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Original article

Radiological assessment of mandibular invasion in squamous cell carcinoma of the oral cavity and oropharynx

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ABSTRACT

Background: Preoperative assessment of mandibular bone invasion in squamous cell carcinoma of the oral cavity and oropharynx is crucial for optimizing bone resection. The principal aim of this study was to evaluate the diagnostic value of CT and MR imaging for the diagnosis of mandibular bone invasion compared to the histological reference. In addition, we assessed the survival impact of bone invasion.
Patients and methods: A single-center retrospective study included all consecutive patients treated by mandibular bone interruption for squamous cell carcinoma of the oral cavity and/or oropharynx.
Results: Sixty-eight patients were included. Prevalence of bone invasion on histology was 43%. Sensitivity, specificity and positive and negative predictive value were respectively 70%, 71%, 66% and 76% for CT compared with histologic analysis, 83%, 50%, 59% and 78% for MRI, and 83%, 62% 62%, 83% for associated CT and MRI. The two tests showed good agreement, with kappa index 0.69 (95% CI, 0.49–0.89) ($P < 0.0001$). There was no difference in overall survival (log-rank > 0.70) between the groups with and without bone invasion.
Conclusion: CT and MRI are complementary for preoperative assessment of mandibular bone invasion, be it cortical and/or medullary, and in some cases may allow mandibular bone-sparing.

1. Introduction

With 600,000 new cases diagnosed each year (WHO 2014 data), head and neck is the 6th most frequent cancer location worldwide. In France, incidence was 14,600 new cases and almost 4,100 deaths in 2012 [1]. Oral cavity and oropharyngeal locations account for half of cases, and are at risk of mandibular bone invasion.

French guidelines recommend work-up including cervicofacial magnetic resonance imaging (MRI) and cervicothoracic computed tomography (CT) for oral cavity and oropharyngeal squamous cell carcinoma extension assessment [2], ideally performed ahead of biopsies and dental care, so as to limit artifacts. Preoperative diagnosis of radiologic bone invasion is essential to plan optimally oncologic surgery that is as non-invasive as possible. Depending on the report, bone invasion on histology concerns 22–55% of mandibular resections. The sensitivity of CT compared to histology is 40–60%, with 89–100% specificity [3–5], while MRI shows 56–94% sensitivity and 73–100% specificity [6,7]. The literature reports wide diagnostic variation for both. Moreover, the prognostic predictive value of bone invasion is controversial: in some studies, it correlated with poorer survival, especially in case of medullary involvement [8], while others reported no significant difference [9].

The main objective of the present study was to assess the diagnostic contribution of CT and/or MRI compared to histology in detecting bone invasion ahead of mandibular interruption surgery. The secondary endpoint was overall survival in groups with and without histologic bone invasion.

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2. Patients and methods

A single-center retrospective study included medical information department data for consecutive patients for the period January 1, 2010 to January 1, 2014.

2.1. Population

2.1.1. Inclusion criteria

Inclusion criteria comprised oropharyngeal and/or oral cavity squamous cell carcinoma managed by mandibular bone

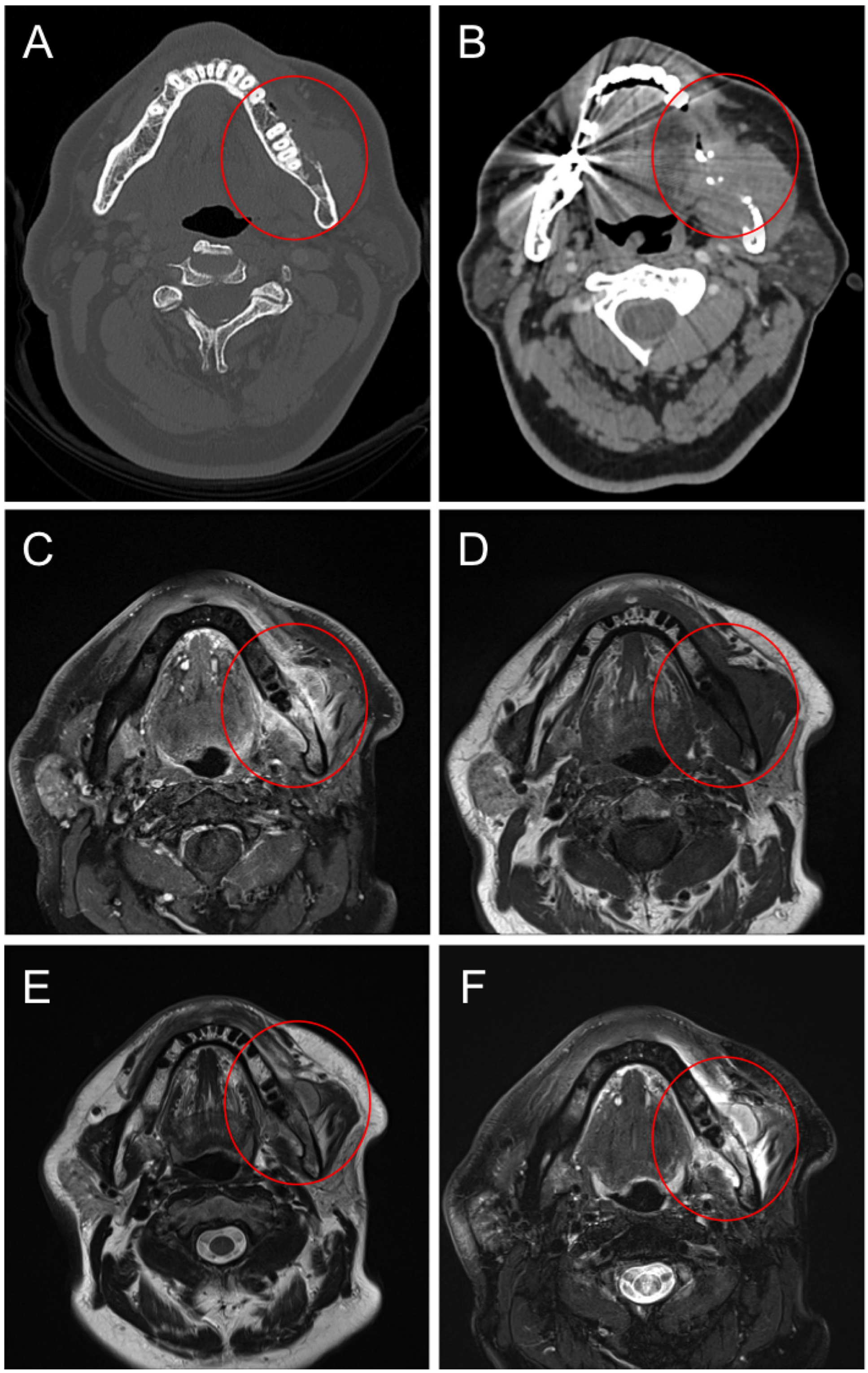

Fig. 1. A. Bone window: lateral cortical lysis with rupture. B. Parenchymal window: tumoral contrast uptake including horizontal mandibular branch. C. Gadolinium-enhanced T1 FAT SAT sequence: lesion contrast uptake and medullary contrast uptake. D. T1 sequence: low-intensity lesion on T1, loss of medullary signal, replacement of medullary bone by tumor. E. T2 sequence: high-intensity medially lesion. F. T2 FAT SAT sequence: lesion in hypersignal on T2.

interruption, with last follow-up on January 1, 2017. Work-up comprised cervicofacial contrast-enhanced CT and/or MRI. Salvage cases following failure of medical treatment were also included. Epidemiological data (age, gender), TNM staging (UICC 7th edition, without invasion depth) and CT/MRI data were collected.

2.1.2. Exclusion criteria

Patients with non-interruptive mandibulectomy or non-interpretable imaging due to dental artifacts were excluded.

2.2. Study design

Imaging was interpreted, according to French Radiology Society (SFR) guidelines, blind to initial radiology and histology results, in a treatment decision-making multidisciplinary team meeting, including a radiologist who had not been involved in prior image interpretation. CT criteria for mandibular bone invasion comprised: cortical erosion, cortical rupture, mandibular nerve canal infiltration or periosteal reaction; MRI criteria comprised: mandibular nerve canal infiltration, low-intensity lesion on T1 with contrast uptake (indicating replacement of medullary bone by tumor) or high-intensity lesion on T2 (Fig. 1). Bone invasion was dichotomized as positive for at least 1 radiologic criterion.

Histologic specimen analysis was conducted in our center's pathology laboratory, and data were collected from the pathology reports in the digitized patient files. Bone analysis was performed after bone margin marking, serial sampling and a decalcification step. HPV status was not systematically recorded in oropharyngeal locations and was therefore not included in analysis.

Minimum follow-up was 3 years. Follow-up data were collected from digital and paper records. In case of loss to follow-up, the date of last follow-up was recorded after checking possible decease in the patient's local deaths registry.

2.3. Statistical analysis

Qualitative variables were reported as number and percentage, normally distributed quantitative variables as mean and standard deviation, and non-normally distributed quantitative variables as median and interquartile range. Normal distribution was checked graphically and on Shapiro-Wilk test.

Sensitivity and specificity for CT and MRI, separately and in association, were calculated against histology, and compared on McNemar test. Agreement between CT and MRI was assessed on kappa coefficient.

Overall survival (percentage survival over a given period) was estimated at various time points on Kaplan-Meier curves and compared according to bone invasion on log-rank test.

Statistical analysis was performed by the center's methodology and biostatistics unit on SAS software (SAS Institute version 9.4), with the significance threshold set at 5%.

3. Results

3.1. Epidemiology

Sixty-eight patients were included, with a male/female sex ratio of 4.2, and median age at diagnosis of 59 years. There were 22 oropharyngeal locations, 42 oral cavity and 4 combined. There were 17 cT2 stages at diagnosis, 12 cT3 and 39 cT4; there were no cases of metastasis. Salvage surgery was performed in 14 cases. Postoperative staging found 25 pT2, 14 pT3 and 29 pT4. Fifty-one patients had MRI, 62 CT and 46 both (Table 1). Three had non-interpretable CT scans (4.8% of patients with CT) and 1 had non-interpretable MRI (2%). Bone invasion prevalence on histology was 43%. Bone margins were positive in 4 cases (6% of patients).

Table 1
Epidemiology, tumor characteristics and types of imaging.

	Number($n = 68$)	(%)
Female/male	13/55	20/80
M/F sex ratio	4.2	
Median age at diagnosis (years)	59 ± 9.27	
Tonsils	12	17.6
Tongue base	2	2.9
Gingival crest	10	14.7
Oral floor	16	24.5
Glossotonsillar groove	9	13.2
Intermaxillary commissure	11	16.2
Other	8	11.8
cT2/pT2	17/25	25/36.8
cT3/pT3	12/14	17.6/20.6
cT4a/pT4a	39/29	57.3/42.6
cN0/pN0	31/33	45.6/48.5
cN1/pN1	14/11	20.6/16.2
cN2a/pN2a	3/1	4.4/1.5
cN2b/pN2b	12/17	17.6/25
cN2c/pN2c	8/6	11.8/8.8
Salvage	14	20.6
MRI	51	75
CT	62	91.2
MRI + CT	46	67.6

MRI: magnetic resonance imaging; CT: computed tomography.

3.2. Diagnostic values of CT and MRI

Sensitivity (Se) was 70% for CT, 83% for MRI and 83% for the combination. Specificity (Sp) was respectively 71%, 50% and 62%. Positive predictive value (PPV) was respectively 66%, 59% and 62%, and negative predictive value (NPV) 76%, 78% and 83%. The kappa coefficient for agreement between CT and MRI was 0.69 (95% CI, 0.49–0.89) ($P < 0.0001$): i.e., good agreement in detecting mandibular bone invasion. Sp and Se did not significantly differ between CT and MRI on McNemar test: respectively, $P > 0.25$ and $P > 0.12$ (Table 2).

3.3. False negatives

All false negatives on CT showed tumor bone contact on palpation (Table 3). In patients 30, 65 and 68, in whom neither MRI nor CT showed bone invasion, whether cortical or medullary, non-conservative surgery was indicated based on clinical aspect and bone proximity (Table 3).

In all false negatives on MRI, no bone invasion was suspected on CT (Table 3), whereas palpation revealed bone contact.

3.4. Overall survival

Three-year overall survival in the whole population was $41 \pm 6.7\%$: $42.5 \pm 11\%$ with and $40 \pm 8\%$ without bone invasion (non-significant; $P > 0.7$) (Fig. 2).

4. Discussion

In surgical management of oral cavity and oropharyngeal tumor, it is essential to assess involvement of the mandibular bone in contact with the tumor: in case of clinical and imaging suspicion, mandibular interruption should be performed, with free flap reconstruction, ideally including a bone component [10]. This requires 2 surgery teams, long operative time and hospital stay, and entails non-negligible morbidity and mortality with esthetic and functional sequelae for swallowing and speech [11]. Precise

Table 2
Diagnostic values of CT, MRI and CT + MRI versus histology.

Imaging	Se 95% CI	Sp 95% CI	PPV95% CI	NPV95% CI	Kappa concordance95% CI
CT	0.70 0.49–0.86	0.71 0.53–0.85	0.66 0.45–0.82	0.76 0.57–0.89	0.69 0.49–0.89 $P < 0.0001$
MRI	0.83 0.68–0.98	0.50 0.31–0.68	0.59 0.40–0.75	0.78 0.52–0.93	
CT + MRI	0.83 0.69–0.96	0.62 0.46–0.77	0.62 0.46–0.77	0.83 0.69–0.96	–

CT: computed tomography; MRI: magnetic resonance imaging; Se: sensitivity; Sp: specificity; PPV: positive predictive value; NPV: negative predictive value.

Table 3
Analysis of false negatives on CT and MRI.

False negatives on CT[a]			
Patient	Sublocation	Bone invasion on MRI	Medullary invasion on MRI
n° 1	Oral floor	No MRI	NK
n° 30	Pelvilingual groove	No	NK
n° 39	Tonsil	Yes	Yes
n° 41	Oral floor	Yes	No
n° 53	Intermaxillary commissure	Yes	Yes
n° 65	Gingival crest	No	NK
n° 68	Oral floor (local recurrence)	No	NK
n° 80	Gingival crest (2nd location)	Yes	Yes
False negatives on MRI[b]			
Patient	Sublocation	Bone invasion on CT	
n° 26	Gingival crest	No CT	
n° 30	Pelvilingual groove	No	
n° 65	Gingival crest	No	
n° 69	Oral floor (local recurrence)	No	

NK: not known.
[a] Patients without CT signs of bone invasion but bone invasion found on histology.
[b] Patients without MRI signs of bone invasion but bone invasion found on histology.

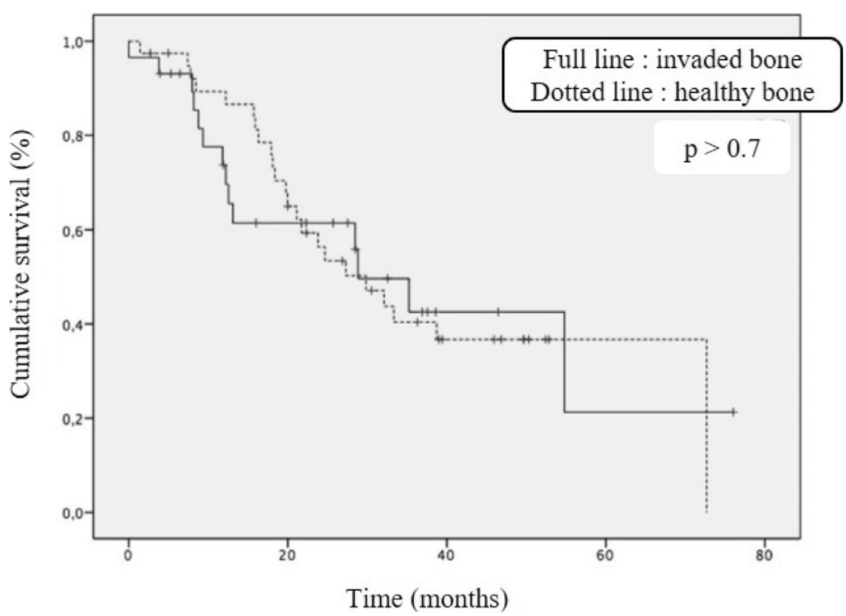

Fig. 2. Overall survival according to bone invasion.

preoperative radiological assessment of mandibular bone invasion can allow bone-sparing and surgical de-escalation.

The prevalence of bone invasion on histology was 43%. Rates in the literature range from 23% to 82%. This may be due to procedural differences (interruptive or not), series with the lowest prevalences including patients treated with non-interruptive resection [3,4,12–17]. In the present series, non-interruptive mandibulectomy was excluded, so as not to bias bone invasion prevalence estimates: in non-interruptive surgery, resection aims only to be oncologic, with healthy margins, there being no clinical or radiological suspicion of bone invasion. In a literature review, Rao et al. advocated conservative mandibulectomy for non-irradiated patients with cortical but not medullary or canal infiltration on imaging [11]. Reports of 5-year survival after interruptive

Table 4
Diagnostic values in recent literature.

Reference	*n*/prevalence on histology(%)	Imaging	Se(%)	Sp(%)	PPV(%)	NPV(%)	Accuracy(%)
Hendrickx et al. [3]	23/48	IRM	82	67	69	80	74
Gu et al. [4]	46/26	CT	42	100	NA	NA	85
		MRI	58	97	NA	NA	87
Bolzoni et al. [12]	43/34	MRI	93	93	88	96	93
Rajesh et al. [13]	23/82	MRI	10	75	95	100	96
Vidiri et al. [14]	36/39	CT	79	82	73	86	81
		MRI	93	82	76	95	86
Abd-el-hafez et al. [15]	114/32	MRI	97	61	55	98	73
Dreiseidler et al. [16]	77/32	CT	80	100	100	75	NA
Silva et al. [17]	58/40	CT	52	79	70	63	68
		MRI	74	73	65	80	73
		CT and MRI	91	74	68	93	80
Goerres et al. [19]	34/35	CT	92	100	100	96	97
Imaizumi et al. [20]	51/23	CT	10	88	100	89	94
		MRI	96	54	93	67	74
Handschel et al. [22]	107/43	CT	83	87	83	87	NA
Our study or u	29/68	CT	70	71	66	76	
		MRI	83	50	59	78	
		CT and MRI	83	62	62	83	

versus conservative mandibulectomy are divergent, but medullary or canal involvement seems clearly to indicate interruption in view of the poor prognosis for survival [11,18].

In the present series, sensitivity and specificity were respectively 70% and 71% for CT and 83% and 50% for MRI, and PPV and NPV were respectively 66% and 76% for CT and 59% and 78% for MRI. In the literature, the diagnostic values of CT and MRI vary widely: sensitivity and specificity of CT respectively from 42% to 100% and from 79% to 100%, and respectively from 58% to 100% and from 54% to 100% for MRI (Table 4). Many authors report high specificity for CT in detecting mandibular bone invasion, due to the density of normal cortical bone on CT, enabling good detection of the slightest erosion, conferring a good PPV [16,19,20].

In the present study, MRI showed greater Se and NPV (83% and 78%) than CT (70% and 76%), and can thus usefully contribute to the analysis of bone invasion, sometimes ruling it out. CT, on the other hand, showed better Sp and PPV, at 71% and 66%. MRI showing bone invasion should be completed by CT scan to rule out false positives if cortical rupture is not clinically clear. However, only 68% of patients had both examinations in extension assessment, mainly due to iodized contrast medium intolerance and contraindications for MRI. Missing data and the retrospective study design prevented analysis of diagnostic value between associated MRI plus CT versus MRI alone or CT alone.

In the literature, MRI false positives mainly concern medullary edema, which is difficult to distinguish from tumoral infiltration. Rajesh et al. advocate MRI alone, diagnostic value not being improved by association to CT [13]. In the present study, combined analysis improved NPV (83%) compared to CT or MRI alone (76% and 78% respectively), as CT can rule out MRI false positives [15]. Only 3 of the 8 CT false negatives were negative on MRI; it would be interesting to know if the bone involvement in these cases was purely medullary.

We chose not to exclude salvage surgery (14 patients; 20%) following failure of medical treatment, so as to have a representative cohort. This may have introduced a bias, underestimating the diagnostic value of imaging due to treatment-induced signal changes: external radiation therapy induces mucosal edema, decreasing tumor tissue discrimination on MRI [21].

Radiologic bone invasion was dichotomized. A prospective study with a well-defined diagnostic algorithm, specifying cortical and/or medullary invasion and periosteal reaction, could well provide further information. In the literature, these signs analyzed separately each have diagnostic value. Perimandibular periosteal reaction or cortical erosion on CT was reported to be significantly associated with bone invasion on histology [17,22].

Three-year overall survival was 41%, in line with the literature. This may be due to our inclusion criteria for all patients with indications for interruptive resection for locally advanced disease. For Shaw et al., 5-year overall survival was 50% and 5-year recurrence-free survival 68%, in a prospective cohort of 100 patients with 35 managed by marginal bone resection, both interruptive and non-interruptive, for tumor of varying advancement and prognosis [18]. In the present series, there was no significant difference in overall survival according to histologic bone invasion, in line with the literature. For Ash et al., mandibular bone invasion was not a significant factor of poor prognosis [9]. Likewise, for Ebrahimi et al., cortical invasion was not a negative factor, whereas medullary invasion was associated with poorer overall survival and increased risk of distant metastasis; 103 of the 498 patients managed surgically for oral cavity squamous cell carcinoma showed bone invasion on histology, and medullary invasion was an independent factor significantly associated with lower overall survival. The authors advocated revising the TNM classification to upgrade T stage in case of medullary invasion [8].

Studies of the diagnostic value of PET-CT to analyze mandibular invasion had small cohorts of around 20 patients; nevertheless, PET-CT with fusion images seems to show better specificity than MRI, with fewer false positives. Even so, false positives do occur, as in inflammation or infection, and PET-CT has mediocre anatomic resolution even with fusion images [23]. It is thus more specific but less sensitive than MRI [15]. Other tracers under development, such as 18F-α-methyl tyrosine, seem to give better specificity than MRI or 18 F-FDG PET/CT [24].

The present series comprised 68 patients, and was larger than in the recent literature. Diagnostic values of CT and MRI vary between reports. Major invasion is easy to detect, but early stages are difficult to diagnose and bone invasion assessment is a real problem. CT and MRI are complementary in studying mandibular bone invasion; rapid imaging within 1 month of surgery should be the basic work-up for oral cavity and/or oropharyngeal tumor ahead of treatment.

5. Conclusion

The present study showed that combined CT and MRI enabled precise analysis of mandibular invasion in oral cavity and oropharyngeal cancer. The two should ideally be associated, adhering to good practice criteria, within 4 weeks before surgery. This optimization of radiologic assessment allows treatment to be adapted, avoiding over-resection and improving postoperative course and limiting long-term sequelae.

Disclosure of interest

The authors declare that they have no competing interest.

References

[1] Les cancers en France, les données, INCa; 2014.
[2] Vergez S, Morinière S, Dubrulle F, Salaun P-Y, De Monès E, Bertolus C, et al. Initial staging of squamous cell carcinoma of the oral cavity, larynx and pharynx (excluding nasopharynx). Part I: locoregional extension assessment: 2012 SFORL guidelines. Eur Ann Otorhinolaryngol Head Neck Dis 2013;130(1):39–45.
[3] Hendrikx AWF, Maal T, Dieleman F, Van Cann EM, Merkx MAW, Cone-beam CT. in the assessment of mandibular invasion by oral squamous cell carcinoma: results of the preliminary study. Int J Oral Maxillofac Surg 2010;39(5):436–9.
[4] Gu DH, Yoon DY, Park CH, Chang SK, Lim KJ, Seo YL, et al. CT, MR, (18)F-FDG PET/CT, and their combined use for the assessment of mandibular invasion by squamous cell carcinomas of the oral cavity. Acta Radiol Stockh Swed 1987 2010;51(10):1111–9.
[5] Brekel MWM, van den, Runne RW, Smeele LE, Tiwari RM, Snow GB, et al. Assessment of tumour invasion into the mandible: the value of different imaging techniques. Eur Radiol 1998;8(9):1552–7.
[6] Uribe S, Rojas L, Rosas C. Accuracy of imaging methods for detection of bone tissue invasion in patients with oral squamous cell carcinoma. Dentomaxillofacial Radiol 2013;42(6):20120346.
[7] Li C, Yang W, Men Y, Wu F, Pan J, Li L. Magnetic resonance imaging for diagnosis of mandibular involvement from head and neck cancers: a systematic review and meta-analysis. PLoS ONE 2014;9(11):e112267.
[8] Ebrahimi A, Murali R, Gao K, Elliott MS, Clark JR. The prognostic and staging implications of bone invasion in oral squamous cell carcinoma. Cancer 2011;117(19):4460–7.
[9] Ash CS, Nason RW, Abdoh AA, Cohen MA. Prognostic implications of mandibular invasion in oral cancer. Head Neck 2000;22(8):794–8.
[10] De Bree R, Rinaldo A, Genden EM, Suárez C, Rodrigo JP, Fagan JJ, et al. Modern reconstruction techniques for oral and pharyngeal defects after tumor resection. Eur Arch Oto-Rhino-Laryngol 2008;265(1):1–9.
[11] Rao LP, Shukla M, Sharma V, Pandey M. Mandibular conservation in oral cancer. Surg Oncol 2012;21(2):109–18.
[12] Bolzoni A, Cappiello J, Piazza C, Peretti G, Maroldi R, Farina D, et al. Diagnostic accuracy of magnetic resonance imaging in the assessment of mandibular involvement in oral-oropharyngeal squamous cell carcinoma: a prospective study. Arch Otolaryngol Neck Surg 2004;130(7):837–43.
[13] Rajesh A, Khan A, Kendall C, Hayter J, Cherryman G. Can magnetic resonance imaging replace single photon computed tomography and computed tomography in detecting bony invasion in patients with oral squamous cell carcinoma? Br J Oral Maxillofac Surg 2008;46(1):11–4.
[14] Vidiri A, Guerrisi A, Pellini R, Manciocco V, Covello R, Mattioni O, et al. Multidetector row computed tomography (MDCT) and magnetic resonance imaging (MRI) in the evaluation of the mandibular invasion by squamous cell carcinomas (SCC) of the oral cavity. Correlation with pathological data. J Exp Clin Cancer Res 2010;29(1):1.
[15] Abd El-Hafez YG, Chen C-C, Ng S-H, Lin C-Y, Wang H-M, Chan S-C, et al. Comparison of PET/CT and MRI for the detection of bone marrow invasion in patients with squamous cell carcinoma of the oral cavity. Oral Oncol 2011;47(4):288–95.
[16] Dreiseidler T, Alarabi N, Ritter L, Rothamel D, Scheer M, Zöller JE, et al. A comparison of multislice computerized tomography, cone-beam computerized tomography, and single photon emission computerized tomography for the assessment of bone invasion by oral malignancies. Oral Surg Oral Med Oral Pathol Oral Radiol Endodontology 2011;112(3):367–74.
[17] Silva M, Zambrini EI, Chiari G, Montermini I, Manna C, Poli T, et al. Pre-surgical assessment of mandibular bone invasion from oral cancer: comparison between different imaging techniques and relevance of radiologist expertise. Radiol Med (Torino) 2016;121(9):704–10.
[18] Shaw RJ, Brown JS, Woolgar JA, Lowe D, Rogers SN, Vaughan ED. The influence of the pattern of mandibular invasion on recurrence and survival in oral squamous cell carcinoma. Head Neck 2004;26(10):861–9.
[19] Goerres GW, Schmid DT, Schuknecht B, Eyrich GK. Bone invasion in patients with oral cavity cancer: comparison of conventional CT with PET/CT and SPECT/CT. Radiology 2005;237(1):281–7.
[20] Imaizumi A, Yoshino N, Yamada I, Nagumo K, Amagasa T, Omura K, et al. A potential pitfall of MR imaging for assessing mandibular invasion of squamous cell carcinoma in the oral cavity. Am J Neuroradiol 2006;27(1):114–22.
[21] Lell M, Baum U, Greess H, Nömayr A, Nkenke E, Koester M, et al. Head and neck tumors: imaging recurrent tumor and post-therapeutic changes with CT and MRI. Eur J Radiol 2000;33(3):239–47.
[22] Handschel J, Naujoks C, Depprich RA, Kübler NR, Kröpil P, Kuhlemann J, et al. CT-scan is a valuable tool to detect mandibular involvement in oral cancer patients. Oral Oncol 2012;48(4):361–6.
[23] Babin E, Desmonts C, Hamon M, Bénateau H, Hitier M. PET/CT for assessing mandibular invasion by intraoral squamous cell carcinomas. Clin Otolaryngol 2008;33(1):47–51.
[24] Kim M, Higuchi T, Arisaka Y, Achmad A, Tokue A, Tominaga H, et al. Clinical significance of 18F – α – methyl tyrosine PET/CT for the detection of bone marrow invasion in patients with oral squamous cell carcinoma: comparison with 18F-FDG PET/CT and MRI. Ann Nucl Med 2013;27(5):423–30.