Use of preoperative MR to predict dural, perineural, and venous sinus invasion of skull base tumors.

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Use of Preoperative MR to Predict Dural, Perineural, and Venous Sinus Invasion of Skull Base Tumors

Marc D. Eisen, David M. Yousem, Kathleen T. Montone, Mark J. Kotapka, Douglas C. Bigelow, Warren B. Bilker, and Laurie A. Loevner

PURPOSE: To assess the accuracy of MR imaging in predicting dural, venous sinus, and perineural invasion by skull base tumors. METHODS: The preoperative MR images of 22 patients who had resection of skull base neoplasms were evaluated for the following characteristics: dural enhancement, pial enhancement, local perineural invasion by adjacent tumor, and venous sinus invasion by tumor. The greatest width of dural enhancement was measured, and the character of dural enhancement was noted. The pathologic and surgical reports were reviewed retrospectively with specific attention to dural, venous, and local perineural invasion. RESULTS: Of the 22 patients studied, dural invasion by tumor was confirmed in eight patients, vascular invasion in six patients, and perineural invasion in four patients. The sensitivity of dural enhancement in predicting invasion was 88%, the specificity 50%, and the accuracy 64%. When enhancement and focal nodularity were present, the sensitivity remained at 88% however, specificity was 100% and accuracy 95%. If the dural enhancement was more than 5 mm thick, sensitivity, specificity, and accuracy were 75%, 100%, and 91%, respectively. Predicting tumor invasion of the dura by the presence of pial enhancement was 50% sensitive and 100% specific. Venous sinus/jugular vein invasion was predicted with 100% sensitivity, 94% specificity, and 95% accuracy. Local perineural invasion was predicted with 100% sensitivity, 50% specificity, and 59% accuracy. CONCLUSIONS: The presence of pial enhancement, focal dural nodules, or dural thickening of more than 5 mm is highly accurate in predicting the presence of neoplastic dural invasion. Linear enhancement of dura does not imply dural infiltration by tumor. Venous invasion by tumor can be predicted accurately with preoperative MR imaging.

Index terms: Magnetic resonance, in treatment planning; Skull, base; Skull, neoplasms


The cooperation of multiple medical disciplines and the technological advances in neurophysiological monitoring, preoperative imaging, intraoperative microscopy, and multispecialty surgery have advanced the frontiers in the management of skull base neoplasms. Current therapeutic techniques include surgical resection, radiation therapy, and chemotherapy. No broadly accepted treatment protocols have been established, however, primarily because of the rarity of skull base tumors and the variability of their histology. Surgical resection of these tumors, while offering potential cure, may involve significant morbidity, including cranial nerve dysfunction. The value of aggressive surgical resection must be weighed against the natural history of the neoplasm.

Intracranial extension is an important prognostic issue and may dictate the treatment of skull base tumors. In a recent study of squamous cell tumors of the temporal bone, patients who had carcinomatous involvement of the dura mater did not have improved survival rates with surgical management (1). Patients whose tumors invaded through the dura died within 5 months of attempted resection, while patients whose disease did not extend intracranially had...
approximately a 50% 5-year survival rate after surgical resection.

Before the advent of magnetic resonance (MR) imaging, invasion of the dura, the venous sinuses, and the cranial nerves was assessed during surgery. However, the degree of soft-tissue resolution achieved with MR imaging has enabled improved delineation of tumor extent. An accurate prediction of invasion of these structures with MR imaging provides hope for a clearer prognosis at presentation and more appropriate treatment decisions. MR imaging has the advantages of multiplanar capabilities and good soft-tissue contrast as compared with other imaging techniques. With the development of MR contrast agents, the value of MR imaging as a diagnostic tool for skull base neoplasms was further increased.

In this study we sought to assess the accuracy of MR imaging in the prediction of dural, perineural, and venous sinus invasion. MR findings were compared retrospectively with the intraoperative report and with the pathologic findings of the resected specimen.

### Materials and Methods

Subjects for the study were chosen retrospectively from the medical records of all patients (n = 64) who had had resection of skull base neoplasms between January 1992 and November 1995. Patients from this group were selected for the study if (a) preoperative T1-weighted, T2-weighted, and contrast-enhanced T1-weighted MR images had been obtained at our institution, and (b) either resected specimens were available for assessment or surgical reports specifically mentioned dural, perineural, or vascular invasion. Twenty-two patients (13 men and nine women) with a mean age of 53 years (range, 19 to 85 years) met these requirements.

A 1.5-T imaging unit was used for all examinations. The imaging protocol included sagittal T1-weighted images (400–600/11–17/2 [repetition time/echo time/excitations]) and axial T1-weighted images (500–700/11–20/2). Fast spin-echo T2-weighted images (3000–5000/80–108/2) were also obtained. Contrast-enhanced images were obtained with parameters similar to those for the noncontrast T1-weighted axial images. The contrast agent was administered at a concentration of 0.1 mmol/kg, and imaging was performed immediately after injection of the agent. Other imaging parameters included a section thickness of 5 mm and a 256 × 192 matrix. A volume neck coil (Medical Advances, Milwaukee, Wis) or a quadrature head coil (GE Medical Systems, Milwaukee, Wis) was used depending on the site of origin of the tumor.

The MR images were examined retrospectively by an experienced head and neck radiologist who was unaware of the pathologic findings. The scans were evaluated for the following characteristics: dural enhancement, pial enhancement, perineural invasion by tumor, and venous sinus invasion by tumor. Dural enhancement was further classified as either nodular if the enhancement had focal sections of variable width or linear if the enhancement had uniform thickness throughout. If the dura showed both linear and nodular enhancement, the enhancement was recorded as nodular. If a tumor such as a meningioma appeared to be within the dura, the adjacent tail of enhancement was examined, as opposed to the enhancement of the tumor itself. The greatest width of dural enhancement was measured. Enhancement extending into the sulci or parenchyma of the brain was considered to represent pial involvement.

Venous sinus invasion was established if vascular occlusion, wall displacement, or narrowing of a venous sinus or the jugular vein was seen. Perineural invasion was recorded if cranial nerves were enhanced, obscured, or encased by tumor. Localized tumor invasion of the nerves with encasement was used as the criterion for positive perineural invasion; biopsies of the nerve distal or proximal to the primary tumor involvement were not performed to assess for more distant spread. Therefore, this phenomenon should not be considered the same as perineural extension of tumor.

Selected cases in which invasion was not clear were reevaluated, still blinded, by the neuroradiologist after a 3-week period to assess intraobserver variability. Intraobserver variability was noted in two of 22 cases, and a second neuroradiologist was consulted to make a final decision in these two cases.

Tumor histology was determined by the surgical pathology staff from permanent sections taken from surgical specimens. The most common histologic findings were meningioma (n = 4) and squamous cell carcinoma (n = 4). The site of origin of the tumors varied. A summary of the findings is given in Table 1. The histology was verified by a second, independent review of the pathology slides. The slides from each case were then reviewed retrospectively with specific attention to dural, venous, and perineural invasion by an experienced head and neck pathologist. Confirmation of perineural and venous sinus invasion was corroborated by the surgeon’s assessment in the surgical report. Perineural invasion was assessed at the primary tumor site rather than at remote antegrade or retrograde locations. If no cranial nerve or venous sinus invasion was noted in the surgical report, invasion was assumed to be absent; provided pathologic evaluation also did not show invasion.

Five characteristics of tumor invasion were examined by MR imaging in the study (pial, dural, linear, and nodular enhancement, and the width of dural thickening). To compare the accuracy of these characteristics in predicting true tumor invasion, we used the exact form of McNemar’s test for matched samples (2). A confidence level (P value) that approaches 0.5 represents equally accurate tests. As the confidence levels stray from 0.5, the likelihood that
### Fig 1. Nodular, pial enhancement; positive dural and cortical invasion.

A. Invasion through the skull base into the underlying brain parenchyma can be seen on this sagittal T1-weighted (500/11/1) unenhanced MR image. The edema of the frontal lobe can be identified (curved arrow) as the mass (M) infiltrates the cortical tissue. This is evidence of transdural (pial) invasion.

B. Contrast-enhanced fat-suppressed T1-weighted (600/11/1) MR image through the frontal lobes shows contrast-enhancing neoplasm (N) infiltrating the cortex of both frontal lobes, right greater than left.

### TABLE 1: Imaging and histopathologic findings in 22 patients with tumors of the skull base

<table>
<thead>
<tr>
<th>Case</th>
<th>Age, y</th>
<th>Histology of Tumor/Location</th>
<th>Findings on MR Imaging</th>
<th>Intraoperative and Pathologic Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Type of Enhancement/ Width, mm</td>
<td>Pial Perineural Spread (Cranial Nerve Affected)</td>
</tr>
<tr>
<td>1</td>
<td>63</td>
<td>Meningioma/petroclival</td>
<td>LD/3</td>
<td>–</td>
</tr>
<tr>
<td>2</td>
<td>67</td>
<td>Squamous cell carcinoma/scalp</td>
<td>. . .</td>
<td>–</td>
</tr>
<tr>
<td>3</td>
<td>33</td>
<td>Meningioma/L parietal</td>
<td>LD/4</td>
<td>–</td>
</tr>
<tr>
<td>4</td>
<td>44</td>
<td>Meningioma/R skull base</td>
<td>LD/5</td>
<td>–</td>
</tr>
<tr>
<td>5</td>
<td>42</td>
<td>Basal cell carcinoma/frontal sinus</td>
<td>ND/8</td>
<td>+</td>
</tr>
<tr>
<td>6</td>
<td>46</td>
<td>Adenocarcinoma/ethmoidal sinus</td>
<td>. . .</td>
<td>–</td>
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<tr>
<td>7</td>
<td>60</td>
<td>Chordoma/clivus</td>
<td>ND/19</td>
<td>–</td>
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<tr>
<td>8</td>
<td>24</td>
<td>Cholesterol granuloma/petrous apex</td>
<td>. . .</td>
<td>–</td>
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<tr>
<td>9</td>
<td>40</td>
<td>Cholesteatoma/R mastoid</td>
<td>LD/1</td>
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<tr>
<td>10</td>
<td>85</td>
<td>Squamous cell carcinoma/periorbital</td>
<td>LD/2</td>
<td>–</td>
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<tr>
<td>11</td>
<td>57</td>
<td>Chordoma/clivus</td>
<td>ND/8</td>
<td>–</td>
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<tr>
<td>12</td>
<td>19</td>
<td>Chondrosarcoma/R temporal bone</td>
<td>. . .</td>
<td>–</td>
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<tr>
<td>13</td>
<td>49</td>
<td>Squamous cell carcinoma/periorbital</td>
<td>LD/2</td>
<td>–</td>
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<tr>
<td>14</td>
<td>67</td>
<td>Mucoepidermoid/parotid</td>
<td>. . .</td>
<td>–</td>
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<tr>
<td>15</td>
<td>35</td>
<td>Meningioma/L petrous apex</td>
<td>LD/2</td>
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<tr>
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<td>17</td>
<td>70</td>
<td>Esthesioneuroblastoma/crteriform plate</td>
<td>ND/32</td>
<td>–</td>
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<tr>
<td>18</td>
<td>70</td>
<td>Basal cell carcinoma/mastoid</td>
<td>. . .</td>
<td>–</td>
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<tr>
<td>19</td>
<td>62</td>
<td>Renal cell carcinoma metastasis/skull</td>
<td>ND/27</td>
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<tr>
<td>20</td>
<td>51</td>
<td>Chondrosarcoma/nasal septum</td>
<td>. . .</td>
<td>–</td>
</tr>
<tr>
<td>21</td>
<td>65</td>
<td>Squamous cell carcinoma/R nasopharynx</td>
<td>ND/6</td>
<td>–</td>
</tr>
<tr>
<td>22</td>
<td>81</td>
<td>Chordoma/clivus</td>
<td>ND/4</td>
<td>–</td>
</tr>
</tbody>
</table>

Note.—LD indicates linear enhancement of dura; ND, nodular enhancement of dura; –, negative finding; and +, positive finding.
one characteristic is more accurate than the other increases.

Results

Fourteen of the 22 cases had dural enhancement. Seven of the 14 cases showed uniformly linear enhancing dura while seven cases showed nodular enhancement. Four cases showed pial enhancement (Fig 1). All four of these cases also showed nodular enhancement. The width of enhancing dura ranged from 1 to 32 mm (mean, 6.7 mm) (Fig 2). Six of seven tumors with nodular enhancement had dural thickening greater than 5 mm. Three cases showed MR findings of nodular enhancing dura, perineural spread, and venous invasion. Five cases showed perineural enhancement alone, whereas four cases showed MR findings suggestive of perineural invasion and linear dural enhancement. Four cases showed perineural and nodular enhancement. Two cases showed venous invasion and linear enhancement. Six cases fulfilled MR criteria of venous invasion and nodular enhancement. In 13 cases, MR images were reported to show perineural invasion, and seven cases were interpreted as showing venous sinus or jugular vein invasion.

Of the 22 patients studied, dural invasion was confirmed histologically in eight. Of these eight cases, the most common histologic type was a chordoma (n = 3). Six of the cases showed vascular invasion by tumor. One of these was discovered at histopathologic examination while the other five were determined by the surgeon during surgery. Four of the cases showed perineural invasion, reported during surgery. One of these showed perineural invasion only while three case had dural, perineural, and cavernous sinus invasion. Two cases had venous and dural invasion only. Eleven cases showed no invasion at all (Table 1).

All patients with dural thickening greater than 5 mm (n = 6) had confirmed dural invasion, while 14 of 16 patients with dural thickening of 5 mm or less had no neoplastic invasion (Fig 3). One case had confirmed dural invasion but no dural enhancement at all (false negative). Of the seven cases that showed linear enhancement alone, none had confirmed dural invasion. Seven of the 22 cases showed nodular enhancing dura and all seven were confirmed to have dural invasion (Table 1).
The sensitivity of all types of dural enhancement in predicting invasion was 88%, the specificity was 50%, and the accuracy was 64%. If the rule that nodular enhancement indicated dural invasion while linear enhancement indicated no invasion was applied, the specificity improved to 100% and the accuracy to 95%. The sensitivity, specificity, and accuracy of predicting tumor invasion by a width of dural thickening of more than 5 mm were 75%, 100%, and 91%, respectively (Table 2). Predicting tumor invasion by pial enhancement was 100% specific and 50% sensitive.

When the data were separated on the basis of the histology of the tumor, we found the accuracy of predicting dural invasion by nodular enhancing dura to be 100% for meningiomas and squamous cell carcinomas. All four of the meningiomas in the study showed linear enhancement adjacent to the mass. None of these cases showed remote dural invasion, and noneshowed nodular enhancement. Predictions as to dural invasion were correct for all four squamous cell carcinomas (three negative, one positive) (Fig 3). Of two adenocarcinomas, one was accurately predicted not to invade dura while the other was considered a false-negative finding, with confirmed dural invasion (Fig 4). One basal cell carcinoma and three of three chordomas were correctly predicted to invade dura (Figs 5 and 6).

McNemar’s test (2) was used to compare the accuracies of linear, nodular, and pial enhancement in predicting dural invasion. The accuracy of linear enhancement was significantly different from (worse than) that of pial enhancement (P < .001), nodular enhancement (P < .001), and a width of dural thickening of 5 mm or more (P < .001). Pial enhancement, nodular dural enhancement, and width of dural thickening of 5 mm or more did not have significantly different accuracies (P > .125). The implication of this analysis is that pial enhancement, nodular enhancement, and wider dural thickening are
significantly more accurate in predicting dural invasion of tumor than is linear enhancement.

Only four patients had perineural tumor according to surgical notes, yet 13 of the 22 patients were judged to have perineural invasion on the basis of preoperative MR images. The criterion used for a positive intraoperative finding was focal macroscopic encasement of or extension along a nerve rather than microscopic invasion seen histopathologically (no distal biopsies were performed). Radiologically, either focal tumor in the expected location of a cranial nerve or actual enhancement of the nerve was considered a positive finding. The four positive cases were correctly predicted on imaging studies, but there were nine false-positive MR examinations. With only four positive cases it is difficult to assess truly the sensitivity of MR imaging (four of four correct); however, the specificity was 50% (nine of 18), and the accuracy was 59% (13 of 22).

Seven of the 22 patients were thought to have vascular invasion on the basis of MR findings; six of these were confirmed to have vascular invasion. There was one false-positive study, a petroclival meningioma that was interpreted as displacing the wall of the cavernous sinus but that did not invade the sinus by intraoperative assessment. The sensitivity and specificity of vascular invasion were 100% and 94%, respectively, and the accuracy was 95%.

Discussion

Cancer of the head and neck represents 4% of all malignant tumors in the United States (3). Worldwide, head and neck cancer represents the sixth most prevalent cancer (4). Improvements in surgical technique, including microvascular surgery and modern surgical reconstruction, make surgical excision or primary...
radiation therapy the most favorable treatment options for the majority of head and neck tumors. If the tumor has progressed to the point that negative margins are not attainable, curative or palliative treatment with radiation therapy for malignant tumors is often recommended; surgery may still be used for debulking large tumors. The extent of tumor invasion thus dictates the surgical approach and has significant prognostic implications.

The extent of dural invasion of skull base tumors has been shown to be an important prognostic indicator. In a retrospective review of 21 patients who underwent craniofacial reconstruction for anterior skull base tumors, the patients who had dural involvement had a 22% survival rate after 3 years while patients without dural involvement had a survival rate of 83% (5). Studies of other skull base tumors showed similar survival rate differences for tumors that invaded dura and those that did not (6–8). Other studies, however, did not find intracranial extension of tumor to be a significant prognostic factor (9, 10). Dural invasion of tumor also guides the surgical approach. If dura is to be excised, preparation for pericranial flaps or fascial grafts is important.

Perineural invasion of tumor also has prognostic significance. Perineural invasion was shown to correlate significantly with increased mortality due to tumor and local or regional tumor recurrence (10–12).

Tumor invasion is determined by clinical examination, by imaging studies, and during surgery. Preoperative determination of invasion is a potentially valuable component of tumor staging and surgical planning. Imaging can provide essential information about the sites of involvement that elude clinical examination. MR imaging and computed tomography (CT) are the common imaging techniques used to evaluate head and neck neoplasms. CT has the advantages of wide availability, speed, and good delineation of the osseous structures, especially at the skull base. It is not uncommon, however, to find erosion of the bone unaccompanied by CT-detectable gross intracranial tumor extension (13). Compared with CT, MR imaging has the advantages of multiplanar capabilities and improved soft-tissue contrast. Vessels and their relationship to the tumor are readily demonstrated by MR imaging without intravenous injection of contrast material. The disadvantage of MR imaging is its poorer availability compared with CT, especially in developing countries where many head and neck cancers are more prevalent than they are in the United States.

The use of contrast agents has greatly improved the sensitivity of MR imaging. Many tumors of the head and neck have intermediate rather than high signal intensity on T2-weighted images, owing to high cellularity and decreased free water (14). In the epidural space, these tumors become difficult to differentiate from brain parenchyma. Van Tassel and Lee (15) looked at noncontrast MR images of sinonasal tumors and found that in six of eight patients, the margins of the epidural component of the sinonasal tumor could not be assessed accurately. After administration of contrast material, however, all eight tumors enhanced and could be clearly delineated.

The physiology of dural enhancement is currently debated between reactive dural changes and tumor invasion. Recent studies show that the pattern of enhancement is more indicative of tumor involvement than the actual presence of enhancement itself. Ahmadi and coworkers (16, 17) showed that dural invasion is present if there is no hypointense zone on T1-weighted images between the enhancing dura and the tumor. These studies also showed that dural invasion corresponded to a discontinuous band of dural enhancement. These and other studies have proposed that a linear pattern of enhancement represents reactive changes in the dura due to adjacent tumor rather than to tumor invasion (16, 18). Our data support this and in addition show that focal, nodular dural enhancement, rather than a discontinuous band of enhancement, represents dural tumor invasion. Focal nodularity of dural enhancement was significantly more accurate than linear enhancement at predicting dural invasion (P < .001). We have also shown that dural thickening of more than 5 mm and pial enhancement, also indicate invasion. Both are significantly more accurate than linear (P < .001) or generalized dural (P < .05) enhancement at predicting dural invasion.

The one tumor confirmed to invade the dura but not correctly predicted at MR imaging is shown in Figure 4. This is a case of adenocarcinoma of the ethmoidal sinus extending into the left orbit (case 6). In this Figure, there is a questionable area of enhancement. Because this enhancement was seen on only one section
and was not clearly dural enhancement, it was interpreted as no dural enhancement by two independent reviewers. This represents the one MR examination in this study that was falsely negative for dural invasion.

The width of dural enhancement was also a significant predictor of dural invasion, as seen in Figure 2. A cut-off of 5 mm was an accurate means of predicting invading versus noninvading tumor. Dural enhancement of 5 mm or less was associated with dural invasion in only one case, whereas every tumor associated with dural enhancement of more than 5 mm was confirmed to invade dura. Unfortunately, we had no instances of nonnodular dural enhancement of more than 5 mm to determine whether this finding was valid, even with a linear pattern. There was one case of nodular enhancement with a width of 4 mm that was positive for dural invasion at histopathologic examination; this may suggest that the type rather than the width of enhancement may be more accurate for predicting dural invasion.

One hypothesis to explain linear enhancement states that the enhancement of the dura is a result of increased meningeal vascularity as a reaction to tumor proximity (17). To examine the possibility that linear enhancement represented increased dural vascularity, the cases of meningiomas in the study were reviewed again to look for dural vascularity. Histopathologic examination did not show increased vascularity of the dura in these samples.

Another possible cause of linear dural enhancement in the region of skull base tumors is reactive change, such as inflammation around or hypertrophy of the dura. Evidence supporting this hypothesis from our study can be found in the surgical report of one case, in which linear enhancement was seen with no dural invasion, yet thickened tissue was present in the epidural region. However, evidence against this hypothesis was supported by a different case, in which a 2-mm area of irregularity of the dura was found, which was discolored and appeared thickened, despite a preoperative MR image that showed no dural enhancement.

Head and neck neoplasms can spread by direct extension or by distant metastasis. Two routes for distant metastasis are along vascular channels or along nerve sheaths. Involvement of cranial nerves has been shown to be a poor prognostic sign (10), and vascular involvement is most likely associated with a poor prognosis as well. Our results show that MR imaging is a good predictor of vascular tumor invasion, as the accuracy of prediction was 95% in our study. All of the cases of venous sinus/jugular vein invasion were confirmed by intraoperative reports rather than with pathologic findings. Since the vascular invasion could be seen grossly by the surgeon during the operation, the invaded venous sinus or jugular vein would most likely be large enough to be seen on MR images. Invasion of smaller cortical vessels would be more difficult to predict with MR imaging.

The ability to assess the accuracy of MR imaging in predicting perineural invasion in this study is tempered by the small number of positive cases (n = 4) and the difficulty in obtaining reliable surgical and histopathologic confirmation. Our large number of false-positive findings could be falsely elevated because we considered perineural invasion to be negative if neural involvement was not specifically mentioned by the surgeon or the pathologist. On the other hand, our radiologic assessment was somewhat liberal: proximity to the expected location of a cranial nerve was used as a positive MR criterion in addition to enhancement and enlargement of the nerve. Therefore, a lesion invading the cavernous sinus, such as the chordoma in case 11 (see Table 1, Fig 6A) or in case 6, the patient with the adenocarcinoma growing through the cribriform plate (Fig 4A), was called “radiologically positive” even if the suspected cranial nerve was not enhancing or thickened.

Therefore, in conclusion, MR imaging can accurately predict dural invasion by skull base tumors if there is pial enhancement (82%) or if the dural enhancement is nodular (95%) or more than 5 mm thick (91%). Linear enhancement of dura does not imply dural infiltration by tumor. Venous invasion of tumor can be predicted accurately (95%) with preoperative MR imaging if the invasion involves the venous sinuses or the internal jugular veins. The ability of MR imaging to show perineural invasion was not definitively assessed in this study, because of the few positive cases (n = 4) and the lack of specific neural biopsies performed.

The preoperative determination of dural, perineural, and venous invasion has significant impact on surgical planning and on discussions of prognosis with patients before attempted curative resections.
References