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MR of Mandibular Invasion in Patients with Oral and Oropharyngeal Malignant Neoplasms

Tae Sub Chung, David M. Yousem, Howard M. Seigerman, Bruce N. Schlakman, Gregory S. Weinstein, and Richard E. Hayden

PURPOSE: To investigate whether MR imaging is an accurate means of assessing mandibular invasion in patients with carcinoma. **METHODS:** We retrospectively studied the MR scans of 22 patients with pathologic or surgical confirmation of mandibular invasion from oral and oropharyngeal cancers. The MR images were blindly analyzed using primary criteria of: (a) cortical breakdown, (b) replacement of bone marrow fat, or (c) gadopentetate dimeglumine enhancement of a mass at the bone marrow defect. Secondary criteria of: (a) contiguous soft-tissue mass, and (b) mass on both sides of the mandibular cortex were also examined. Mandibular invasion was graded as periosteal/cortical, medullary, or no invasion. **RESULTS:** Primary positive findings of cortical breakdown and abnormal bone marrow signal were highly sensitive (100%) for periosteal/cortical invasion and medullary involvement, respectively. However, a high rate of false-positive studies hampered the MR accuracy, which fell into the 73% to 77% range. A negative MR study was highly predictive, but a positive study was less valuable. Gadolinium enhancement added little to the MR study's accuracy. False-positive studies mainly occurred in the setting of prior irradiation, osteoradionecrosis, and odontogenic infections. **CONCLUSIONS:** MR imaging is a sensitive method for detecting mandibular invasion but has a low positive predictive value. A negative study virtually excludes cortical/periosteal or bone marrow invasion.

Index terms: Mandible; Carcinoma; Mouth, magnetic resonance; Mouth neoplasms

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When squamous cell carcinoma extends to the mandible, the likelihood of a cure by radiation therapy is greatly reduced, and surgery must be considered. The surgeon must decide on the type of mandibular resection and the form of mandibular reconstruction. Various studies such as clinical examination, dental films, panoramic radiography, and bone scintigraphy have been limited by either low sensitivity or specificity for evaluating mandibular invasion by oral and oropharyngeal carcinomas

(1, 2). Although computed tomography (CT) has a lower false-positive rate (8.3%) than other examinations, dental amalgam and dense bone can obscure CT images (3). Magnetic resonance (MR) images are not as degraded by dental amalgam or by the dense bone of the mandible. Even though root canal surgery and metal bridge work cause artifacts on MR, the image distortion is limited to the immediate area of the offending material and does not produce the sort of global image disruption that occurs on CT scans (4). Moreover, MR imaging has the advantage of better demonstration of soft tissue and tumor interfaces.

Treatment failures of oral squamous cell carcinoma usually result from local recurrence. To minimize recurrence, resection of the tumor must include a margin of normal tissue. Sometimes, a more conservative operation may be recommended to preserve the function of the oral cavity. For these reasons, exact location of the tumor margin will help preserve the function

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of the oral cavity and pharynx and reduce the chance of local recurrence.

The accurate prediction of tumor invasion will also lead to more appropriate patient informed consent and preoperative planning for resection and construction. The purpose of this study was to investigate whether MR imaging is an accurate means of assessing the mandible in patients with possible invasion.

Materials and Methods

The MR scans of 22 patients who had open mandibular biopsy (5 patients), mandibular resection (14 patients), and intraoperative surgical assessment with adjacent biopsies (3 patients) of the mandible for oral and oropharyngeal malignant neoplasms during the past 4 years were retrospectively reviewed. All patients had clinically suspected and pathologically confirmed malignancies adjacent to the mandible. Ten patients had no pathologic evidence of mandibular invasion; 12 patients had cortical or periosteal invasion, and of these 12, 5 had medullary involvement.

The MR images were blindly and retrospectively analyzed for the findings of: (a) cortical breakdown by tumor invasion, (b) inhomogeneity of bone marrow by tumor invasion on T1-weighted images, and (c) gadopentetate dimeglumine enhancement of a mass at the bony defect. Secondary findings of a contiguous soft-tissue mass or a mass along both the lingual and buccal surface of the mandible were also reviewed. The 22 studies were presented in random order with no clinical or pathologic information. The data were analyzed to determine sensitivity, specificity, positive predictive value, negative predictive value, and accuracy rates of each criterion (Tables 1–3).

MR was performed with a 1.5-T Signa imager (General Electric Medical Systems, Milwaukee, Wis). For the purposes of this study, only axial short-repetition-time (TR) and short-echo-time (600–800/11–30/1–2 [TR/echo time/excitations]), long-TR fast spin-echo (2000–4000/30–35,80–90/0.5–2), and postcontrast short-TR (600–800/20–35/1) spin-echo images were provided for interpretation. Sagittal and coronal scans were later reviewed to determine any additional benefit but were not used in the data-collection part of the study. Nineteen of the 22 patients had postcontrast images. Gadopentetate dimeglumine (Magnevist, Berlex, Wayne, NJ) was administered at a dose of 0.1 mmol/kg, with imaging performed immediately after injection. Superior and inferior presaturation pulses were applied. Frequency selection fat suppression was used on all T2-weighted and postgadolinium scans. Section thickness for all pulse sequences was 5 mm, with contiguous sections obtained in all cases. The matrix size was 256×192 for all short-TR sequences and either 256×128 or 256×192 for the long-TR sequences. A volume neck coil (Medical Advances, Milwaukee, Wis)

was used in most cases to obtain optimal signal-to-noise ratios while maintaining an adequate imaging range.

Results

Cortical/Periosteal Invasion (Fig 1)

Twelve patients had cortical/periosteal invasion by cancer, and in 7 of these cases the disease did not involve the marrow. In five of the 12 the disease also invaded the marrow space. The selected criteria for cortical invasion from oral and oropharyngeal carcinoma showed wide variation in sensitivity, specificity, and accuracy (Table 1). Primary findings of cortical defects and gadolinium enhancement at a cortical defect showed 100% sensitivity for mandibular invasion. However, the specificities of these criteria were low (40% and 38%, respectively) because of high rates of false-positive studies.

Inhomogeneity of the bone marrow as a secondary finding was not particularly sensitive (58%), because bone marrow replacement does not occur in those patients with disease limited to the cortical/periosteal area. The secondary finding of a contiguous soft-tissue mass showed 100% sensitivity and 10% specificity for cortical/periosteal erosion. The positive predictive value of this finding was 57%, and accuracy was 59%. Similarly, a mass seen on both sides of the mandible did not correlate well with cortical/periosteal invasion, because the mass may pass around the inferior or superior surface of the mandible. This finding yielded a sensitivity of 67%, a specificity of 40%, and accuracy of 55%.

Medullary Invasion (Fig 2)

Replacement of high signal on T1-weighted scans of mandibular medullary fat was a highly sensitive primary finding on MR (Table 2). All cases of pathologically proved medullary invasion had bone marrow replacement on MR. Normal marrow fat signal was never seen in cases of medullary invasion. However, a 50% false-positive rate was present. The specificity was 71%, yielding an accuracy of 77%.

The secondary findings of cortical erosion and gadolinium enhancement at a cortical breakdown site showed even higher false-positive rates and thus lower accuracies, because they implied cortical/periosteal invasion, not necessarily medullary involvement. Other findings of contiguous masses and masses on both sides of the mandible showed sensitivities

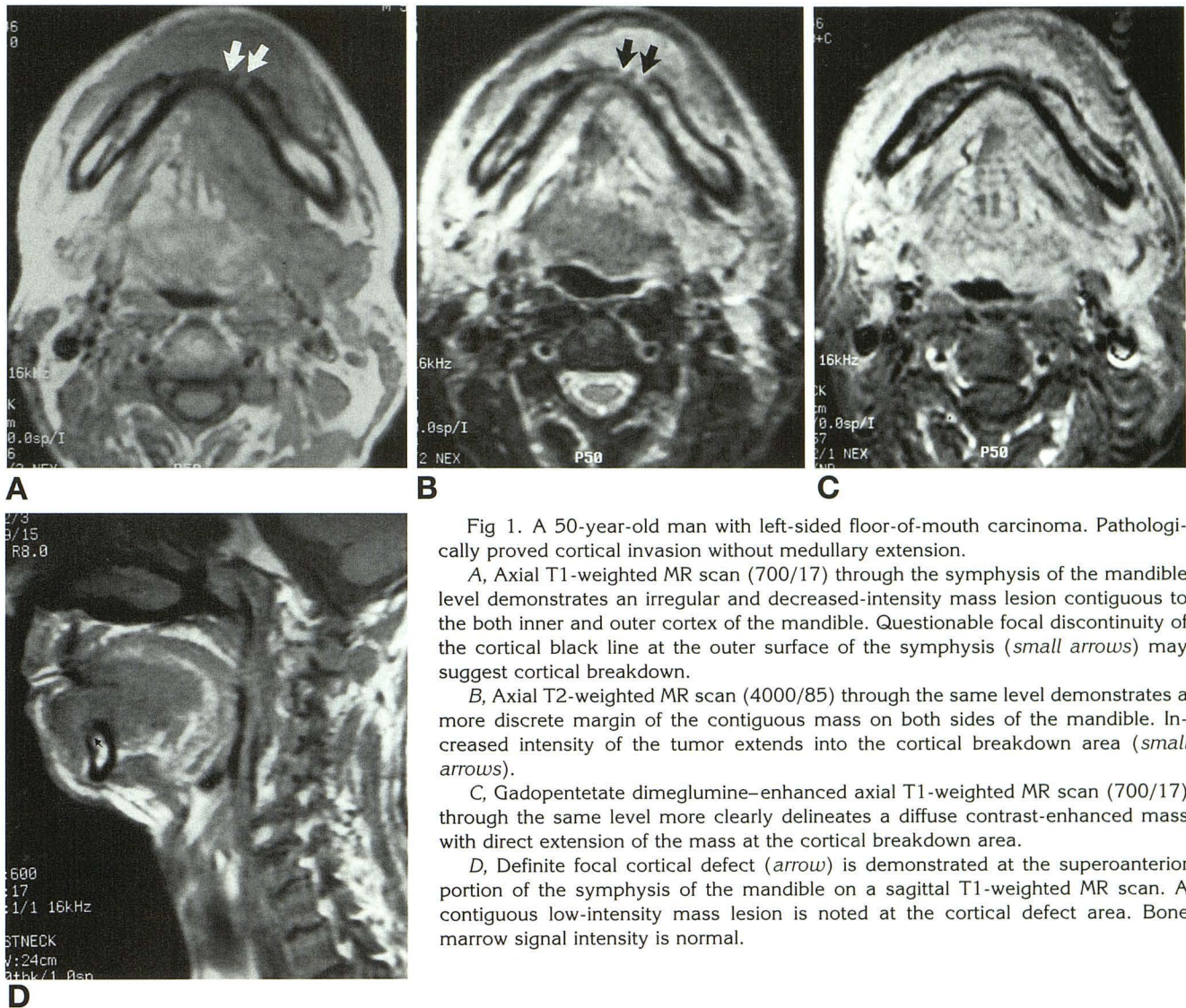


Fig 1. A 50-year-old man with left-sided floor-of-mouth carcinoma. Pathologically proved cortical invasion without medullary extension.

A, Axial T1-weighted MR scan (700/17) through the symphysis of the mandible level demonstrates an irregular and decreased-intensity mass lesion contiguous to the both inner and outer cortex of the mandible. Questionable focal discontinuity of the cortical black line at the outer surface of the symphysis (*small arrows*) may suggest cortical breakdown.

B, Axial T2-weighted MR scan (4000/85) through the same level demonstrates a more discrete margin of the contiguous mass on both sides of the mandible. Increased intensity of the tumor extends into the cortical breakdown area (*small arrows*).

C, Gadopentetate dimeglumine-enhanced axial T1-weighted MR scan (700/17) through the same level more clearly delineates a diffuse contrast-enhanced mass with direct extension of the mass at the cortical breakdown area.

D, Definite focal cortical defect (*arrow*) is demonstrated at the superoanterior portion of the symphysis of the mandible on a sagittal T1-weighted MR scan. A contiguous low-intensity mass lesion is noted at the cortical defect area. Bone marrow signal intensity is normal.

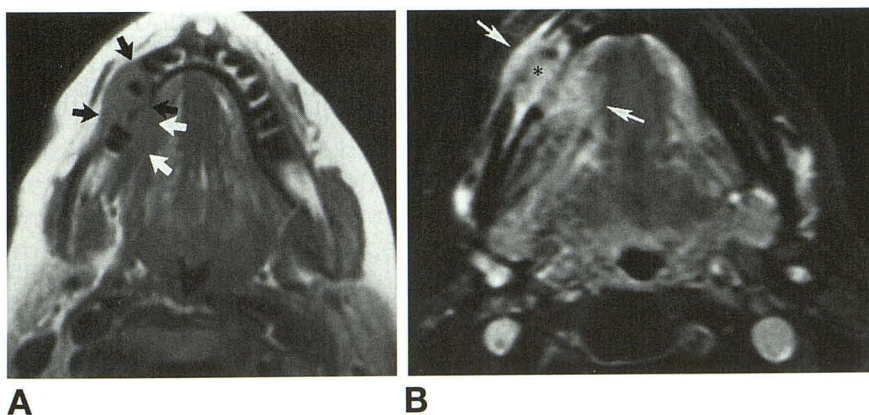


Fig 2. A 62-year-old man with right-sided floor-of-mouth carcinoma.

A, Axial T1-weighted MR scan (800/17) through the mandibular body level demonstrates an irregular decreased-intensity mass with cortical defects (*black arrows*) and inhomogeneity of bone marrow in the right mandible. The floor-of-the-mouth component (*white arrows*) is seen.

B, The extension of tumor on both sides of the mandible (*arrows*) and invasion of the marrow space (*asterisk*) is well seen on this postcontrast, fat-suppressed T1-weighted image.

TABLE 1: Periosteal/cortical involvement: comparison of criteria in 22 cases

Criterion	Sensitivity, %	Specificity, %	Positive Predictive Value, %	Negative Predictive Value, %	Accuracy, %
Primary					
Cortical defect	100	40	67	100	73
Enhancement at cortical defect*	100	38	69	100	74
Secondary					
Bone marrow fat replacement	58	70	70	58	64
Contiguous mass	100	10	57	100	59
Mass on both sides of mandible	67	40	57	50	55

*Only 19 of 22 patients received contrast.

TABLE 2: Medullary involvement: comparison of criteria in 22 cases

Criterion	Sensitivity, %	Specificity, %	Positive Predictive Value, %	Negative Predictive Value, %	Accuracy, %
Primary					
Bone marrow fat replacement	100	71	50	100	77
Secondary					
Cortical defect	100	26	28	100	41
Enhancement at cortical defect*	100	20	25	100	37
Contiguous mass	100	6	24	100	27
Mass on both sides of mandible	80	41	29	88	50

*Only 19 of 22 patients received contrast.

of 100% and 80%, respectively, but specificities and accuracies at or less than 50% (Table 2).

Soft-Tissue Masses

All patients had to have pathologically proved malignant neoplasms in proximity to the mandible to be enrolled in this study. A contiguous soft-tissue mass was seen by MR in every patient. Secondary findings of cortical defects, medullary replacement, enhancement in a cortical defect, and masses on both sides of the mandible had sensitivities from 45% to 82% (Table 3). One cannot assess the specificity and negative predictive value of the MR findings in this study, because there were no pathologically negative cases for a soft tissue mass.

False-Positive Studies for Mandibular Invasion

What accounted for the false-positive studies? There were pathologically proved cases of radiation fibrosis, osteoradionecrosis, and chronic inflammation that accounted for some of the cases, with abnormal marrow signal thought to represent tumor infiltration (Fig 3). Four cancers had narrow tumor bases with partial attachment to the mandible. Two of these

four cases were radiologically false-positive (pathologically negative) for invasion of the bony cortex. These two cases had well-defined postextraction bony defects, which marginally contacted with the narrow base of the tumor mass on the upper surface of the mandible. The high incidence of odontogenic disease may have contributed to other false-positive cases—numerous carious teeth were noted in pathologic specimens. The dental disease led to inaccurate diagnosis of erosion along the alveolar ridge portion of the mandible. Partial volume effects may also simulate cortical erosions. One unusual pattern of tumor spread showed invasion through the mandibular foramen without cortical breakdown.

Discussion

Approximately 91% of oral cavity carcinomas are of the squamous cell or epidermoid type (2). This carcinoma is aggressive, usually spreading by direct invasion and lymphatic channels. The incidence of mandibular invasion of oral and oropharyngeal malignancies ranges from 11% to 39% (2, 5, 6).

Three important issues emerge in the treatment of the mandible: (a) presence and extent

TABLE 3: Soft-tissue involvement: comparison of criteria in 22 cases

Criterion	Sensitivity, %	Positive Predictive Value, %	Accuracy, %
Primary			
Contiguous mass	100	100	100
Secondary			
Cortical defect	82	100	82
Bone marrow fat replacement	45	100	45
Enhancement at cortical defect*	58	100	58
Mass on both sides of mandible	64	100	64

Note.—There were no cases in which pathologically there was not a cancer adjacent to the mandible, so specificity and negative predictive values are not relevant.

*Only 19 of 22 patients received contrast.



Fig 3. False-positive case of mandibular invasion in a patient with radiation fibrosis on pathologic sectioning. This T1-weighted scan suggested mandibular involvement because of the diffuse replacement of the fatty marrow signal with low signal (asterisk) and the adjacent soft-tissue mass (arrows) near the angle of the mandible at the site of the original primary tumor. The mass was squamous cell carcinoma, but the mandible showed no evidence of tumor.

of mandibular involvement by tumor; (b) symphysis involvement to preserve function after mandibular resection; and (c) consistency of the mass, because necrotic and solid areas within the same tumor behave and are treated very differently (1). Preoperative evaluation of mandibular invasion of oral and oropharyngeal malignancies can influence whether the mandibular resection will be full thickness, partial thickness, or periosteal. If tumor is adjacent to but not invading the body of the mandible, the periosteum may be resected as a margin. If there is tumor along the alveolar ridge (near the teeth sockets), some bone may need to be resected even without demonstration of cortical erosion because of the propensity for microscopic spread in this area. If the cortex is eroded

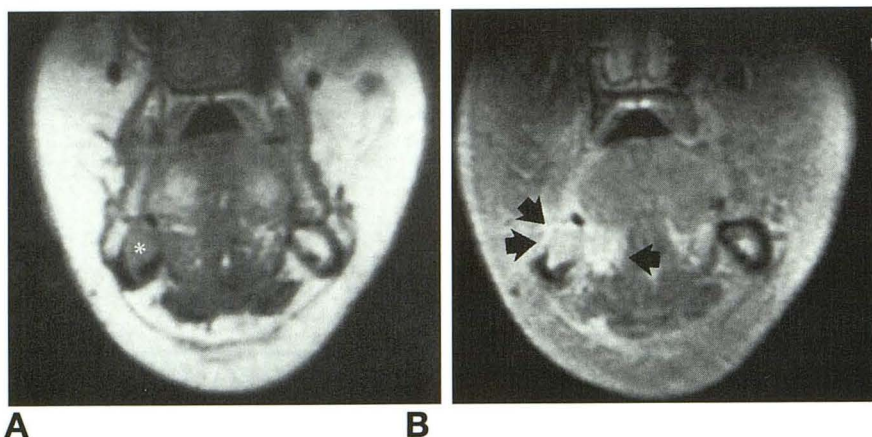
without marrow invasion, a marginal mandibulectomy may sometimes be performed, depending on the extent of disease. If tumor erodes through the cortex into the marrow space, segmental resection of the mandible is necessary, because frozen section analysis of margins is difficult on nondecified specimens. From the standpoint of sites of involvement, the symphysis of the mandible has to be preserved or reconstructed during surgery to save the function of the remaining tongue and uninvolved mandible. Involvement of the symphysis by tumor is important to note, as is invasion of the inferior alveolar canal, because this requires scrutiny of the mandibular division of the trigeminal nerve. In summary, the exact location of the tumor border can prevent unnecessarily wide resection, preserve better function of the tongue and mandible, and ultimately lead to a better outcome.

Although many studies (plain radiography, panoramic view, bone scintigraphy, and CT) have been evaluated for mandibular invasion of the oral and oropharyngeal carcinoma, all have high false-positive and false-negative rates. Clinical evaluation can also be unreliable in defining the extent of mandibular involvement because surrounding inflammation may obscure the purported tumor margins (7). Routine mandible x-ray films have a 40% to 50% false-positive rate and a 5% to 7% false-negative rate (2, 5). Although bone scintigraphy seems to be a more accurate study than panoramic radiography (8), bone scans also produce a false-positive rate of as high as 53% and a false-negative rate of 12% due to superimposed dental disease (5). CT has been advocated as an imaging technique for lesions of the mandible because of good bone detail and good soft-tissue definition with a low false-positive (8.3%) rate (3). How-

Fig 4. A 59-year-old man with right-sided floor-of-mouth carcinoma.

A, Coronal T1-weighted MR scan (600/29) demonstrates irregular bony defect with hypointense bone marrow (*asterisk*) in the right mandibular body.

B, Contrast-enhancing irregular mass (*arrows*) is better seen along both the inner and outer sides of the bony defect area (500/16).



ever, there can be difficulties in using CT scans because of large dental amalgam artifacts and poor prediction of the soft-tissue extension of disease (3, 7). Hence, whereas CT seems to be sensitive, it still has limitations as an imaging technique. MR has been proposed to be competitive with CT in terms of imaging the mandible for tumor extent in soft tissue, cortex involvement, and bone marrow invasion (7).

Inherent in this study is the bias that, because the mandible or perimandibular region was biopsied or resected, there was a strong selection prejudice toward patients with suspected mandibular invasion. Surgeons do not biopsy the periosteum if the tumors are remote from the mandible or if they do not believe cancer may reside there. Thus we believe that we have included an appropriate study population. Nonetheless, we did garner 10 cases of negative mandibular specimens in patients suspected of having cancer. A potential pitfall lies in the fact that several cases had tumor margin biopsies of periosteum or adjacent tissue that were negative, and we assumed this meant no mandibular invasion despite suspicious MR scans. Because cancer rarely "skips" regions, we feel that this analysis is justifiable, even though we may not have had an explanation for the imaging findings.

In evaluating MR findings of mandibular invasion of oral and oropharyngeal malignancies, we found that invasion of the cortex is easily demonstrated by replacement of low signal cortex with intermediate signal tumor on T1-weighted images. Involvement of the symphysis (genial tubercles) of the mandible where the genioglossus and geniohyoid attach is one of the crucial points in treatment of patients with oral cancer. Tubercle involvement is well demonstrated by MR (1). We noted that sagittal

locating images were particularly useful in the symphysis area (Fig 1D), and coronal images were sometimes useful for lesions of the mandibular body and ramus (Fig 4).

Because cortical invasion of oral and oropharyngeal malignancies is closely related to the distance of the primary tumor from the mandible (9, 10), a contiguous soft-tissue mass is a highly sensitive finding. Thirty percent of the patients whose tumors are clinically fixed to the mandibles have bone invasion, compared with 8% in whom the lesions do not appear to be fixed (2). Proximity to the bone, not tumor size, is the greatest determining factor in mandibular involvement by tumor (9). Interposition of normal tissue between tumor and mandible usually means no direct mandibular invasion from tumor. Radiologically contiguous soft-tissue mass at the cortical breakdown area can be divided into two appearances: broad and narrow (partially attached) tumor base. Most of our cases of a radiologically contiguous mass had a broad-based tumor mass on the bony cortex of the mandible, and most of them were pathologically positive for invasion of the bony cortex.

Inhomogeneity of bone marrow has been regarded as a sensitive and specific criterion for mandibular invasion by malignancy. Because the oral hygiene and the general condition of patients with oral cavity malignancy are often poor, the chance of tooth extractions from dental caries and inflammatory disease is high. Furthermore, the volume of supporting bone marrow in the mandible may not be great in patients with odontogenic disease and extracted teeth. Therefore, secondary changes from tooth extraction, inflammatory odontogenic disease, postradiation fibrosis, osteoradionecrosis, and/or partial volume averaging of mandibular cortex and marrow can create false-positive cases

of inhomogeneous bone marrow. Inhomogeneity of bone marrow by tumor invasion is detectable by replacement of high-signal bone marrow by lower-signal tumor (1). Because CT shows only gross changes in the bone marrow, MR imaging is considered superior in evaluating the pathologic change in this location (3).

Some normal variations, physiologic thinning of portions of the inner cortex of the mandibular ramus, and orifices of mandibular foramina can simulate cortical tumor erosion (11, 12). Sometimes, chemical-shift artifact of fat intensity of bone marrow can obscure the black line of bony cortex and mimic a cortical defect. A bony cortical defect without a contiguous soft-tissue mass suggests normal variation with thinning of the cortex. We believed that gadopentetate dimeglumine enhancement of a cortical defect with a contiguous tumor mass could differentiate tumor from other causes, such as tooth extraction or associated inflammations, but this was not necessarily the case. In every case the gadolinium-enhanced defect interpretation followed that of the cortical erosion criterion. However, gadopentetate dimeglumine enhancement provided additional information regarding the soft-tissue tumor infiltration not available on the unenhanced scans in 2 of 12 patients (Fig 4).

We also hypothesized that a mass on both sides of the inner and outer cortex of the mandible would be a sensitive finding for invasion of the mandible implying penetration of tumor through the flat shape of the mandible (3). However, our data show low sensitivity and specificity of this finding. Tumor mass seems to cross easily over or under the edge of the mandible without passing through the bone. Tumor can also spread across the gingiva between the teeth without eroding the mandible or may spread from one side to another by growth under the mandible.

What can be concluded about the evaluation of the mandible by MR? If one has a negative MR

study for cortical erosion, bone marrow fat replacement, and/or gadolinium enhancement at a cortical defect, there is little chance that periosteal/cortical or medullary invasion exists. In other words, a negative MR study has great value (100% negative predictive value). If medullary or cortical invasion exists, the MR will be positive (100% sensitivity). However, a positive MR study, particularly in the face of prior irradiation, inflammatory odontogenic disease, or extensive tooth extraction defects, may be misleading with regard to predicting mandibular invasion, be it cortical or medullary. Secondary findings of contiguous masses on one or both sides of the mandible are supportive findings but also lead to false-positive studies.

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