

Mandibular involvement diagnostic capacity of four imaging modalities in patients with Oral Squamous Cell Carcinoma

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Abstract

Background: Mandibular bone resection in patients suffering from oral squamous cell carcinoma (OSCC) is a challenging and crucial decision requiring precise diagnosis. Selecting the most suitable imaging system is one of the essential paraclinical records with this regard. **Objective:** In this study we attempted to compare the accuracy of four routine imaging modalities in pre-surgical diagnosis of mandibular bone involvement due to OSCC.

Methods and Materials: In this descriptive retrospective in-vivo study, 67 patients diagnosed with peri-mandibular OSCC undergone marginal or segmental mandibular bone resection were included. The final pathology reports of mandibular resections were considered as the gold standard for diagnosis of mandibular involvement by tumor. The reports of the four imaging modalities: panoramic view, bone scintigraphy, computed tomography (CT) and magnetic resonance imaging (MRI) were compared based on the clinical observations and pathological reports.

Results: MRI had the best diagnostic power and accuracy (with 100% positive predictive value) among the four imaging modalities. No false positive results was revealed in CT and MRI groups.

Conclusion: Although MRI is known to be more accurate in assessment of soft tissue rather than hard tissue, the result of the current study, considering all the limitations revealed that mandibular hard tissue involvement could be determined more efficiently by MRI in tumor involvement cases compared to other imaging methods.

Keywords: Oral Squamous Cell Carcinoma, Mandible, Panoramic Radiography, computed Tomography, Magnetic resonance imaging

INTRODUCTION

SCC is the most common malignancy in the oral cavity and peri-mandibular region (1). This disease entails tremendous side effects such as: pathological fractures, facial disfigurement, infection, chronic ulcers and death. Accurate and prompt diagnosis of the tumor and the following proper treatment plans are the keys for achieving good curative results (2-4). The primary treatment of SCC is aggressive surgical resection. Deciding on whether or not having

a mandibular bone resection is one of the most important and burdening clinical resolutions. Mandibular bone resection could lead to impaired integrity of the mandibular bone and requirement of extensive reconstructive surgeries. On the other hand, preserving SCC-invaded mandibular bone may be followed by recurrence of malignancy, distant metastases and eventually succumbing to the tumor (5-10).

There are several preoperative diagnostic methods to detect initial tumor and mandibular invasion by the tumor. Among those imaging modalities contribute a significant role in cancer diagnosis and surgical treatment planning (11-13). The result of a recent study showed that although the T-stage is the most widely used and reliable staging system but, the imaging-histologic features are a more reliable and powerful prognostic factor than T-stage per se for mandibular SCC (14).

Accurate diagnosis of the mandibular bone invasion is a controversial issue in the literature (15). Although there are reported studies about the sensitivity and specificity of the diagnostic methods for this purpose, there is no consensus among clinicians on which approach is the best to be utilized for patients (15). False negative results of any preoperative diagnostic methods might lead to insufficient surgical intervention and consequently, tumor recurrence and poor prognosis.

On the other hand, false positive results may lead to subsequent overtreatment and hence its complications such as functional and esthetic complications. Therefore, determining the sensitivity and specificity of these diagnostic imaging systems in SCC tumor detection is critical. Computed tomography (CT) and magnetic resonance imaging (MRI) are useful advanced imaging systems which are vastly used to determine mandibular involvement by the tumor; however, their sensitivity and specificity with this regard are reported variously in previous studies (15-20). Thus, this study sought to determine and compare the preoperative diagnostic accuracy of four routinely used imaging systems panoramic view, bone scintigraphy, CT and MRI in patients suffering from oral SCC with possible mandibular involvement.

MATERIALS AND METHODS

Inclusion criteria

67 patients referred to the hospitals affiliated to Saint-Luc University (UCL, Brussels, Belgium) during 129 months, from February 2002 to October 2013, diagnosed with oral SCC were included in this descriptive retrospective in-vivo study. The evaluated cases revealed SCC indicators in the buccal mucosa, alveolar mucosa retromolar pads, and palatine tonsils. There were no cases with the involvement of the mouth floor or base of the tongue. All the detected tumors were above 1 centimeter, which indicated the need for mandibulectomy. Written informed consent was obtained from all patients, which allowed researchers to use their files for research purposes and the study was approved by the Ethics Committee of Saint-Luc University. The patients were diagnosed based on the clinical presentation of visible tumor mass, chronic ulceration with red and white exophytic appearance. All the patients were treated surgically and their mandibular bones were resected either marginally or segmentally. The data available from their diagnostic investigations consisting of panoramic images, bone scintigraphy, CT (18, 20) and MRI were used to determine mandibular involvement by the tumor. The results were compared with microscopic pathological report of the resected bones, which was considered as the gold standard in this study.

The panoramic images that were taken in digital setting (ProMax, Proline XC, Helsinki, Finland), were evaluated by two maxillofacial surgeons and were then divided into involved and non-involved groups. The reports of the bone scintigraphy was performed with administration of 600 MBq Tc-99m-methylene-diphosphonate and recorded with dual-head

gamma camera equipped with low-energy high-resolution parallel whole collimators. 140 keV photopeak with a 15% window, 128_28 matrix, 256 angles and 10 s/angle, were considered as mandibular involvement by this method. Some of the oral cavity SCC-invaded cases showed some uptake of the Tc99m but with the consultation of the nuclear specialist, only mandibular bone uptake was considered in this study.

Panoramic images interpretation

In panoramic images, radiolucency with ill-defined margins at the tumor site (in the absence of dental diseases) was considered as bone involvement (figure 1). To assess lesion margins in panoramic view, the margin was considered as well defined if the border between radiolucency and radio-opacity was clear and otherwise it was considered as ill-defined.

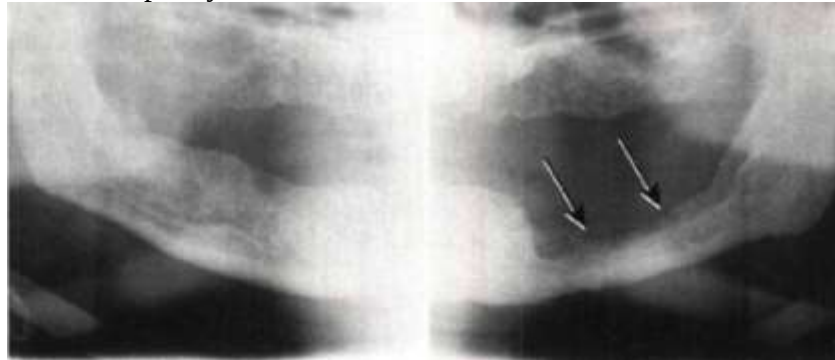


Figure 1. Panoramic image indicating ill-defined border

Scintigraphy results interpretation

In scintigraphy results interpretation, asymmetrical activity in the bone (in the absence of dental disease), indicating the presence of hot spots in the bone or activity in the adjacent bone as active spots was considered as bone involvement (Figure 2).

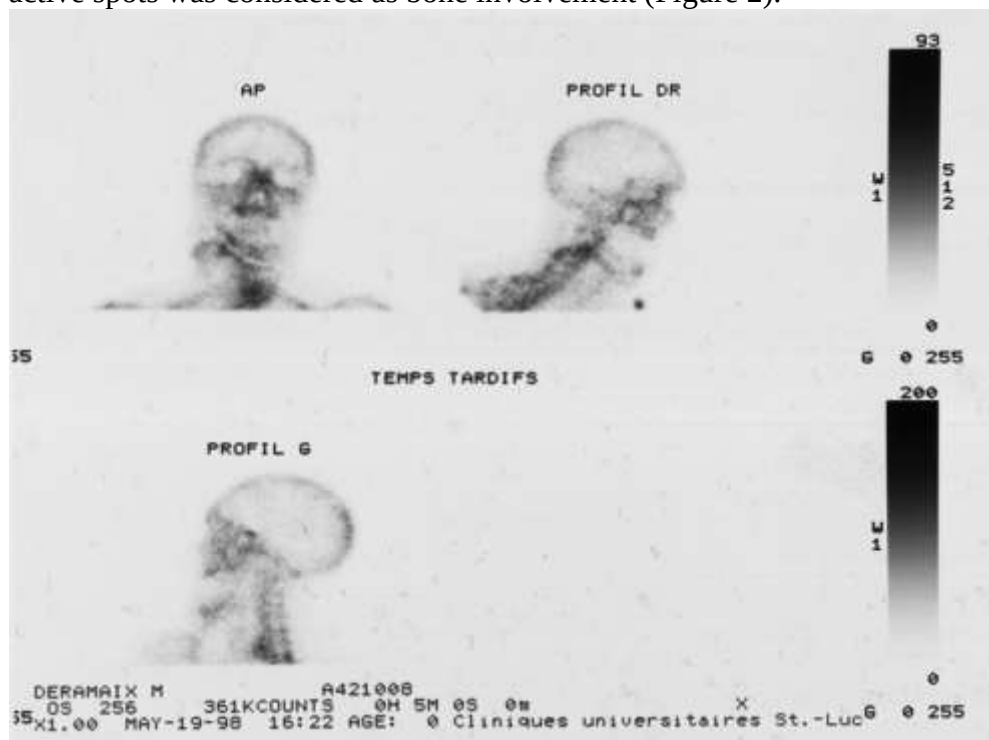


Figure 2. Scintigraphy indicating hot spot

CT images interpretation

The CT (Somatom, Siemens, Erlangen, Germany) images that were obtained in coronal and axial sections in soft and hard tissues views in spiral manner, were evaluated by a single maxillofacial surgeon and a single radiologist jointly and then grouped as involved and non-involved with respect to the mandibular involvement. In interpreting CT scans, radiolucency adjacent to the tumor with ill-defined borders despite dental disease was considered as diseased, in addition to defects of the bone cortex or bone marrow as radiolucency (figure 3). To assess lesion margins in CT scans, the margins were considered as well defined if the border between radiolucency and radio-opacity was clear. Otherwise it was considered as ill-defined. Slices' thickness in MRI and CT scan were adjusted at 2 millimeters.



Figure 3. CT scan indicating dentate border.

MRI images interpretation:

The MRI (Vision, Siemens Medical Systems, Erlangen, Germany) images in T1 and T2 weight in both coronal and axial cuts were assessed and divided exactly in the same manner for CT images. For MRI, cortical bone defects, omitted bone marrow signal, and removal of the spongy bone trabeculation associated with cortical bone defect were considered as bone involvement (figure 4). Although the tumor margins are more clearly delimited after contrast injection, lack of contrast injection in our patients was due to the fact that ordering contrast injection is not a routine request in this clinical setting with the aim of investigating bone erosion or involvement. Sagittal views of CT scans and MRI were reconstructed images and were not applied in this study to avoid artifacts and false positive diagnosis probability.

All the assessments were performed blindly by the radiologist and maxillofacial surgeon. Missing data were excluded from the statistical analysis. Finally, sensitivity, specificity, positive and negative predictive values were recorded. Chi-square test was applied to compare diagnostic modalities properties. $P < 0.05$ was considered to be statistically significant.

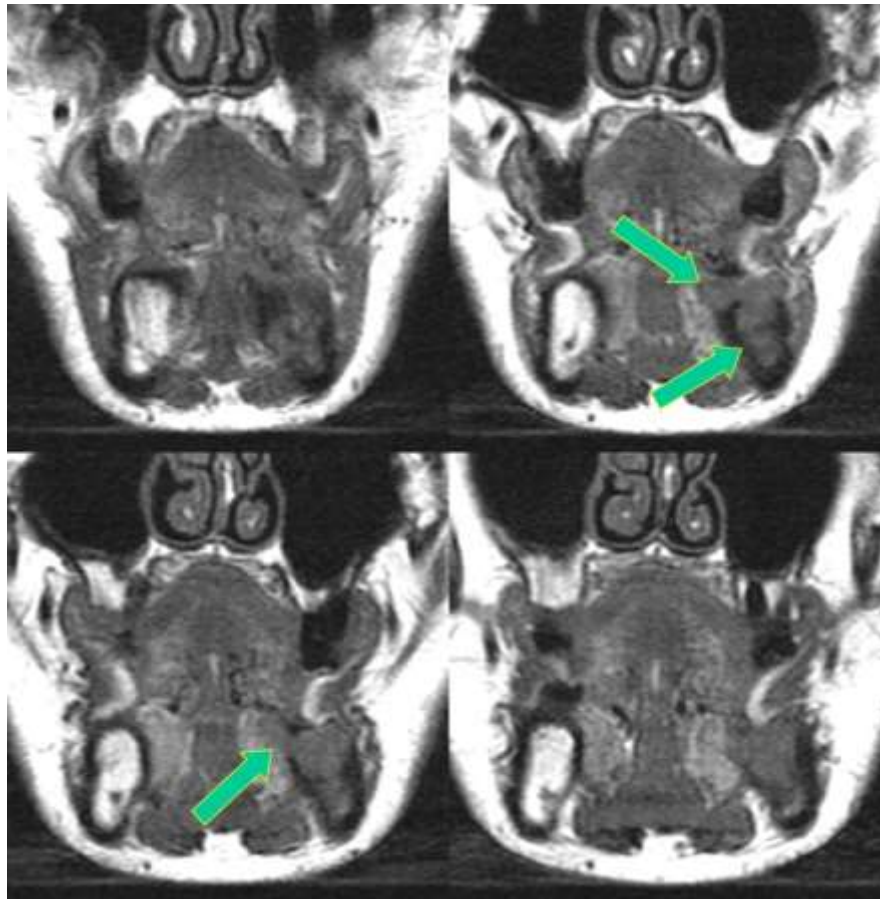


Figure 4. MRI results; the arrows indicate omitted signal of bone marrow compared with the other side in the above images and perforation of lingual cortex in posterior mandible in the below images

RESULTS

Participants' demographic information

The patients' mean age was 57.5 (4.4) years. The patients' gender participating in the research was more in male compared to female (80.6% male and 19.4 female) more detailed information is shown in table 1. The number of each type of surgery performed is demonstrated in details in table 1.

Table 1. The gender and surgical procedure distribution of the studied patients

Type of surgery	Marginal Mandibulectomy	Segmental Mandibulectomy	Total (Number/percent)
Gender			
Male	34	20	54 (80.6%)
Female	10	3	13 (19.4%)
Total	44 (65.7%)	23 (34.3%)	67

Diagnostic tests' evaluation

Diagnostic test evaluation for panoramic, bone scintigraphy, CT, and MRI modalities are demonstrated in details in table 2. The positive sign (+) indicates mandibular bone involvement and negative sign (-) means lack of mandibular bone involvement in the tables. There were no false positive results in CT and MRI groups so their specificity and positive predictive values were maximum. The minimum specificity belonged to Scintigraphy. The minimum sensitivity was recorded for CT. The maximum sensitivity recorded was for MRI

imaging modality. The minimum negative predictive value belonged to CT and the minimum positive predictive value belonged to Scintigraphy. The maximum number reported as diagnostic accuracy was for MRI. The minimum number reported as diagnostic accuracy was for CT imaging modality. The negative likelihood ratio was minimum in MRI and maximum in CT. All diagnostic parameters for each imaging modality are illustrated in details in table 3.

Table 2. Diagnostic test evaluation for panoramic imaging, bone scintigraphy, CT and MRI in the patients with squamous cell carcinoma referred to the Saint-Luc University hospitals (UCL Brussels Belgium) from February 2002 to October 2013

	Panoramic (+)	Panoramic (-)	Scintigraph y(+)	Scintigraphy (-)	CT (+)	CT (-)	MRI (+)	MRI (-)
Pathological assessment (+)	15(26.3%)	11(19.3%)	13(28.8%)	7(15.5%)	7(16.6 %)	13(30.9%)	11(33.3%)	3(9.1%)
Pathological assessment (-)	3(5.3%)	28(49.1%)	5(11.1%)	20(44.6%)	0(0%)	22(52.5%)	0(0%)	19(57.6 %)
Total	18	39	18	27	7	35	11	22

Table 3. Diagnostic parameters for each diagnostic method used for the patients with squamous cell carcinoma referred to the Saint-Luc University hospitals

	Number	Sensitivity	Specificity	*PPV	*NPV	*LR ⁻	*DA
Panoramic	57	57.7%	90.3%	83.3%	71.8%	0.4	75.4%
Scintigraphy	45	65%	80%	72.2%	74.1%	0.4	73.3%
*CT	42	35%	100%	100%	62.9%	0.6	69%
*MRI	33	78.6%	100%	100%	86.4%	0.2	90.9%

PPV: positive predictive value, NPV: negative predictive value, *LR⁻ : negative likelihood ratio,* DA: diagnostic accuracy, *CT: computed tomography, *MRI: magnetic resonance imaging

DISCUSSION

Controversy on the diagnostic value of different routinely used imaging modalities for bone SCC-invaded cases motivated us to investigate this issue (21). The results of our investigation indicated that MRI with T1 and T2 weights had the best diagnostic capacity in diagnosis of tumor invaded mandibular bone compared to panoramic, scintigraphy, and CT considering all aspects such as sensitivity which was the highest in MRI . This result is in line with a recent study results which showed more sensitivity and specificity of MRI compared to CT for detecting OSCC bone invasion. Also the authors declared that MRI detection of bone invasion was associated with greater disease-specific mortality while, it was not statistically significant for CT (22). The lowest sensitivity in this study was related to CT (35%), although it had 100% specificity. The very low sensitivity of CT in the present study questions this imaging method as a diagnostic tool for the initial diagnosis of mandibular invasion by SCC, although the 100% specificity of CT makes this tool an appropriate imaging method for patients' follow-up. The results of the study by Gu *et al.* also showed a low sensitivity for CT (41.7%) for diagnosis of mandibular invasion by SCC (23), which is consistent with the results of our study. Other studies have also reported a low sensitivity of about 50% for CT in the assessment of mandibular invasion (16, 17) while there are some other reports showing a higher sensitivity for this diagnostic method (24-26). The differences between the diagnostic accuracy of CT in diagnosis of mandibular invasion by SCC may be related to inter-operator bias, different techniques of acquisition in each setting, and sample size limitations.

The next lowest sensitivity in the present study was related to panoramic imaging (57.7%), while it had an acceptable specificity (90.3%). Hendrikx AW *et al*, compared the diagnostic accuracy of three imaging modalities in diagnosis of mandibular invasion of oral SCC and reported a similar sensitivity and specificity for panoramic imaging (55% and 92%, respectively). Furthermore, they declared that panoramic imaging had the lowest sensitivity and specificity, compared to cone beam CT (CBCT) and MRI (27). Other researchers have also reported a lower sensitivity for panoramic imaging than CBCT for diagnosis of mandibular invasion of lower gingival carcinoma (28), while in the present study, CT had the lowest sensitivity. The difference between the results of these studies and ours, in terms of the lower sensitivity of CT than panoramic imaging, could be due to the fact that we used conventional CT, which resulted in the lowest sensitivity (35%), while they have used CBCT, which has a higher accuracy, as the results of previous studies had confirmed (29, 30). Moreover, the results of our study confirmed that of previous reports on the poor diagnostic power of panoramic imaging (27, 28), which may be due to its structural limitations like two-dimensional setting and minimum bone decalcification required in the image for correct diagnosis. All in all, the results of the present study, in line with that of previous reports, discourage the use of panoramic imaging as the only diagnostic method for diagnosis of mandibular invasion (27, 28). Although, its use as an initial imaging or screening tool or in combination with other methods is desirable.

The other modality used in this study was scintigraphy, which had sensitivity (65%) close to panoramic imaging (57.7%), while its specificity was lower than that of panoramic imaging (80%). Bone scintigraphy is a method based on nuclear radioisotope uptake and subsequent scanning, so the procedures of its operation and interpretation are different from other methods evaluated in this study. The results of the study by Jamdade AS, John A showed similar sensitivity and specificity for bone scintigraphy compared with that we found in our study (31), although the initial specificity in their study was 50%, which increased to 83% after the scintiscan was used with PR under outlined criteria (31). Specificity of mandibular bone invasion by SCC was reported to be 48% in SPECT technique (13, 32) and 66.7% for bone scintigraphy (33) while more recent studies, like that of Van Cann EM, Koole R, Oyen WJ, de Rooy JW, de Wilde PC, Slootweg PJ, *et al* reported a 100% sensitivity for bone scintigraphy (34). Despite the high sensitivity, the researchers have also concluded that bone scintigraphy is not an ideal single diagnostic test (34). Jamdadeh *et al*. also reported the enhanced diagnostic value of simultaneous panoramic and scintigraphy evaluation (31). Other researchers have also reported that a combination of diagnostic methods should be used for the initial diagnosis of mandibular invasion (15, 34, 35). Although more advanced imaging modalities are widely at hand nowadays, but the results of a recent study indicated that the use of more sophisticated imaging modalities such as SPECT in oncologic staging in addition to CT and/or MRI is not always beneficial. The authors concluded that only negative SPECT results showed greater specificity and accuracy while the sensitivity remained unaffected. Thus, the use of SPECT is only recommended in specific cases to rule out bone invasion when positive CT or MRI results are uncertain (36-39).

The most interesting finding in this study was no false positive results in MRI, which caused high positive predictive value for this method. Also, the highest sensitivity was related to MRI (78.6%). We found that MRI systems can predict true mandibular tumor involvements completely. Few studies have investigated the diagnostic accuracy of MRI. Bolzoni A *et al*. have reported a sensitivity and specificity of 93% (40). Rajesh and colleagues reported 100% sensitivity and 75% specificity for MRI in diagnosis of bone invasion in patients with oral SCC (41). Mukherji SK *et al*. have also confirmed a high specificity for MRI (93%), higher than CT (42). Our findings support the use of MRI over CT as a modality of choice in

determining mandibular bone invasion. The results of these studies confirm our findings on the high power of MRI in determining mandibular osseous invasion, although the specificity of MRI in our study (100%) was higher than that in the previous reports (40-42). MRI is considered as an appropriate tool for assessment of mandibular SCC due to the high fat tissue content of SCC (34, 43) and high power of MRI in detection of soft tissue and invasion depth (44). Contrary to these results, Imaizumi A *et al.* argued about the low specificity of MRI (24). The difference between the results reported in their study could be related to interpreter's accuracy in diagnosing these types of imaging.

In contrast to our findings, the results of a recent study demonstrated that MRI tends to over-estimate bone invasion because of similarities in signal of tumoral tissue and peritumoral inflammation or infection. Also, the author claimed that because MRI is known for multiple artifacts related to tissue, motion or technique, it is not considered as a suitable diagnostic method for SCC-related bone per se. They claimed that no single perfect diagnostic method or algorithm is suggested to determine mandibular involvement by the tumor. Thus, using combined MRI and CT findings might be needed to overcome the probable insufficiency that may exist in specificity and sensitivity of each of these imaging systems (21).

The main strength of the present study was the comparison of different imaging modalities by a single practitioner to determine the best technique. Although investigation of all diagnostic evaluations performed by a single practitioner could minimize the effects of inter-examiner bias, the present study could have limitations. One of the limitations of this study could be the clinician's preference on patients' selection for specific imaging.

CONCLUSIONS

In conclusion, among the four imaging techniques (panoramic imaging, bone scintigraphy, CT, and MRI), the latter showed the highest accuracy on the initial determination of mandibular invasion in oral SCC. According to the results, 100% specificity of CT and MRI suggested these two modalities as appropriate diagnostic options for mandibular bone invasion follow-up in affected patients, while panoramic imaging and bone scintigraphy are not suggested as the only diagnostic methods and a combination of imaging techniques are suggested for the initial diagnosis, when panoramic imaging or bone scintigraphy is used. Further prospective diagnostic research comparing these diagnostic methods are recommended to confirm the results obtained in the present study.

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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