ORIGINAL ARTICLE

Diagnostic Accuracy of Magnetic Resonance Imaging in the Assessment of Mandibular Involvement in Oral-Oropharyngeal Squamous Cell Carcinoma

A Prospective Study

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Objective: To evaluate the sensitivity, specificity, accuracy, and predictive values of magnetic resonance imaging (MRI) in the assessment of mandibular involvement in oral-oropharyngeal squamous cell carcinoma.

Design: Prospective study.

Setting: University hospital.

Patients: Forty-three patients with oral or oropharyngeal squamous cell carcinona undergoing marginal or segmental mandibulectomy between January 1, 1994, and January 31, 2003.

Interventions: Indications for mandibulectomy were MRIs suggestive of bony invasion, tumor involving the retromolar trigone or the alveolar ridge, recurrent or persistent lesion, or intraoperative suspicion of periosteal invasion. Detection of tumor signal replacing the hypointense cortical rim was considered the main radiologic finding for mandibular invasion.

Main Outcome Measures: The MRI findings were subsequently compared with histopathologic data of surgical specimens with reference to the presence of cortical and/or medullary mandibular involvement.

Results: Sixteen patients had MRI findings suggestive of mandibular involvement. Segmental mandibulectomy was performed in 15 cases and marginal resection in the remaining case. In 14 patients, bony invasion was confirmed. All of the other 27 patients who underwent marginal or segmental mandibulectomy with negative MRI findings had no histopathologic evidence of mandibular involvement, except in 1 patient: on histopathologic examination, despite cortical integrity, neoplastic vascular embolization into the bony lacunae was detected. Sensitivity of MRI in detecting mandibular involvement was 93%; specificity, 93%; accuracy, 93%; and negative and positive predictive values, 96% and 87.5%, respectively.

Conclusions: Magnetic resonance imaging is commonly considered the technique of choice for treatment planning in advanced oral and oropharyngeal squamous cell carcinoma because of its accuracy in depicting soft-tissue involvement. This study demonstrates the additional diagnostic value of MRI in detecting bone invasion.

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TREATMENT OF ADVANCED oral-oropharyngeal squamous cell carcinoma (SCC) is based on an appropriate combination of ablative and reconstructive surgery, radiotherapy, and chemotherapy, with the intent to optimize control of the disease and, at the same time, to minimize treatment comorbidities, with special reference to those related to surgical resection. This goal can be achieved only by adequate clinical and radiologic evaluation of tumor extent and careful selection of reconstructive techniques.

The rates of mandibular infiltration reported in the literature range from 22% to 100% in relation to the different oral and oropharyngeal subsites involved and the disease stage.[1-8] A precise assessment of the extent of mandibular invasion is therefore crucial for treatment planning to obtain both radical tumor resection and good functional results. In fact, it is commonly accepted that when a previously untreated mandible appears to be disease free, its integrity can be maintained, except for a rim resection performed to obtain adequate surgical margins in healthy tissues. However, when mandibular involvement is clearly detected during preoperative and/or intraoperative evaluation, mandibulectomy is required. This may be either marginal resection, in the case of early infiltration,[9] or segmental mandibulectomy. The latter more aggressive procedure com-

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Table 1. MR Imaging Protocol

	Sequence		
	Turbo SE T2	SE T1	SE T1*
TR, ms	5680	500	500
TE, ms	15	15	15
Acquisition time	1 min 52 s	2 min 50 s	2 min 50 s
Section thickness, mm	3	3	3
Acquisition plane	Axial, coronal	Coronal	Axial, coronal, sagittal

Abbreviations: MR, magnetic resonance; SE, spin echo; TE, echo time; TR, repetition time.
*After contrast administration.

monly requires additional operative time to provide not only adequate soft-tissue repair but also osseous reconstruction. This is especially true when anterior defects are present and/or in young dentate patients, to improve functional and cosmetic results.[10]

Different preoperative investigations may be applied alone or in combination to assess mandibular involvement. These include pantomography, computed tomography (CT), magnetic resonance imaging (MRI), mandibular and maxillary CT (DentaScan software; General Electric Co, Milwaukee, Wis), scintigraphy, and single-photon emission computed tomography. Intraoperative evaluation of mandibular involvement by means of periosteal stripping[11] or frozen sections on curetted medullary bone[12] may have a role in clearly defining the extent of mandibular resection.[13,14]

Magnetic resonance imaging is regarded as a highly accurate examination in depicting extension of oral-oropharyngeal cancer in the surrounding soft tissues because of its high contrast resolution and multiplanar views.[15,16] For these reasons, MRI has been considered the gold standard for pretreatment assessment by our team for many years. The present analysis was planned with the intent to specifically assess the additional diagnostic value of MRI in detecting bone invasion by contrasting radiologic and postoperative histopathologic findings.

METHODS

Between January 1, 1994, and January 31, 2003, 43 nonconsecutive patients admitted to the Department of Otolaryngology at the University of Brescia in Brescia, Italy, with oral (29 patients) or oropharyngeal (14 patients) SCC underwent surgical treatment that included either marginal or segmental mandibulectomy. These patients included 37 men and 6 women, ranging in age from 37 to 79 years (mean, 57 years). Twenty patients (47%) had previously received unimodal or multimodal treatment: 11 underwent radiotherapy with curative intent, 4 had combined chemoradiotherapy (in 1 case in association with surgery), 3 had surgery followed by complementary radiotherapy, and the remaining 2 patients were treated by surgery alone. Lesions were retrospectively staged according to classification of malignant tumors established by the American Joint Committee on Cancer[17] as follows: 1 T1, 9 T2, 9 T3, 21 T4a, and 3 T4b. Taking into account the different anatomic subsites of the oral cavity and oropharynx, none of the patients had neoplastic lesion involving only 1 subsite: 7 patients (16%) had involvement of 2 subsites (group A), whereas 36 patients (84%) had extensive lesions involving 3 or more oral and/or oropharyngeal subsites (group B).

Magnetic resonance imaging was performed on all patients as the only preoperative radiologic examination. It was acquired on a 1.5-T unit with the use of a high-resolution protocol (**Table 1**). This consisted of turbo spin-echo (SE) T2-weighted sequences (axial and coronal planes) and SE T1-weighted sequences obtained before (axial plane) and after (axial, coronal, and sagittal planes) administration of a contrast agent (gadopentetate dimeglumine, 0.2 mL/kg). All images were acquired with 3- to 3.5-mm section thickness, high-resolution matrix (256×512), small field of view (180-200 mm), and small pixel size (ranging from 0.29×0.64 mm to 0.47×0.74 mm). All MRI examinations were evaluated by the same radiologist (R.M.).

Mandibular infiltration was suspected whenever the hypointense signal of cortical bone was replaced by the signal intensity of tumor on both SE T2-weighted and SE T1-weighted sequences. Replacement of the hyperintense signal of medullary bone by tumor signal intensity (intermediate on turbo SE T2, hypointense on SE T1, and markedly enhancing after contrast administration) was considered suggestive of invasion of bone medulla.

Criteria for mandibulectomy included MRI findings of bony invasion, tumor involving the retromolar trigone or the alveolar ridge to achieve safe surgical margins, persistent or recurrent lesions involving subsites in proximity to the mandible, and intraoperative suspicion of periosteal invasion. A rim mandibulectomy was performed only when a sufficient height of mandible could be preserved to avoid iatrogenic fractures.

The lesion was approached through a median or paramedian mandibulotomy in 41 patients (associated with segmental mandibulectomy in 34 and marginal mandibulectomy in 7), and transorally or via a pull-through in 1 patient each (both patients underwent a marginal mandibulectomy). Thirty-four patients had segmental mandibulectomy, and 9 underwent marginal resection. Intraoperative evaluation of mandibular margins by means of periosteal stripping or frozen sections on curetted medullary bone was performed in only 2 cases in which the radicality of resection was doubtful.

The MRI findings were subsequently compared with histopathologic data, in relation to the presence of cortical and/or medullary mandibular involvement. On the basis of these results, sensitivity, specificity, accuracy, and predictive values of MRI in detecting bone invasion by SCC were calculated.

RESULTS

In 16 patients, MRI was suggestive of mandibular infiltration. In 10 cases, transcortical tumor spread into the medullary space was evident (**Figure 1**), while in the remaining 6 patients involvement confined to the cortex was suspected. Segmental mandibulectomy was performed in 15 cases and marginal resection in 1 case. Intraoperative evaluation of bony margins never modified the extent of mandibular resection performed. In 14 patients, bony invasion was confirmed at histopathologic examination (10 cases with medullary and 4 with exclusive cortical involvement). Only 1 (7%) of these 14 patients had a lesion involving 2 subsites, while the remaining 13 (93%) had extended lesions involving 3 or more oral and/or oropharyngeal subsites. The overall infiltration rate was thus 14% (1/7) in group A and 36% (13/36) in group B. Two patients with MRIs suggestive of cortical invasion of the retromolar trigone underwent segmental mandibulectomy, and results were found to be negative for mandibular involvement (**Table 2**, top section, cases 4 and 7). These were the only 2 false-positive cases (5%) in the present series (**Figure 2**).

Twenty-seven patients with negative findings on MRI received marginal (8 cases) or segmental (19 cases) mandibulectomy, with no pathological evidence of mandibular involvement in 26 cases. In 1 patient who underwent segmental resection for a persistent retromolar trigone SCC previously treated with radiotherapy, neoplastic vascular embolization into the bony lacunae was detected on histopathologic examination (**Figure 3**). Despite cortical integrity observed on MRI (**Figure 4**) and confirmed by the pathologist, this high-grade lesion was also characterized by massive vascular embolization and perineural spread (Table 2, bottom section, case 1). This patient represents the only false-negative case (2%) in the present series. The prevalence of bone invasion was 11% (1/9) for rim mandibulectomies and 41% (14/34) for segmental resections.

Eleven (58%) of the 19 patients who underwent a segmental mandibulectomy with MRI negative for bony involvement had been previously treated by means of unimodal or multimodal treatment, and 15 cases (79%) had lesions involving the retromolar trigone or alveolar ridge. Thirteen (87%) of those 15 cases were at an advanced stage (III and IV).

The sensitivity, specificity, and accuracy of MRI in detection of mandibular involvement were 93%, 93%, and 93%, respectively, while the negative and positive predictive values were 96% and 87.5%, respectively.

COMMENT

Two basic histologic patterns of mandibular invasion were originally documented by McGregor and MacDonald[18] regarding tumor spread in nonirradiated edentulous mandible. The first consisted of an erosive (or expansive) pattern characterized by well-defined U-shaped excavation of the mandibular bone. The second pattern was exemplified by an infiltrative (or invasive) mass, which showed neoplastic nests invading the bone with osseous spicula along irregular margins. These 2 patterns, also observed in subsequent histologic studies, are probably related to several factors that chiefly include the site of the lesion, its extent, and the nature of the anatomic barrier encountered by the tumor during growth. In contrast, the impact of previous treatment, dental status, and the histopathologic characteristics of the tumor appear to play a less clear role.[5,9,19-22] A clear-cut differentiation between erosive and infiltrative patterns cannot always be established during histopathologic examination. In fact, both may be detected in the same specimen at different levels along the front of mandibular infiltration as expression of different neoplastic components of the same lesion.[5,22,23]

We observed an unusual finding of mandibular involvement by neoplastic vascular embolization into the bony lacunae associated with radiologic and histopathologic findings of cortical integrity (Table 2, bottom section, case 1). To the best of our knowledge, this characteristic histologic feature has been reported in a single case.[20] In that report, a single neoplastic island was identified in bone marrow, with no evidence of direct invasion from the retromolar area where the tumor was located. This apparently rare pathway of mandibular involvement might possibly be observed in a higher percentage of patients if mandibular specimens were analyzed in their entirety with macrosections instead of with standard techniques.

Figure 1. Spin-echo T1-weighted magnetic resonance images after contrast administration on axial (A) and sagittal (B) planes. Squamous cell carcinoma of the anterior floor of the mouth is centered on the midline (B, black arrowheads); the lesion obstructs both Wharton ducts, which are dilated (A, white arrowheads). Cortical bone is eroded on both vestibular and lingual sides (black arrows); the lesion invades the medullary bone in its upper third (asterisk).

Neither prognosis nor the risk of local recurrence was related to mandibular invasion, although they are in strict correlation with tumor size, nodal status, and surgical margins.[8,23-26] Therefore, the most important factor in mandibular management is to clearly identify the presence of neoplastic infiltration and its precise extent by

Table 2. Radiologic and Histopathologic Findings in 16 Patients With MRI Suggestive of Mandibular Infiltration and 27 Patients With MRI Negative for Mandibular Infiltration

Patient No./ Age, y	Previous Treatment	RMT or AR Localization	Type of Mandibulectomy	pT	MRI Findings	Pathological Evaluation	Combination
Suggestive MRI Findings							
1/43	RT + S	No	Segmental	4a	Positive M	Positive M	TP
2/60	None	No	Marginal	4a	Positive C	Positive C	TP
3/44	None	No	Segmental	4a	Positive M	Positive M	TP
4/57	None	Yes	Segmental	2	Positive C	Negative	FP
5/42	RT	No	Segmental	4a	Positive M	Positive M	TP
6/46	RT	No	Segmental	4a	Positive C	Positive C	TP
7/53	None	Yes	Segmental	3	Positive C	Negative	FP
8/64	S + RT + CHT	No	Segmental	4a	Positive M	Positive M	TP
9/50	S	No	Segmental	2	Positive M	Positive M	TP
10/52	None	No	Segmental	4a	Positive M	Positive M	TP
11/79	None	Yes	Segmental	4a	Positive M	Positive M	TP
12/58	RT + CHT	Yes	Segmental	4b	Positive M	Positive M	TP
13/49	None	No	Segmental	4a	Positive M	Positive M	TP
14/68	RT	Yes	Segmental	4a	Positive C	Positive C	TP
15/61	RT	Yes	Segmental	4b	Positive C	Positive C	TP
16/48	None	Yes	Segmental	2	Positive M	Positive M	TP
Negative MRI Findings							
1/54	RT	Yes	Segmental	4a	Negative	Positive E	FN
2/60	None	No	Segmental	2	Negative	Negative	TN
3/72	None	No	Marginal	2	Negative	Negative	TN
4/65	RT + CHT	Yes	Segmental	4a	Negative	Negative	TN
5/37	None	Yes	Segmental	4a	Negative	Negative	TN
6/58	None	No	Marginal	2	Negative	Negative	TN
7/53	None	Yes	Segmental	4a	Negative	Negative	TN
8/60	None	No	Marginal	4a	Negative	Negative	TN
9/58	None	Yes	Marginal	4a	Negative	Negative	TN
10/73	None	No	Marginal	1	Negative	Negative	TN
11/54	None	Yes	Segmental	3	Negative	Negative	TN
12/55	None	Yes	Marginal	4a	Negative	Negative	TN
13/63	None	No	Segmental	2	Negative	Negative	TN
14/57	None	No	Segmental	3	Negative	Negative	TN
15/61	None	Yes	Segmental	3	Negative	Negative	TN
16/51	None	Yes	Segmental	4a	Negative	Negative	TN
17/49	RT	Yes	Segmental	3	Negative	Negative	TN
18/57	RT	Yes	Segmental	4a	Negative	Negative	TN
19/61	RT	Yes	Segmental	3	Negative	Negative	TN
20/51	RT	Yes	Segmental	4b	Negative	Negative	TN
21/57	S + RT	Yes	Marginal	4a	Negative	Negative	TN
22/77	None	Yes	Marginal	4a	Negative	Negative	TN
23/49	RT	Yes	Segmental	3	Negative	Negative	TN
24/56	RT + CHT	Yes	Segmental	3	Negative	Negative	TN
25/66	RT	Yes	Segmental	2	Negative	Negative	TN
26/54	RT	Yes	Segmental	2	Negative	Negative	TN
27/50	S	No	Segmental	3	Negative	Negative	TN

Abbreviations: AR, alveolar ridge; C, cortex; CHT, chemotherapy; E, embolization; FN, false negative; FP, false positive; M, medulla; MRI, magnetic resonance imaging; pT, pathologic T stage; RMT, retromolar trigone; RT, radiotherapy; S, surgery; TN, true negative; TP, true positive.

means of preoperative and intraoperative evaluation to obtain adequate oncologic control and to minimize functional sequelae.

Mandibular infiltration is a challenging diagnostic issue in preoperative staging of oral-oropharyngeal cancer. A reliable assessment of bone invasion is obtained by matching complementary information provided by physical examination and imaging studies.[27] The ideal diagnostic tool would consist of the noninvasive and inexpensive demonstration of both cortical erosion and neoplastic replacement of medullary bone, to allow the selection of an appropriate surgical strategy (marginal vs segmental mandibulectomy).[28]

Several previous reports, focusing on mandibular infiltration, have investigated the role of different diagnostic techniques including pantomography, bone scanning, CT, and MRI. Accurate assessment of bone invasion is difficult by conventional radiography, since at least 30% to 75% of cancellous bone must be replaced by tumor to be detected on pantomography.[29,30] In addition, the width of mandibular infiltration is underestimated by pantomography by an average of 13 mm, while the depth of invasion is impossible to assess on a 2-dimensional coronal x-ray film.[31]

Abnormal osteoclastic activity in the area of bone infiltration, confirmed by various histopathologic studies,[5,19,20] is the rationale for radionuclide tracer uptake.

Figure 2. Spin-echo T1-weighted magnetic resonance images (MRIs) after contrast administration on axial (A) and coronal (B) planes. Squamous cell carcinoma of the oropharynx infiltrates the left tonsillar fossa and extends anteriorly to the base of the tongue (A, white arrowhead) and to the retromolar trigone (A, black arrowhead). Focal effacement of medullary bone is detected at the most anterior aspect of the mandibular angle (arrows), suggesting bone invasion. Histopathologic examination did not confirm this finding (false-positive MRI findings).

Although more sensitive than pantomography (functional changes are detectable earlier than morphologic changes), bone scanning provides low specificity (12%-15% false-positive rate),[30,31] as bone uptake can also be observed in the presence of periodontal inflammatory disease, infection, osteomyelitis, and trauma.[29]

Computed tomographic scanning may provide high sensitivity and specificity (96% and 87%, respectively)[32] when proper examination protocols are applied (3-mm or less section thickness; image reconstruction with both soft-tissue and bone algorithm). The recently developed multisection technique enables acquisition of a volume of interest with nearly isotropic voxel, therefore allowing high-quality multiplanar reconstructions comparable to native axial images. Complementary diagnostic value may be added by the application of software (DentaScan) that enables one to reformat a dataset of axial images (acquired with 1-mm section thickness) into multiple cross-sectional and panoramic views.[28,33] The supplementary cost to the patient of the use of this software may be as high as $650, making the real cost-effectiveness of this technique questionable.[28]

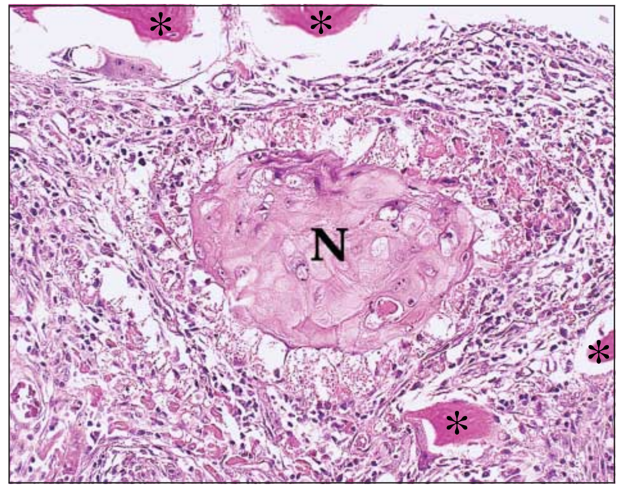

Figure 3. A single island of neoplastic cells (N) in bone tissue (Table 2, bottom section, case 1). The asterisks indicate osseous lamellae (hematoxylin-eosin, original magnification ×40).

Two major drawbacks limit the diagnostic accuracy of CT. Beam hardening artifacts produced by dental amalgam or prosthetic implants spoil the quality of images and limit correct assessment of the mandible. In addition, according to several authors,[18,30,34] mandibular infiltration more frequently occurs by means of direct medullary invasion, in edentulous areas of the alveolar ridge; CT is known to be rather weak at demonstrating early signs of neoplastic replacement of medullary bone.

A relatively limited number of reports focusing on MRI findings of neoplastic infiltration of the mandible have been published.[6,7,35-38] Magnetic resonance imaging provides excellent contrast resolution, allowing unique definition of tumor relationships with adjacent soft-tissue structures (muscles, midline lingual septum, salivary glands and ducts, and vessels). This technique displays cortical bone of the mandible as a continuous, thin layer with a markedly hypointense signal on all sequences, as a result of the lack of freely mobile protons in its molecular structure. Medullary bone, in contrast, exhibits an intermediate-to-high signal on turbo SE T2-weighted sequences and a brightly hyperintense signal on SE T1-weighted sequences because of its high–fat tissue content. Mandibular infiltration is, therefore, suspected in the presence of tumor encroachment of the hypointense cortical layer, as well as when an abnormal signal pattern is detected in the medullary space.

In our experience, MRI demonstrated a very high sensitivity (93%); the single false-negative result was seen in a case in which pathological examination of the speci-

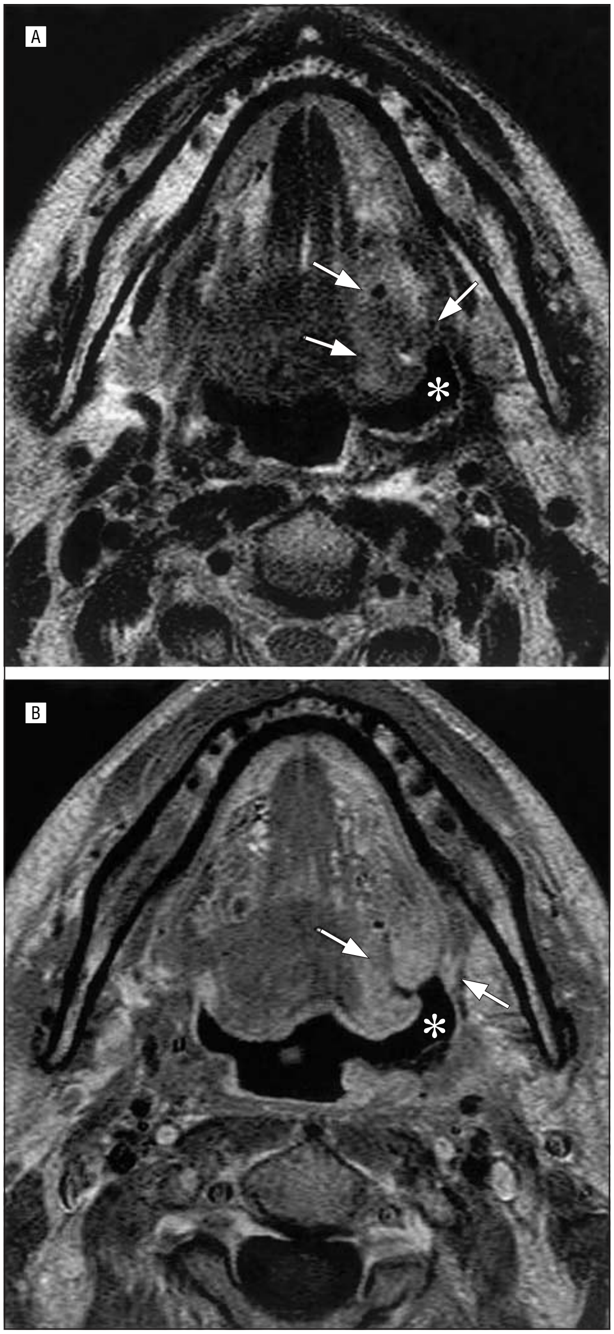

Figure 4. Turbo spin-echo T2-weighted magnetic resonance image (MRI) (A) and spin-echo T1-weighted image after contrast administration (B), axial plane. Squamous cell carcinoma of the retromolar trigone persisted after radiotherapy. A massive ulceration is demonstrated at the level of the left tonsillar fossa (asterisk); neoplastic tissue invades the base of the tongue and glossotonsillar sulcus (arrows). Both cortical and medullary bone of the mandible are normal; pathological examination of the specimen demonstrated medullary infiltration without cortical disruption (false-negative MRI findings).

men demonstrated small nests of neoplastic cells, certainly below the threshold of MRI, into the bony lacunae with possible tumor vascular embolization along Havers channels, with absence of cortical disruption (Table 2, bottom section, case 1). Magnetic resonance imaging yielded 2 false-positive cases (Table 2, top section, cases 4 and 7). The overestimation of cortical invasion is a well-known shortcoming of the technique, as signal changes are comparable in both inflammatory conditions (periodontal disease and peritumoral edema) and neoplastic invasion.

Overall, MRI demonstrated both high accuracy (93%) and negative predictive values (96%). According to the criteria we established for mandibulectomy, no patient in the present series received inadequate treatment in terms of mandibular resection. The specificity of MRI was higher than that recently reported for CT (93% vs 87%, respectively).[32] Nevertheless, 2 patients (Table 2, top section, cases 4 and 7) underwent segmental mandibulectomy because they had MRI findings suggestive of cortical bone infiltration at the level of the retromolar trigone. In these cases, appropriate rim mandibulectomy would have ensured a complete tumor resection with safe margins.

In conclusion, the results presented herein demonstrate the additional value of MRI for evaluation of the relationship between tumor and mandible. In particular, the very high sensitivity (93%) and negative predictive value (96%) indicate the reliability of the technique in ruling out the neoplastic invasion of the mandible.

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