subject movements using the iPlan “eddy-correction” algorithm. The DTI data sets were fused to the MP-RAGE data sets using the “autofuse” algorithm of the iPlan 2.5. The seed point regions for tractography were based on anatomical landmarks used in previously published work by other groups.\textsuperscript{4,18,20,33} Rectangular volumes of interest (VOIs) were defined in the coregistered anatomical data sets (T1-MPRAGE and T2). Two seed points were chosen: the LGB (VOI-1) and the calcarine cortex (VOI-2). The LGB was identified on axial sections at the level of transition from the posterior limb of the internal capsule to the cerebral peduncle, posterolateral to the peduncle.\textsuperscript{18} The VOI-2 was allocated to Brodmann area 19. Fiber tracts passing through both VOIs were considered to compose the OR. Stray fibers extending to the contralateral hemisphere or the frontal lobe were removed using the iPlan 2.5 “exclude” algorithm. A fractional anisotropy threshold of 0.1 and a minimum fiber length of 100 mm were applied as standard settings for all trackings based on tracking algorithms for the OR, as previously used by other groups.\textsuperscript{25,33,34} Shifts of the OR caused by the tumor were visualized in comparison with the fiber tracking of the patient's healthy hemisphere. To gain supplementary quantitative data on tract volumes and numbers of fibers, fiber objects were created using Brainlab’s “create 3D object” function. Using the function “plan content,” the volume of the fiber objects as well as the number of fibers within the chosen fiber object was given. The mean OR volumes and mean number of fibers were compared between the tumor-bearing hemisphere and the healthy hemisphere of each patient.
Integration Into Surgical Planning

Tractography results and reconstructions of the shifted OR were preoperatively presented to the surgeons, who were given the opportunity to consider the data and adjust their surgical approach accordingly. Based on emerging patterns of fiber shifts, tumor locations were assigned to optimum surgical approaches aimed at the best possible sparing of fibers. Postoperative neurological and surgical outcomes were registered.

Evaluation of Visual Field Deficits

Both pre- and postoperative VFDs were compared using computerized perimetry (CP) and finger perimetry. Of the 113 patients included in the study, 54 underwent preoperative and postoperative CP by a board-certified ophthalmologist, whereas 59 patients underwent pre- and postoperative finger perimetry for the evaluation of VFDs. Since the computer-based record of VFDs has better accuracy and must therefore be considered a higher standard, only the 54 patients with CP were statistically analyzed.

All preoperative CP studies were performed within 48 hours before surgery after the patient had already received a course of corticosteroids for several days. All postoperative CP studies were performed between postoperative Days 3 and 6 (usually on the day of discharge), when the immediate postoperative swelling was assumed to have partially subsided. Again, all patients were still on corticoids during postoperative CP. All CP studies were performed at the same institution.

Results

Tumor pathologies are summarized in Table 1. In all 113 patients, the optic tract could be visualized by the chosen tracking algorithm in both hemispheres, regardless of the tumor’s composition, grade, size, or location within the temporal lobe. In none of the cases were fibers pervading the tumor, and neither was there apparent fiber loss or thinning. Even for very large lesions, no distinguishable loss of fibers was noticed (Fig. 1). The mean OR volume in the tumor-bearing hemisphere was $13.59 \pm 2.77 \text{ cm}^3$, as compared with $14.61 \pm 2.20 \text{ cm}^3$ in the healthy hemisphere. Thus, the tract volumes were slightly greater in the healthy hemisphere; however, the 2-tailed p value was 0.058, which is considered not very significant. The slight difference may be explained by compression of the tracts by tumor (Fig. 2).

The number of OR fibers in the tumor-bearing hemisphere was $248 \pm 57.5$ as compared with $257 \pm 71.5$ in the healthy hemisphere. The p value was 0.721, indicating no significant difference (Fig. 3).

Likewise, in invasively growing tumors like glioblastoma multiforme (GBM) or lower grade astrocytoma, no fibers within the tumor mass were detected using the cho-

![Fig. 1. A: Images depicting a very large temporolateral tumor (oligodendroglioma) occupying a great extent of the temporal lobe. B: Tractography revealing maximum medial displacement of the OR (yellow) by tumor (green), which eventually led to a splitting of the OR into a superior and an inferior bundle. There is no apparent destruction of the OR by tumor, even though the lesion is very large. Figure is available in color online only.](image1)

![Fig. 2. Volumetry of the OR comparing the tumor-affected hemisphere with the healthy hemisphere. Values on the y-axis are expressed as the means ± standard deviations in cm³. No significant difference was seen (13.59 ± 2.77 cm³ vs 14.61 ± 2.20 cm³, p = 0.058). Figure is available in color online only.](image2)

### Table 1. Characteristics of 113 patients who underwent temporal lobe surgery for intraaxial tumors

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean patient age in yrs</td>
<td>54 ± 16</td>
</tr>
<tr>
<td>M/F ratio</td>
<td>70:43</td>
</tr>
<tr>
<td>Tumor pathology</td>
<td></td>
</tr>
<tr>
<td>GBM</td>
<td>65</td>
</tr>
<tr>
<td>Astrocytoma GIII</td>
<td>18</td>
</tr>
<tr>
<td>Astrocytoma GII</td>
<td>10</td>
</tr>
<tr>
<td>Oligodendroglioma GII</td>
<td>3</td>
</tr>
<tr>
<td>Metastasis</td>
<td>17</td>
</tr>
</tbody>
</table>

GII, GIII = Grade I, Grade III; GBM = glioblastoma multiforme.
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No difference was noticed in the behavior of fiber shifts between rather sharply bordered tumors, like metastases, and diffusely infiltrating tumors, like GBM. In all cases, clear displacement of the fiber tracts, without apparent injury to the fibers, was observed in proximity to the tumor. The direction of fiber displacement depended on the anatomical tumor location.

**Patterns of Fiber Shifts**

To further analyze possible fiber shift patterns that depended on the anatomical tumor location, we divided the temporal lobe into 4 main regions, based on a previously described anatomical compartmentation of the temporal lobe.7

**Temporolateral Tumors**

Lateral tumors were located in the inferior, middle, or superior temporal gyrus. Thirty-five tumors were lateral. In all of these cases, the OR was shifted medially (Fig. 4). Thus, a lateral transcortical approach to the tumor will not injure any of the fiber tracts.

**Temporopolar Tumors**

The temporopolar region constitutes the most anterior part of the temporal lobe, always including Brodmann area 38. The 8 temporopolar tumors in this study always caused posterior buckling of the OR (Fig. 5). Even though Meyer's loop often could not be clearly distinguished as a separate bundle, we must assume that the anterior bundle was subject to the strongest buckling. An anterior approach by a pterional craniotomy will not transect any of the OR fibers.

**Temporomesial Tumors**

Temporomesial tumors were confined to the hippocampus, parahippocampus, amygdala, and uncus. Those limbic tumors grow from the most medial region of the temporal lobe outwards. For each of the 36 temporomesial tumors included in this study, the fiber tracts shifted laterally (and often cranially). In none of the mesial lesions were fibers shifted medially or inferiorly (Figs. 6 and 7). Consequently, lateral transcortical approaches to the temporomesial region carry a high risk of transecting optic fibers. A medial approach, that is, transsylvian, does not interfere with the course of the OR.

**Temporocentric Tumors**

Even with tumors of the temporal stem, which are located in the midst of the comprehensive white matter network in the temporal lobe, visualization of the OR was
clearly feasible in every case. Each of the 32 temporocentric tumors in this study shifted the optic fibers laterally and superiorly. Again, for none of the temporocentric tumors did we observe a mesial or inferior shift (Fig. 8).

Fusiform Gyrus Tumors
Tumors of the medial and lateral occipitotemporal (fusiform) gyri abut the temporal base. These tumors cause a superior and slightly lateral shift of the optic tract. Hence, a lateral transcortical approach to the basal gyri will transect the optic fibers. The shortest trajectory to the tumor through a subtemporal approach bears no risk of direct injury. However, only 2 temporobasal tumors were in this cohort.

Altogether, there was a high correlation between tumor location and the direction of OR fiber shift. In all cases, the OR fiber shifts followed the above-described unequivocal patterns. Thus, standard surgical approaches could be ascribed to the tumor locations with the aim of minimizing injury to the OR (Fig. 9).

Surgical Outcome
Before operations, the surgeons received the results of
the MRI measurements and performed the operations in all 113 patients according to the recommended approaches. In 102 (90%) patients, gross-total resection was accomplished. In 10 (9%) patients the resection was subtotal, and in 1 (1%) patient the tumor was only partially removed. General neurological (10 [9%] of 113 patients) and surgical (9 [8%] of 113 patients) morbidity rates were similar to previously published rates, as was the overall morbidity rate of less than 10% (Table 2).

To assess visual morbidity, we only used the cohort of 54 patients who had undergone CP by board-certified ophthalmologists (Table 3) because of the higher inaccuracy of analysis and greater likelihood of missing small VFDs in the 59 patients who underwent finger perimetry.
only. (Note, however, that the incidence and distribution of VFDs in the finger perimetry group were comparable to those in the CP group [data not shown].) The overall incidence of new or worsened postoperatively impaired visual fields was 4%. Among the 24% of patients with intact visual fields preoperatively, the incidence of new postoperative visual field morbidity was 8%. Among the 76% of patients with existing visual field deficits preoperatively, a worsening of these deficits was encountered in 2%, whereas 24% of the patients improved postoperatively (Fig. 10).

Discussion

Knowledge of the exact course of the OR in each patient with a temporal tumor may help improve neurological results and avoid visual field deficits. The principal novel finding of our study is that tumors of the temporal lobe, whether gliomas or metastases, displace the OR rather than infiltrate and destroy it. Furthermore, we have identified reproducible patterns of OR fiber shift, which are dictated by the compartment of tumor origin within the temporal lobe. Thus, using our proposed classification system and the corresponding surgical approaches may help to significantly reduce visual field deficits in temporal lobe tumor surgery.

In the last 2 decades, tremendous insight into the anatomy of the OR was obtained through fiber dissection studies. The LGB marks the beginning of the OR (Fig. 11A). In the LGB, as in the whole visual pathway, the optic fibers show a strict retinotopic arrangement. From the LGB onwards, the OR can be subdivided into 3 major fiber bundles: an anterior bundle, a central bundle, and an inferior bundle. The anterior bundle, which contains information from the contralateral upper visual field quadrant, extends anterior and superior to the temporal horn of the ventricle toward the temporal pole, where it forms the Meyer’s loop, and then turns posterior to the primary visual cortex in the occipital lobe, below the calcarine sulcus. The central bundle contains visual information from the fovea centralis. Without forming a loop, it extends above the temporal horn straight to Brodmann area 19. The inferior bundle contains information from the contra-

<table>
<thead>
<tr>
<th>LOCATION</th>
<th>SHIFT</th>
<th>APPROACH</th>
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<tbody>
<tr>
<td>polar</td>
<td>dorsal</td>
<td>pterional</td>
</tr>
<tr>
<td>lateral</td>
<td>medial</td>
<td>lateral</td>
</tr>
<tr>
<td>mesial</td>
<td>lateral</td>
<td>Transsylvian/ suboccipital</td>
</tr>
<tr>
<td>intrinsic</td>
<td>Latero-cranial</td>
<td>Transsylvian/ Transopercular subtemporal</td>
</tr>
</tbody>
</table>

FIG. 9. Allocation of tumor locations within the temporal lobe to their predetermined directions of fiber shift and suggested surgical approaches aiming at maximum sparing of the OR. Figure is available in color online only.

TABLE 2. Summary of temporary and permanent neurological morbidity in 10 patients as well as surgical morbidity in 9 patients

<table>
<thead>
<tr>
<th>Morbidity</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurological*</td>
<td></td>
</tr>
<tr>
<td>New VFD</td>
<td>0/5</td>
</tr>
<tr>
<td>Hemiparesis</td>
<td>3/1</td>
</tr>
<tr>
<td>Aphasia</td>
<td>5/2</td>
</tr>
<tr>
<td>Third nerve palsy</td>
<td>4/2</td>
</tr>
<tr>
<td>Surgical</td>
<td></td>
</tr>
<tr>
<td>Wound healing disorder</td>
<td>7</td>
</tr>
<tr>
<td>Bleeding requiring revision</td>
<td>2</td>
</tr>
</tbody>
</table>

* Listed values represent temporary/permanent morbidities.

TABLE 3. Summary of visual morbidity in 54 patients analyzed with both pre- and postoperative CP

<table>
<thead>
<tr>
<th></th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VFD Preop</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>13 (24)</td>
</tr>
<tr>
<td>Yes</td>
<td>41 (76)</td>
</tr>
<tr>
<td>VFD Postop</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>12 (92)</td>
</tr>
<tr>
<td>Yes</td>
<td>1 (8)</td>
</tr>
<tr>
<td>Better</td>
<td>10 (24)</td>
</tr>
<tr>
<td>Same</td>
<td>30 (73)</td>
</tr>
<tr>
<td>Worse</td>
<td>1 (2)</td>
</tr>
</tbody>
</table>
Patterns and standard deviation; SF = short-term fluctuation. MD = mean deviation; OD = oculus dexter; PSD = pattern standard deviation.

The group that was unaltered postoperatively. CPSD = corrected pattern standard deviation.

The observed direction of fiber displacement was always congruent with the origin of tumor growth. Lateral tumors, which extend medially, entrain the OR medially. Mesial tumors, expanding laterally, shift the fibers laterally. As shown in the coronal section of Fig. 11C, the origin of every temporomesial tumor lies medial to the OR. Thus, the positional relation between tumor and fiber tracts was always retained, even in space-occupying lesions. Polar tumors, which can only expand dorsally, push the OR correspondingly. Central tumors are always embedded within the most intricate architecture of the white matter tracts, which occupy the largest volume of the temporocentral region.11,16,19,21,26,27,32 Besides the OR, this region includes the anterior commissure, the uncinate fasciculus, and the temporopontine and temporothalamic fibers, as well as many others, some of which are not yet fully described or understood.34 Those centric tumors tend to spread along the trajectories of the temporal stem they are incorporated into. Our data suggest that those tumors push the OR laterally and superiorly. We assume that large temporocentric lesions, which grow into the frontal lobe, may therefore pass through the temporal stem medial to the OR. Tumors of the medial occipitotemporal (fusiform) gyrus naturally push the OR cranially.

Today, routine tracking of the OR before every temporal surgery is not (yet) applied by every neurosurgeon for various reasons. Moreover, not every MRI facility offers DTI imaging. And there are patients with temporal tumors (for example, those with pacemakers) who simply cannot undergo DTI processing as part of their preoperative workup. In these cases, knowledge of the fixed allocation of tumor location and fiber shift may prove useful. To minimize injury to the OR, safe approaches can be chosen according to those outlined in Fig. 9.
Fiber tracking for temporal tumors

Previously, we proposed and applied the division of temporal lobe tumors into 4 basic topographic types. The division was based on the graded assembly of the temporal lobe from outer over intermediate to inner layers on axial sections, and thus reflected the ascending ontogenetic ages of the lobe from outer to inner layers. In that earlier study, we also demonstrated that a strict allocation of anatomical tumor location with a surgical approach—that is, lateral and polar tumor location with transcortical approaches and limbic and central/intrinsic tumor locations with transsylvian approaches—resulted in minimal neurological morbidity other than VFDs, including hemiparesis and aphasia, as well as minimal vascular complication and good gross-total resection. Therefore, we conclude that the implementation of the proposed surgical approaches (Fig. 9) leads to good postoperative results in general, beyond the reduction of VFDs.

Our previous classification of approaches was rather intuitive. We found that the applied approaches resulted in a maximum reduction of visual field deficits. After executing the tractography, it became evident that the direction of fiber shifts follows rather rigid patterns that are dependent solely on the anatomical tumor location. Therefore, one can ultimately predict the resulting shift of the OR merely based on the topographic location of a lesion, even without exact knowledge of the DTI data. In fact, one may dispense with DTI fiber tracking to reduce visual morbidity in temporal lobe surgery if one adheres to the classification of approaches outlined in Fig. 9.

Conclusions

Preoperative DTI fiber tracking of the OR may be a valuable tool for planning approaches to temporal lobe tumors. Its use may lead to a reduction in postoperative visual morbidity. Temporal lobe tumors lead to a dislocation of the OR rather than its destruction. The direction of fiber shift depends exclusively on the tumor topography and is therefore predictable. Consequently, the above-proposed allocation of surgical approaches to tumor topography may prove helpful and improve outcomes if DTI is not feasible.

References


Disclosure
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions
Conception and design: Faust. Acquisition of data: Faust. Analysis and interpretation of data: Faust. Drafting the article: Faust. Critically revising the article: Vajkoczy. Approved the final version of the manuscript: Faust. Supervised the study: Vajkoczy. Reviewed the submitted version of manuscript: Faust. Approved the final version of the manuscript on behalf of both authors: Vajkoczy. Statistical analysis: Faust. Administrative/technical/material support: Faust. Study supervision: Vajkoczy.

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