Oral Cavity and Base of the Tongue Tumors. Correlation between Clinical, MRI and Pathological Staging of Primary Tumor

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The diagnosis of oral cavity and oropharyngeal tumors can be obtained through clinical examination and biopsy. CT and MRI can then be used to define the extension of the disease. The aim of this study was to define the accuracy of clinical and MRI T staging of oral cavity and base of the tongue tumors and correlate the results with pathological data. Mandibular involvement, in a subgroup of patients, was determined and sensitivity, specificity, accuracy and positive and negative predictive values were evaluated. Fifty-nine patients affected by squamous cell carcinoma and 1 case of adenoido-cystic carcinoma were examined by means of a superconductive MR unit, using SE T1, and fat-suppressed T2 weighted sequences before contrast medium infusion. SE T1 and T1 fat-suppressed sequences after gadolinium-DTPA infusion were used. T stage accuracy of both clinical examination and MRI were found to be respectively 62% (k 0.459) and 82% (k 0.775). The sensitivity, specificity and accuracy of MRI in the detection of mandibular involvement were 94.1%, 60% and 81.5%, while the positive and negative predictive values were 80% and 85.7%, respectively. The sensitivity, specificity and accuracy of clinical examination in the detection of mandibular involvement were 100%, 30% and 74.1%, while the positive and negative predictive values were 70.8% and 100%.
In the present study, MRI was seen to be an adequate technique for the assessment of oral cavity malignancies, in the evaluation of depth invasion, presence and extension of mandibular involvement.

Key Words: Oral cavity imaging, Base of the tongue imaging, Mandible MRI, Magnetic Resonance Imaging comparative studies

The clinical staging of oral cavity and oropharyngeal tumors usually begins from clinical examination and biopsy. The former can collect data concerning the superficial and intramural extension of the tumor by means of inspection and bimanual palpation (1-4); the latter determines the histology and depth of infiltration through incisional biopsy.

Correct preoperatory staging is fundamental for proper therapeutic planning. CT and MRI (5-7) are of the upmost importance in studying the disease, providing information regarding the extension of the tumor beyond the midline and/or the infiltration of the mandible, considering either the cortical or medullary portion (8-11). The assessment of mandibular status is crucial in treatment planning of oral cavity carcinoma. When the tumor is close to the mandible, it is difficult to determine the presence and rate of bone infiltration, and particularly the involvement of the cortical and/or medullary part of the mandible (10-13). However, MRI proved to be more accurate than CT in the analysis of soft-tissue or bone extension by the tumor, due its high contrast resolution and multiplanar views (14-16).

The aim of the present study is to define the accuracy of MRI in the evaluation of the T stage, correlating MRI to clinical and pathological data. In the subgroups of the tumor close to the mandible, the relationship between tumor and mandible was determined, comparing clinical examination and MRI to pathological data.

Materials and Methods

Clinical data

Between January 2002 and December 2005, 60 non-consecutive patients (44 men and 16 women) with oral and oropharyngeal tumors involving the base of the tongue were studied. The sites of primaries are reported in Table I. Histology was found to be positive to squamous cell carcinoma in 59 cases and to adenoido-cystic carcinoma in one. The median age was 50 years (range 35-86). All patients underwent surgical treatment for primary tumor and cervical nodes and 36 of them required reconstruction through pedicled and/or microvascular flaps.

Before clinical evaluation, all dentures and partial mobile dental prostheses were removed. The oral cavity was examined looking for any sign of trismus, visible or palpable lesions, evaluating dental status, tongue movement and protrusion and soft tissue health. Palpation of the tongue and floor of the mouth was extremely useful in detecting small lesion infiltration and superficial extension. Clinical measurements were carried out manually considering the limits of the tumour identified through visual examination and palpation. The area of the tumor was marked and the two major diameters were measured. In case of trismus, the distance between incisor teeth was measured and recorded. The neurological examination of peripheral nerves of the oropharynx and oral cavity completed the clinical staging and was performed looking for sensory and motor neural deficiencies such as tongue active mobility impairment, uvulo-palatal asymmetry during phonation and hypo-anesthesia of oral, pharyngeal and facial sites.

Imaging

Magnetic Resonance Imaging (MRI) was obtained on a 0.5 T (Philips-Gyroscan) superconductive system. A neck-coil, 5-millimeter-thick slice, two acquisitions and a matrix of 256x256 were used. The study, before the infusion of contrast medium, consisted of spin-echo (SE) T1 sequences (TR 450 ms TE 20 ms) on axial and coronal or sagittal planes, in relation to the site of the tumors (we used sagittal planes for the base of the tongue tumors) and short-tau-inversion-recovery (STIR) T2 weighted sequences (TR 1800 ms, TE 100 ms and T1 10 ms.) on the axial plane. After infusion of gadopentate dimeglumine (Gd-DTPA) at 0,2 mmol/kg, T1 fat-suppressed (SPIR) sequences (TR 400 ms TE 10 ms.) with an acquisition time of 1.43 min. on axial planes and SE T1 sequences on axial, coronal and sagittal planes were used for the evaluation of the tumors and lymphnodes.

In the evaluation of the mandible, SE T1 sequences were used in the coronal or axial plane with 3-millimeter-thick slices before the infusion of the contrast medium. Mandibular involvement was suspected whenever the hypointense signal of the cortex was replaced by the tumor signal intensity and when the high signal intensity on T1 sequences of the medullary bone disappeared.

Table I - Sites of the tumors

Sites	Number
Floor of the Mouth	18
Tongue	16
Base of the tongue	7
Gingiva	9
Retromolar Trigone	6
Cheek	2
Lip	1
Alveolar Ridge	1

Pathology

The whole specimen was fixed in formalin overnight at 4°C.

The resected specimen was oriented and measured in three dimensions.

When intact teeth were included in the specimen, they were removed to shorten decalcification times and reduce decalcification-induced artifacts.

The surgical margins were painted with India ink.

The mucosa and soft tissues were separated from the mandibule with a scalpel. They were cut upward and foreward.

The specimen were kept for decalcification by means of 20% formic acid plus 10% formalin solution and were serially cut at 1 cm interval to determine mandibular invasion.

Afterwards they were embedded in paraffin from which 5 mm sections were cut and stained with hematoxylin and eosin. Bone involvement was distinguished in cortical and marrow infiltration.

The pathological staging (pT) was achieved considering the maximum tumor size after fixation of the specimen in formalin. The tumor was oriented and cut along its major diameters; the assessment of the mandibular involvement was made through the examination of the EE slides after decalcification. All data were finally tabulated and cross-tabulations were prepared.

Statistical Analysis

TNM staging of the oral cavity and oropharynx considered the major diameters. Concordance between clinical, MRI T stage and pathological T stage was assessed using Cohen's k coefficient of agreement.

Landis and Koch proposed categories for judging values: less than 0.0 was poor, 0.00 to 0.20 was light, 0.21 to 0.40 was fair, 0.41 to 0.60 was moderate, 0.61 to 0.80 was substantial and 0.81 to 1.00 was perfect (18-19).

In the evaluation of the T stage the accuracy of clinical and MRI stage was assessed.

In the evaluation of mandible, the sensitivity, specificity, accuracy, predictive positive value (PPV) and predictive negative value (NPV) of the MRI was assessed.

This was a retrospective study. All MRI exams were evaluated by two radiologists who are expert in head and neck tumors; the clinical date were assessed by the same head and neck surgeons and the pathological data by the same pathologist.

Table II - Correlation between clinical data and MRI vs. pathological T stage

		Pathological Data				
		T1	T2	T3	T4a	Total
Clinical Data	T1	3			1	4
	T2	4	11			15
	T3		10	4		14
	T4a	1	6	1	19	27
MRI Data	T1	5				5
	T2	2	22		1	25
	T3		3	5		8
	T4a	1	2		19	22
Total		8	27	5	20	60

Results

In T stage evaluation, the accuracy of clinical data was 62% (K 0.459). Downstaging was present in 1 case and upstaging in 22. MRI accuracy resulted to be 82% (K 0.775), recording downstaging in 1 case and upstaging in 8 cases (Tab. II) (Fig. 1-2).

The results of the clinical staging obtained by means of physical examination (C1) and MRI imaging, (C2) were compared to the pathological data (Tab. III).

At pathological examination bone structures were found to be infiltrated in 17 cases out of 27 clinically staged as T4a (bone): the mandible was affected in 16 cases, the maxilla in one case. Examining the mandibular involvement (16 cases), three main patterns of infiltration were highlighted: transcortical spread into the medullary space and mandibular nerve canal in 10 cases (60.0%); marginal cortical infiltration in 4 cases (26.7%); finally, 2 cases of periosteal infiltration (13.3%).

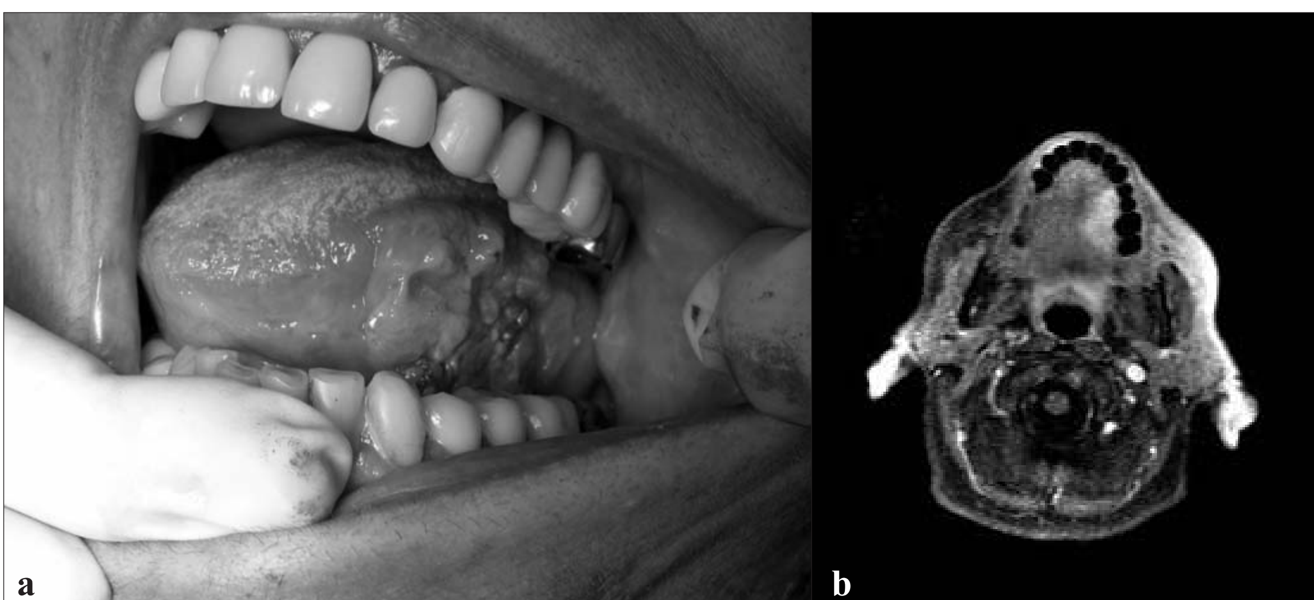


Fig. 1 - Left tongue tumor. Clinical examination shows a lesion in the left tongue **(a).** MRI with fat suppressed sequences after Gd-DTPA infusion **(b)** shows an area with strong enhancement classified as T2 confirmed by pathological data.

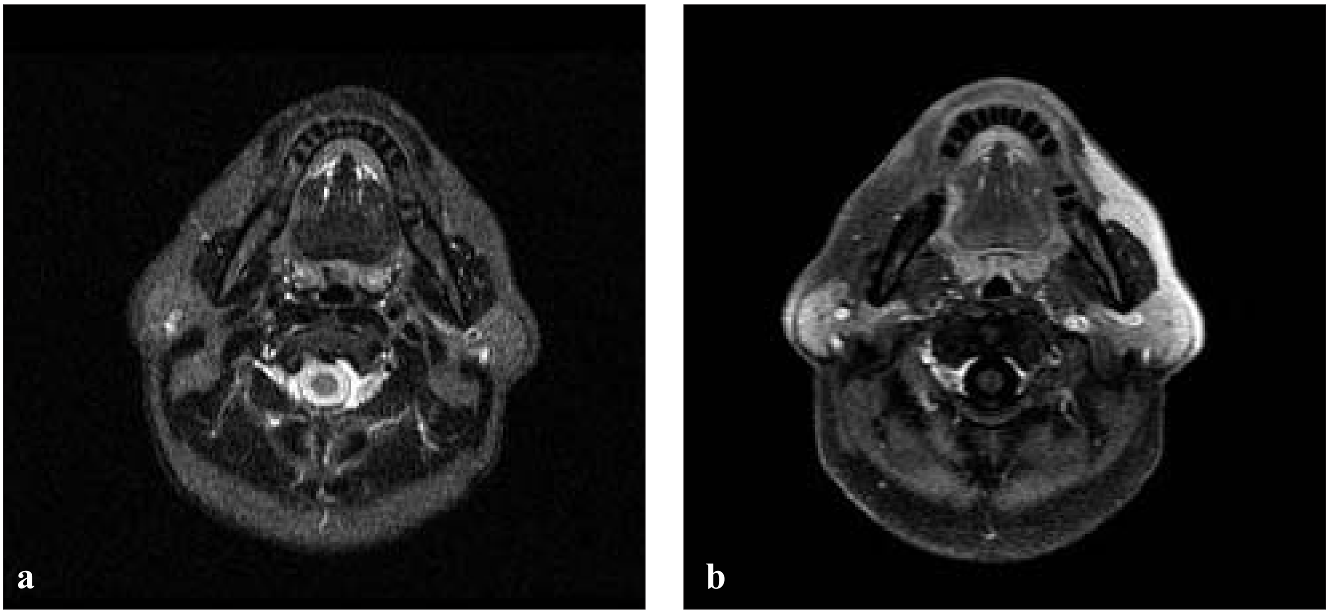
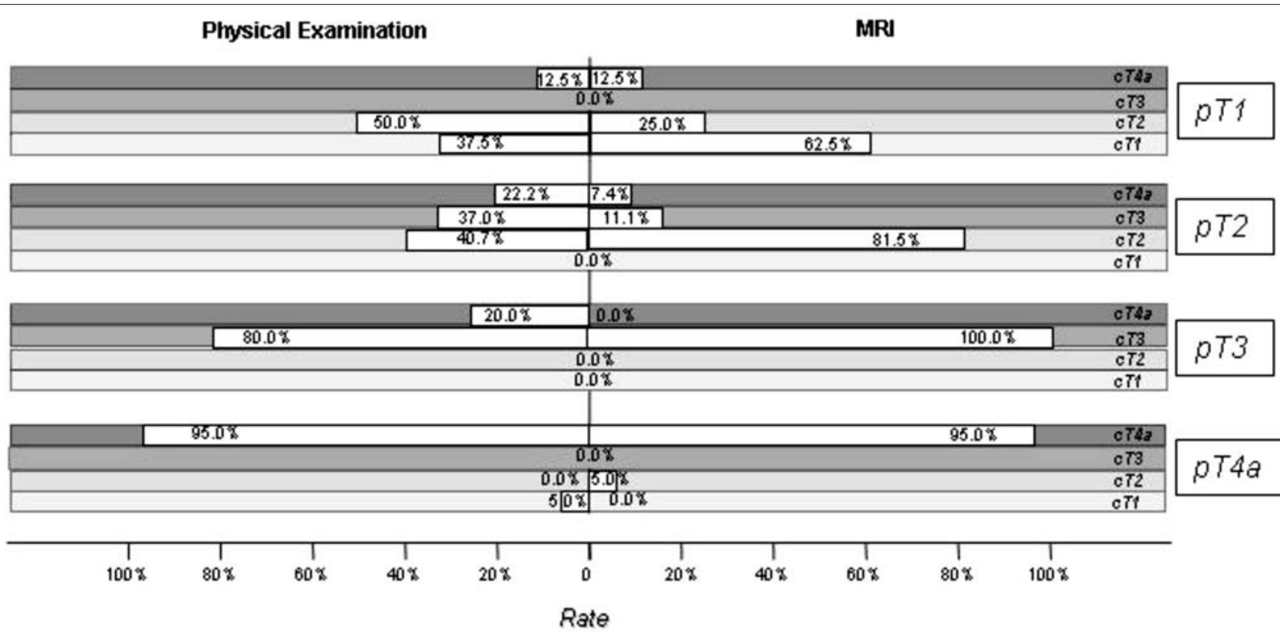


Fig. 2 - Righ floor of the mouth tumor. MRI with fat suppressed sequences before (STIR sequences; **a**) and after (SPIR sequences; **b**) Gd-DTPA infusion shows an area of hyperintensity with strong enhancement classified as T2 (dimension of 22 mm.); at pathological data the lesion resulted T1 (18 mm.).

Table III - Clinical staging rates (cT), at physical examination and MRI imaging, related to each pathological class of T (pT)



Therefore, 4 false positive cases and 1 false negative case were found in the present study on MRI imaging. MRI failed to diagnose one case of initially medullary mandibular infiltration (0,3 mm.) deriving from a floor of the mouth primary tumor. Considering the 4 cases of false positive bone infiltration, having gingiva (two cases) lip and trigone tumors, the supposed cortical infiltration of the mandible was not con-

Fig. 3 - Left floor of the mouth tumor. MRI with SE T1 sequences at 3 millimeter-thick slices in coronal plane before Gd-DTPA infusion shows a lesion in the floor of the mouth with an infiltration of the mandibular cortex; the signal intensity of medullar bone is normal. The lesion was classified as T4a by clinical data and MRI. At pathological data the lesion was classified T4a.

firmed at histological examination, so pathological staging resulted as pT1 (one case) and pT2 (two cases), respectively; maxillary infiltration was supposed at MRI exam in one case of retromolar trigone tumor, which did not result at pathological staging. Therefore, the patient was finally classified as pT2.

No case of mandibular infiltration was missed at the joint physical and MRI examination.

Although at physical examination no T4a, for bone infiltration, resulted understaged, 5 cases of T2, one of T3 and one of T1 tumors were overstaged, being considered to have mandibular involvement.

The sensitivity, the specificity and the accuracy of MRI in the detection of mandibular involvement were 94.1% , 60% and 81.5% respectively, while the positive and negative predictive values were 80% and 85.7% respectively. The sensitivity, the specificity and the accuracy of clinical examination in the detection of mandibular involvement were 100%, 30% and 74.1% respectively while the positive and negative predictive values were 70.8% and 100% respectively (Figg. 3-4) (Tab. IV).

Discussion

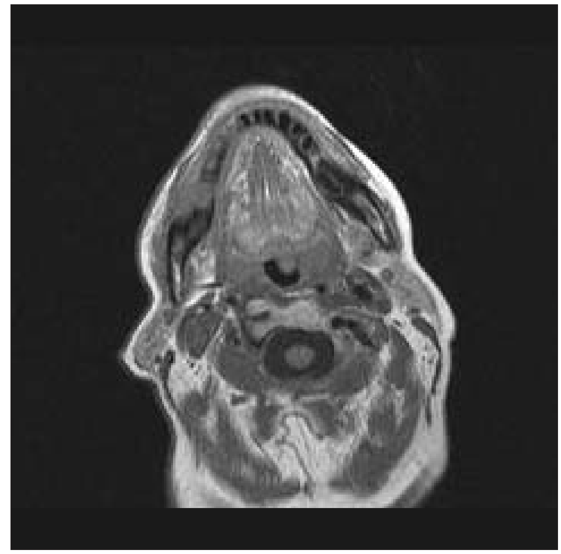
An adequate assessment of tumor stage in the oral-cavity and base of the tongue tumors is essential for appropriate planning of surgical and radiation therapy (1-4). The possibility of obtaining a correct evaluation of oral-cavity tumors depends on the ability to evidence the depth and extension of soft tissue and bone infiltration. This is particularly true when the mandible is involved, considering both its cortical and medullary components. The grade of mucosal and muscular infiltration influences not only the extent of primary excision and the reconstructive options, but also the risk of lymphatic spread and consequently the type of neck dissection and the necessity of complementary radiation therapy (17-19, 22-23).

MRI was used to determine the local extension of oral-cavity and base-of-the-tongue tumors (7-14,18-19). To obtain higher T stage definition, after Gadolinium-DTPA infusion, fat suppressed sequences were recorded using short acquisition time after bolus injection of contrast medium, so as to obtain a stronger tumor enhancement. This technique determined an accuracy of 82%, 20% higher than clinical evaluation, which was assessed at 62%.

A general tendency to overstage the tumor was observed both for physical or MRI evaluation (8 cases of overstaging compared to only 1 case of downstaging), This appeared more evident in cases of physical examination than MRI and could be partly due to the shrinkage of the formalin-fixed specimen, which, especially in muscular tissue, can reach 30% of the volume (20).

These data, arising from physical examination and MRI, should be evaluated considering the different pathological stages and some more interesting observations can as well be made.

The accuracy of MRI seems to be far higher than physical examination in case of small and middle-size tumors (T < 4cm), whereas this difference tends to be reduced progressively with the increase of T-size (T > 4cm). Considering pT1-2 tumors, physical examination appeared to overstage frequently, whereas the results were significantly lower for MRI. This phenomenon cannot obviously be explained only with the fixation-determined volume reduction of the specimen. It is likely due to the difficulty in determining the deep extension of the tumor in soft tissue organs, such as the tongue and/or the floor of the mouth, through only inspection and palpation. MRI and physical examination never determined downstaging errors in case of pT2-3 tumors.



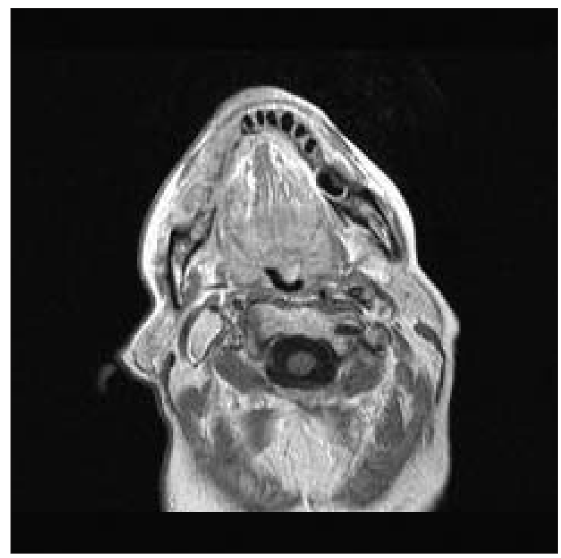


Fig. 4 - Right cheek tumor. Clinical examination **(a)** and MRI with SE T1 sequences at 3 millimeter-thick slices in axial planes before **(b)** and after Gd-DTPA infusion **(c)** shows a lesion in close relationship with the mandibular cortex, which appear infiltrated; the medullary bone shows hypointense signal intensity before contrast medium infusion **(b)** and enhancement after contrast medium infusion **(c)** which could indicate an infiltration; the lesion was classified by clinical data as T3 and by MRI as T4. Histopathologic examination did not confirm this finding (false-positive MRI findings); the lesion was classified as T2 .

The latter technique was inadequate in detecting minimal bone and/or extrinsic muscle infiltration (pT4a), while it was difficult to detect minimal cortical infiltration through MRI.

In cases of huge tumors (pT3), both physical evaluation and MRI led in most cases to correct staging (MR accuracy=100%), although the former confirmed its tendency to overstaging.

Considering those tumors classified as pT4a, invading extrinsic muscles and/or bone structures, such as the mandible or maxilla, the accuracy of physical examination and imaging were both very high, characterized by downstaging low risk, due to the difficulty in evidencing minimal bone infiltration. This tendency appeared evident mostly in those cases, in which the tumors arose on the floor of the mouth (10 cases) and on the retromolar trigone (5 cases). Furthermore, they may also occur in cases of small tumors close to the maxilla (superior or inferior), whose cortical infiltration is difficult to be evidenced with these methods, or in case of minimal alveolar or mandibular canal invasion, determining medullary tumor spread.

There are two main patterns of mandibular invasion by squamous carcinoma which are, in fact, considered as two consequent phases, which may be present simoultaneously in different points of the same tumor: erosive, characterized by well-defined U-shaped excavation of the mandibular cortex with/without the medullary part, which radiologically appears as a well-defined radiolucency lesion without spicules bone; the second pattern is referred to as an infiltrative mass which radiologically appears as an ill-defined and irregular lesion (10). Another unusual pattern of the mandible's invasion is represented by neoplastic vas-

Table IV - Sensitivity, specificity, accuracy, predictive positive value (PPV), negative predictive value (NPV) of MRI and clinical data in the evaluation of mandibular involvement

	MRI Data	Clinical Data
- Sensibility	94,1%	100%
- Specificity	60,0%	30%
- Accuracy	81,5%	74.1%
- PPV	80,0%	70,8%
- NPV	85,7%	100%

cular embolization with cortical integrity (18). The more aggressive tumors have a prevalent infiltrative pattern.

There are various entry routes for the tumor into the mandible; squamous cell carcinoma spreads along the mucosal surface and the submucosal soft tissue until it approaches gingiva where the tumor may come into contact with the mandible periosteoum. The dental sockets represent the mandible entry way in dentate patients; the tumor cells migrate into the occlusal surface of the alveolus in the edentulous patients and enter the mandible via dental pits. Therefore, the subsites in which mandibular invasion is most frequently evidenced are the alveolus (78%) and retromolar trigone (75%) (12).

Panoramic X-ray (OPG) (24), CT scans, MRI and CT-PET (25-27) represent the imaging techniques for early assessment of the mandibular invasion. OPG efficacy in evidencing early mandibular invasion ranges between 60% and 64% - high rate of false negative results is reported (13). CT scans and Dentascan may are excellent techniques for the evaluation of bone erosion with a sensitivity of 95% and specificity of 79%, as reported in a recent work considering 39 patients affected by squamous cell carcinoma of the oral cavity studied through Dentascan (20-21). MRI is superior to CT in the evaluation of the medullary bone space invasion. Van den Brekel *et al.* (10) assessed mandible invasion on 29 patients and found that MRI had the highest sensitivity (94%), but low specificity (73%). CT and panoramic X rays have a lower sensitivity (64% for CT and 63% for x-rays) but higher specificity (89% and 90%, respectively). A previous study on the evaluation of the tongue and floor-of-the-mouth tumors by Crecco *et al.* (17) reported an accuracy of MRI in the evaluation of the mandibular invasion of 93%. Recently, Bolzoni *et al.* (18) found high sensitivity, specificity and accuracy using MRI (93%); the predictive positive value was 87.5% and the negative value was 96%. Imaizumi *et al.* (26) found a sensitivity and specificity for mandibular cortical invasion of 96% and 54% for MRI and 100% and 88% for CT, while for the inferior alveolar canal involvement the sensitivity and specificity were 100% and 70% for MRI and 100% and 96% for CT. In the study of Wiener *et al.* (25) MRI was superior to multislice CT in the detection of bone infiltration with a sensitivity of 100% versus 71.6%, a specificity of 93.3% versus 95.5% and an accuracy of 94.2% versus 92.3%.

In our study the sensitivity, the specificity and the accuracy of MRI in the detection of mandibular involvement were 94.1%, 60% and 81.5% respectively while the positive and negative predictive values were 80% and 85.7%, respectively.

In conclusion, in order to obtain correct clinical staging of oral cavity and oropharyngeal tumors involving the base of the tongue, MRI must be considered as the optimal mean of detection for the primary and locoregional nodes. Moreover, it can optimally visualize the parapharyngeal space, which could be involved directly by the neoplastic mass or by deep pharyngeal nodal spread.

In cases of small tumors, the goals of MRI examination are the analysis of the depth of infiltration and the search for bone invasion (T4a).

The adequate assessment of locally advanced tumors can be achieved by physical examination, both for T extension and/or eventual bone invasion, but the necessity of surgical planning requires a detailed analysis of the structures involved in the disease; among them in particular those whose invasion constitutes a local contra-indication to radical surgical treatment (T4b), such as masticatory space invasion, pterygoid plates, skull base and internal carotid artery. For these reasons, MRI must be considered as the first choice exam for all tumors of the base of the tongue and oral cavity, independently from subsite, origin and extension.

In the future, the development of new diagnostic procedures, integrating the morphologic and metabolic features of the neoplastic lesions (PET-TC), will probably lead to new sharper instruments, able to perform "one shot" comprehensive study of these complex and polymorphic diseases. At present MRI still appears to be the optimal synthesis of morphological evaluation and metabolic related analysis of oral and pharyngeal carcinoma.

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