Original Article

Patterns of Mandibular Invasion in Oral Squamous Cell Carcinoma

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Abstract

Background: Mandibular resections are routinely carried out for achieving a tumor free resection margin for oral cancers. However, the need of mandibular resection to achieve this has always been questioned. The present study was carried out to assess the patterns of mandibular involvement in carcinoma of the mandibular region.

Methodology: A total of 23 consecutive patients who had undergone mandibular resection and were found to have mandibular invasion were studied in a prospective open fashion. After decalcification, the specimens were serially sectioned at a 0.5-1 cm interval to identify gross invasion and .3 to .5 micron cut by microtome to identify pattern of mandibular invasion. Preoperative contrast enhanced CT scan was also used to record and analyze the type of invasion.

Result: Two types of invasion pattern were found: “erosive” and “invasive”. Out of 23 patients, the mandibular pattern of invasion was infiltrative (invasive) in 7 (30.4 percent) and erosive in 7 (30.4 percent) and no invasion in 9 (39.1 percent). In 6/7 cases of perineural invasion (or 75% of all cases), there was an infiltrative (invasive) trend. The contrast-enhanced computed tomography scan revealed 8 (34.8%) erosive bone involvement, 5 (21.7%) infiltrative (invasive) disease, and 10 (43.5%) no involvement of bone in the 23 individuals investigated. CECT's sensitivity, specificity, NPV, PPV, and accuracy were respectively 71.4%, 66.7%, 60.9%, 76.4%, and 70%.

Conclusions: Larger or higher TNM staged tumors are more likely to invade the mandible and show the more aggressive (invasive) form of tumor spread. The accuracy of identifying mandibular invasion by CECT was 70%, indicating a certain degree of sampling error and variability in interpretation.

Key Words: Oral squamous cell carcinoma, mandibular invasion, pattern of invasion, infiltrative, erosive, contrast enhanced CT scan.

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Introduction

Globally, oral cancer is the sixth most common cancer.[1] Every year, over 550000 people are diagnosed globally, with approximately 300,000 deaths.[2] The highest prevalence is seen among the south Asian population.[3] In Bangladesh, oral cancer is the third common cancer. More than 7000 people are newly diagnosed each year, and among them, mortality is about 6.6%.[4]

The incidence is more common in males than in females. And the most common age group of presentation is above 50 years.[5] However, the incidence of oral cancer is increasing among the young population aged less than 45 years.[6]

Approximately 85 to 95% of all diagnosed oral cancers are squamous cell carcinoma (SCC).[7] Among all head and neck SCCs, oral SCC with mandibular invasion has the highest recurrence rate and one of the lowest 5-year overall survival rates.[8,9]

The prevalence of oral SCC with mandibular bone involvement is reported to range from 12% to 56% of cases.[10,11,12]

Carcinoma involving the mandibular alveolar ridge, lower buccal sulcus, sublingual sulcus, and mandibular retromolar trigone is defined as oral carcinoma of the mandibular region.[13] Carcinoma of the mandibular region usually involves the mandible, frequently by direct extension and sometimes by other routes.[14.15] The prevalence of mandibular bone involvement ranges from 12 to 56%.[16,17,18] The prognosis of these lesions is usually poor with a primary site recurrence rate of nearly 70% that ultimately causes death.[19,20]

Mandibular involvement in these cases occurs mainly due to direct infiltration of the mandible by the tumor. The main route of entry into the mandible is reported to be through the alveolar crest and lingual cortex if the tumor is located medial to the mandible.[21,22] Other routes of infiltration are also described, of which spreading through the canal of the inferior alveolar nerve is most important in the present scenario, where a lot of emphasis is being placed on conserving the mandible. Too many mandibles are sacrificed without histological evidence of mandibular invasion.[23] For reasons of quality of life, it is important to preserve the continuity of the mandible, if oncological safety can be assured.[24] Oral squamous cell carcinoma can invade the mandible by two well-recognized patterns.[25,26,27,28,29,30] In the invasive pattern of disease, fingers and islands of tumor advance independently into the cancellous spaces, with little osteoclastic activity and no intervening layer of connective tissue. In the erosive pattern, the tumor advances on a broad front, with a connective tissue layer and active osteoclasts separating the tumor from the bone. This is similar to the osteoclastic-independent phase (invasive) and the osteoclastic dependent phase (erosive).[25] The evidence for a progression from the erosive to the invasive pattern of disease, depending on the extent of invasion by the description of what they termed the mixed pattern of spread.[29] Besides, they found that the depth of tumor invasion of the mandible was related to the presence of the invasive pattern of spread.

Moreover, by knowing the characteristics of the different patterns of invasion, the prognosis and recurrence can also be predicted. The pushing type (erosive) of invasion has a low recurrence rate and a better prognosis than the infiltrative pattern of invasion.[23]

There remains little detailed histologic examination of the routes of tumor entry into the dentate mandible, and in some previous reports, a large proportion of patients have received primary radiotherapy and have undergone salvage procedures.[25] In this patient group, it is difficult to be sure whether the pattern of tumor entry and spread is related to the effects of the tumor or influenced by the effect of radiotherapy on bone.[31]

Bone invasion alters the clinical staging and management of oral carcinoma on the assumption that resection of the bone invaded by the tumor can result in disease progression and poor outcome.[32] Detecting oral carcinoma involvement of the mandibular bone prior to definitive therapy is challenging for head and neck surgeons.[18,32] Despite recent improvements, mandibular reconstruction results are still not functionally satisfactory, necessitating extended surgery and microvascular surgery expertise. Therefore, determination of bone invasion and setting of resection margins is imperative in the overall assessment of patients undergoing surgery. Various techniques available for the evaluation of the mandible prior to surgery includes radiographs of mandible, bone scans, computed tomographic (CT) scans, magnetic resonance imaging (MRI) scans, and single photon emission computed tomographic (SPECT) scans.[33] Although all these tests play definite roles in the evaluation of the mandible, all of them have specific pitfalls and

controversy still exist as to what is the best way to image the mandible in oral cancer.[34]

This study was carried out for histopathological, and contrast enhanced computed tomographic assessment for mandibular invasion pattern in oral squamous cell carcinoma.

Materials and Methods

The descriptive cross-sectional study was carried out at the Oral & Maxillofacial Surgery Department of Bangabandhu Sheikh Mujib Medical University, Dhaka Dental College Hospital and Shaheed Suhrawardy Medical College Hospital Dhaka, Bangladesh from 1st of October 2020 to the 31st of October 2021. A total 23 patients of either sex who had with mandibular bone invasion undergone surgery for oral SCC were included in this study. A purposive sampling technique was used for this study. The patterns of invasion of the mandible was detected by contrast enhanced computed tomography (CECT) and post-operative histopathological study. Twenty-three samples were collected: 7 from the Oral & Maxillofacial Surgery Department of Bangabandhu Sheikh Mujib Medical University, 11 from Oral & Maxillofacial Surgery Department of Dhaka Dental College Hospital, and 5 from Oral & Maxillofacial Surgery Department of Shaheed Suhrawardy Medical College Hospital, Dhaka, Bangladesh. Ethical clearance for the study was taken from the Institutional Review Board (I.R.B) of BSMMU prior to the commencement of this study and permission from the aforementioned institutions. Data was processed and analyzed by SPSS 24 (Statistical program for Social Sciences).

RESULTS AND OBSERVATION

The present study included 23 histologically confirmed squamous cell carcinoma patients who had undergone marginal or segmental mandibulectomy, out of which, 14 (60.9 %) were female and 9 (39.1%) were male. The male to female ratio was 0.6:1. (Figure 1)

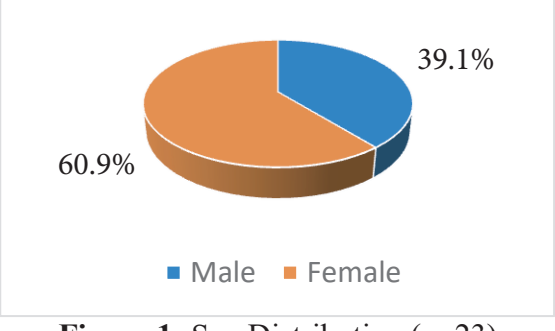


Figure 1: Sex Distribution (n=23)

The mean age of the studied respondents was 59.04±10.5 (SD) years. Nineteen (82.61%) of the patients were aged above 50 years and 4 (17.39%) were equal to or below 50 years of age. Females above 50 years of age had the highest (12) occurrence of SCC, whereas those below 50 years had only 2 (8.7%).

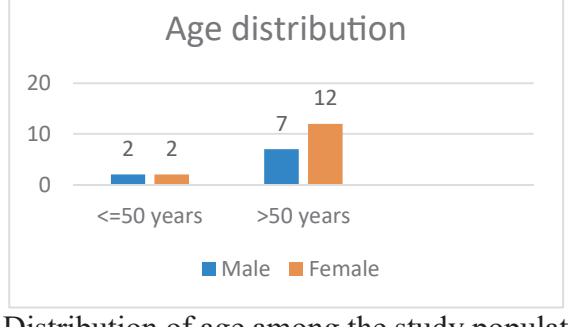


Figure 2: Distribution of age among the study population (n=23)

In contrast enhanced CT scan, out of 23 patients, 8 (34.8%) had erosive bone involvement, 5 (21.7%) infiltrative (invasive) and 10 (43.5%) had no invasion. (Table 1)

Table 1: CT scan findings for bone invasion (n=23)

Pattern of invasion	Frequency	Percent
No signs of involvement	10	43.5
Erosive	8	34.8
Invasive	5	21.7
Total	23	100.0

Out of 23 patients, 7 (30.4%) had erosive bone involvement, 7 (30.4%) had infiltrative (invasive) and 9 (39.1%) had no invasion. Overall, 60.8% bone involvement was present. (**Table 2**)

Table 2: Histopathological invasion pattern (n=23)

Invasion pattern	Frequency	Percent
No invasion	9	39.1
Erosive	7	30.4
Invasive (infiltrative)	7	30.4
Total	23	100.0

Buccal mucosa 10(43.5%) and lower alveolar ridge 10 (43.5%) were the most common site followed by tongue 2(8.7%) and retromolar 1(4.3%). 7 (70%) out of 10 buccal mucosa tumour involved bone (5 erosive and 2 invasive) and 5(50%) out of 10 lower alveolar ridge tumour had bone involvement (1 erosive and 4 invasive). 57.1 % (4 out of 7) of all invasive tumour was at the lower alveolar ridge. (Table 3)

Table 3: Histological invasion pattern in relation to site of the lesion (n=23)

	Histopathological invasion pattern		
Site	**No invasion n (%)**	**Erosive n (%)**	**Invasive n (%)**
Buccal mucosa	3 (30)	5 (50.0)	2 (20.0)
Lower Alveolar ridge	5 (50.0)	1 (10)	4 (40)
Retromolar area	1 (100)	0	0
Tongue	0	1 (50)	1 (50)

Fisher's Exact test, p= 0.287 (>0.05)

The perineural invasion was present in 8 (34.8%) cases among which 6 (85.7%) were invasive tumour. 7 out of 7 erosive tumour was devoid of perineural invasion. (**Table 4**)

Table 4: Histological invasion pattern in relation to perineural invasion (n=23)

	Histopathological invasion pattern			
Perineural invasion	No invasion n (%)	Erosive n (%)	Invasive n (%)	Total
Absent	7 (77.8)	7(100.0)	1(14.3)	15(65.2)
Present	2 (22.2)	0	6(85.7)	8(34.8)

Fisher's Exact test, p= 0.003 *(< 0.05)*

Out of 23 tumors, 10 (43.5%) were well differentiated and 13 (56.5%) were moderately differentiated. 71.4% (5) invasive tumor were moderately differentiated.(**Table 5**)

Table 5: Histopathological invasion pattern in relation to histopathological grading (n=23)

	Histopathological grading	
Histopathological invasion pattern	Well differentiated n (%)	Moderately differentiated n (%)
No invasion	5 (55.6)	4 (44.4)
Erosive	3 (42.9)	4 (57.1)
Invasive	2 (28.6)	5 (71.4)
Total	10(43.5)	13 (56.5)

out of 7 invasive pattern bone involvements, 3 (42.9%) were at stage IVA, 4 (57.1%) were at stage IVB. Out of 4 (17.4%) Stage IV B tumors, 4 (100%) involved bone in an invasive pattern. Among the erosive patterns, 7 (85.7%) were in stage IVA and 1 (14.3%) was in stage II. There were 13 (56.5%) stage IVA diseases, among them no invasion in 3 (30.8%), erosive in 7 (46.2%) and invasive in 3 (23.1%). (**Table 6**)

Table 6: Histological invasion pattern in relation to pathological TNM staging (n=23)

	Pathological TNM staging			
Histopathological invasion pattern	Stage II **n (%)**	Stage III **n (%)**	Stage IV A **n (%)**	Stage IV B **n (%)**
No invasion	0	5 (55.6)	4 (44.4)	0
Erosive	1 (14.3)	0	6 (85.7)	0
Invasive	0	0	3 (42.9)	4 (57.1)
Total	1 (4.3)	5 (21.7)	13 (56.5)	4 (17.4)

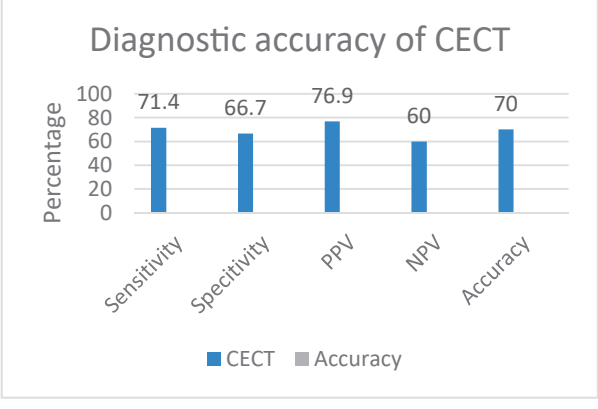
Fisher′s Exact test, p= 0.001 (<0.05)

CECT could truly predict bone involvement in 10 patients out of 14 patients. Among 9 patients who didn't have bone invasion, CECT could predict in 6 patients accurately not having invasion.(**Table 7)**

Table 7: Bone invasion in CECT in relation to bone invasion in Histopathology (n=23)

	Bone invasion in Histopathology		
Bone invasion in CECT	**Positive**	**Negative**	Total
Positive	10	3	13
	TP	FP	TP+FP
Negative	4	6	10 FN+TN
	FN	TN	
Total	14	9	23
	TP+FN	FP+TN	

TP=True positive, FP=False positive, FN=False Negative, TN=True Negative Fisher's Exact test, p=0.102 (P > 0.05)



PPV: Positive Predictive Value, NPV: Negative Predictive Value

Figure 3: Diagnostic accuracy of CECT

CECT showed 71.4% sensitivity, 66.7% specificity, 76.9% positive predictive value, 60% negative predictive value and 70% accuracy.

Discussion

The mainstay of treatment for oral squamous cell carcinoma was composite resection of the cancer with en bloc resection of a segment or hemi mandible with a probable recurrence preventive adequate healthy margin, including neck node dissection.[35] With a better understanding of the disease's spread and biology, it's now clear that most of the oral cancer spread to the mandible occurs through direct infiltration of the tumor through the alveolar ridge or lingual and buccal cortical plate.[21,29] Tumors also enter at the point of abutment, which is the junction of reflected and attached mucosa in both edentulous and dentulous mandibles. It has long been assumed that if there is normal tissue between the tumor and the bone, the mandible can be saved. But determining the involvement of the mandible preoperatively can be difficult, and subsequent preservation of the mandible can result in positive resection margins if the canal has not been excised. Also, it has been shown that invasive disease patterns are visible at shallower depths.[29]

Dubner & Heller[36] found that marginal resection of the mandible resulted in significantly higher local

recurrence rates, regardless of the size of the primary or the involvement of the nodes. They also discovered that neither tumor invasion of the mandible nor the addition of radiotherapy influenced recurrence rates. Similar findings were found in a study of Ord, et al.[23]

CT has been reported to be the most accurate method in evaluating discrete cortical bone involvement.[16] However, CT scans are hampered by artifacts produced by metallic dental prostheses and false-negative CT findings are reported to occur as well.[37]

The present study included 23 histologically confirmed squamous cell carcinoma patients, out of whom, 14 (60.87%) were female and 9 (39.13%) were male which is contrary to the findings of a study5 probably due to late reporting of female patient than male in our country.

The age range in this study was from 25 years to 75. The mean age of all patients was 59.04 (SD 10.542) and most (82.61%) of the patients were aged above 50 years that is similar to the findings of Vidiri, et al.[38]

In our study Buccal mucosa 10(43.5%) and lower alveolar ridge 10 (43.5%) were the most common sites. Seven (70%) out of 10 buccal mucosa tumour involved bone. And 5(50%) out of 10 lower alveolar ridge tumors had bone involvement that is significantly lower than the incidence (89%) found by Kalavrezos et al.[33] and Tsue et al.[37]

Our findings of histopathological invasion patterns: we found two types of invasions: “Erosive” and “Invasive” and that is consistent with the study of Brown & Browne29and Müller & Slootweg.[27] Among 23 patients’ invasions were as follows: no invasion in 9 (39.1%), erosive bone invasion in 7 (30.4%), and invasive bone invasion in 7 (30.4%) and overall, 60.8% bone involvement was present.

Contrast-enhanced computed tomography scan had a Sensitivity of 71.4%, which is higher than the observation (41.7%) found by Gu et al.[39] and close to the findings (83%) of Uribe, et al.40 and (75%) Kushraj et al.[32] And Specificity of 66.7%, which is lower than the findings (100%) both by Gu, et al.39 and Uribe et al.40 The positive and negative predictive value of CECT was respectively 76.9% which is lower than (100%) Kushraj et al.[32] and 60% slightly lower than (78%) Kushraj et al.[32]

Out of 7 patients with invasive pattern bone involvement, 3 (42.9%) were at stage IVA, 4 (57.1%) were at stage IVB. Out of 4 Stage IV B tumors, 4 (100%) involved bone in an invasive pattern, p= 0.001 (<0.05).

In our findings out of 23 tumors, 10 (43.5%) were well differentiated and 13 (56.5%) were moderately differentiated. 71.4% (5) of invasive tumor were moderately differentiated. But degree of differentiation was not strongly associated with the patterns of bone invasion, p=0.68 (>0.05) which supports the findings of Lukinmaa et al.[26]

In contrary to the findings of Hong et al.[41], invasive patterns had perineural invasion in 85.7% (7) cases and out of 7 (30.4%) erosive patterns, 7 (100%) had no perineural invasion. These findings were statistically significant p= 0.003 (<0.05).

Conclusion

The results of our study suggest that oral cancer can invade mandible by two patterns: ‘erosive’ and ‘invasive’. Contrast enhanced computed tomography had a sensitivity of 71.4%, Specificity of 66.7% and Positive and negative predictive value was respectively 76.9%, and 60%. Most (71.4%) of the invasive tumour were moderately differentiated but degree of differentiation was not associated with the patterns of bone invasion. Invasive patterns commonly (85.7%) had perineural invasion. The accuracy of identifying mandibular invasion by CECT was 70%, indicating a certain degree of sampling error and variability in interpretation.

Limitations of the study

The limitation of this study was the small number of subjects available. It was not feasible to take more samples due to limited indoor facilities, of the ongoing COVID pandemic situation as well as a limited time period for the study. An accurate preoperative assessment of mandibular invasion cannot be justified.

Recommendations

Based on the findings of our study, review of literature and in accordance with the pattern of mandibular invasion, we recommend combined preoperative radiographic assessment tools besides clinical assessment to detect mandibular invasion. As the types of tools cannot be recommended from this study, further study is needed for accurate preoperative diagnosis of mandibular invasion.

Conflict of Interest: none

References

1. Kumar M, Nanavati R, Modi TG, Dobariya C. Oral cancer: Etiology and risk factors: A review. Journal of cancer research and therapeutics. 2016 Apr 1;12(2):458-63.

2. Saba NF, Goodman M, Ward K, Flowers C, Ramalingam S, Owonikoko T, Chen A, Grist W, Wadsworth T, Beitler JJ, Khuri FR. Gender and ethnic disparities in incidence and survival of squamous cell carcinoma of the oral tongue, base of tongue, and tonsils: a surveillance, epidemiology, and end results program-based analysis. Oncology. 2011 Sep 8;81(1):12-20.

3. Shah JP, Gil Z. Current concepts in management of oral cancer–surgery. Oral oncology. 2009 Apr 1;45(4-5):394-401.

4. Sultana N, Malik M. The overview of oral cancer and risk factors in Bangladesh. International Journal of Dental Sciences and Research. 2014 Sep 18;2(5A):8-10.

5. Stell & Maran's textbook of head and neck surgery and oncology. London: Hodder Arnold; 2012.

6. Hussein AA, Helder MN, de Visscher JG, Leemans CR, Braakhuis BJ, de Vet HC, Forouzanfar T. Global incidence of oral and oropharynx cancer in patients younger than 45 years versus older patients: a systematic review. European Journal of Cancer. 2017 Sep 1;82:115-27.

7. Harris CM, Ghali GE. Oral Cancer: Etiology, diagnosis, classification and staging. Peterson's Principles of Oral and Maxillofacial Surgery, Milaro MM, Ghali GE, Larsen PE, Waite PD (eds). 3rd ed. Connecticut: People's Medical Publishing House. 2011:677-92.

8. Batsakis JG. Surgical excision margins: a pathologist's perspective. Advances in anatomic pathology. 1999 May 1;6(3):140-8.

9. Langdon JD, Harvey PW, Rapidis AD, Patel MF, Johnson NW, Hopps R. Oral cancer: the behaviour and response to treatment of 194 cases. Journal of Maxillofacial Surgery. 1977 Jan 1;5:221-37.

10. Chen YL, Kuo SW, Fang KH, Hao SP. Prognostic impact of marginal mandibulectomy in the presence of superficial bone invasion and the nononcologic outcome. Head & neck. 2011 May;33(5):708-13.

11. Hoffmannová J, Foltán R, Vlk M, Šipoš M, Horká E, Pavlíková G, Kufa R, Bulik O, Šedý J. Hemimandibulectomy and therapeutic neck dissection with radiotherapy in the treatment of oral squamous cell carcinoma involving mandible: a critical review of treatment protocol in the years 1994–2004. International journal of oral and maxillofacial surgery. 2010 Jun 1;39(6):561-7.

12. Kolk A, Schuster T, Chlebowski A, Lange P, Scheidhauer K, Kesting M, Bissinger O, Schwaiger M, Dinges J, Weitz J. Combined SPECT/CT improves detection of initial bone invasion and determination of resection margins in squamous cell carcinoma of the head and neck compared to conventional imaging modalities. European journal of nuclear medicine and molecular imaging. 2014 Jul;41:1363-74.

13. Söderholm AL, Lindqvist C, Hietanen J, Lukinmaa PL. Bone scanning for evaluating mandibular bone extension of oral squamous cell carcinoma. Journal of oral and maxillofacial surgery. 1990 Mar 1;48(3):252-7.

14. Carter RL, Tsao SW, Burman JF, Pittam MR, Clifford P, Shaw HJ. Patterns and mechanisms of bone invasion by squamous carcinomas of the head and neck. The American Journal of Surgery. 1983 Oct 1;146(4):451-5.

15. Marchetta FC, Sako K, Murphy JB. The periosteum of the mandible and intraoral carcinoma. The American Journal of Surgery. 1971 Dec 1;122(6):711-3.

16. Bahadur S. Mandibular involvement in oral cancer. The Journal of Laryngology & Otology. 1990 Dec;104(12):968-71.

17. Barttelbort SW, Bahn SL, Ariyan S. Rim mandibulectomy for cancer of the oral cavity. The American Journal of Surgery. 1987 Oct 1;154(4):423-8.

18. Rao LP, Das SR, Mathews A, Naik BR, Chacko E, Pandey M. Mandibular invasion in oral squamous cell carcinoma: investigation by clinical examination and orthopantomogram. International journal of oral and maxillofacial surgery. 2004 Jul 1;33(5):454-7.

19. Langdon JD, Harvey PW, Rapidis AD, Patel MF, Johnson NW, Hopps R. Oral cancer: the behaviour and response to treatment of 194 cases. Journal of Maxillofacial Surgery. 1977 Jan 1;5:221-37.

20. Snow Jr JB, Gelber RD, Kramer S, Davis LW, Marcial VA, Lowry LD. Randomized preoperative and postoperative radiation therapy for patients with carcinoma of the head and neck: preliminary report. The Laryngoscope. 1980 Jun;90(6):930-45.

21. Brown JS, Lowe D, Kalavrezos N, D'Souza J, Magennis P, Woolgar J. Patterns of invasion and routes of tumor entry into the mandible by oral squamous cell carcinoma. Head & Neck: Journal for the Sciences and Specialties of the Head and Neck. 2002 Apr;24(4):370-83.

22. Huntley TA, Busmanis I, Desmond P, Wiesenfeld D. Mandibular invasion by squamous cell carcinoma: a

computed tomographic and histological study. British Journal of Oral and Maxillofacial Surgery. 1996 Feb 1;34(1):69-74.

23. Ord RA, Sarmadi M, Papadimitrou J. A comparison of segmental and marginal bony resection for oral squamous cell carcinoma involving the mandible. Journal of oral and maxillofacial surgery. 1997 May 1;55(5):470-7.

24. Van Cann EM, Dom M, Koole R, Merkx MA, Stoelinga PJ. Health related quality of life after mandibular resection for oral and oropharyngeal squamous cell carcinoma. Oral Oncology. 2005 Aug 1;41(7):687-93.

25. Carter RL, Foster CS, Dinsdale EA, Pittam MR. Perineural spread by squamous carcinomas of the head and neck: a morphological study using antiaxonal and antimyelin monoclonal antibodies. Journal of clinical pathology. 1983 Mar 1;36(3):269-75.

26. Lukinmaa PL, Hietanen J, Söderholm AL, Lindqvist C. The histologic pattern of bone invasion by squamous cell carcinoma of the mandibular region. British Journal of Oral and Maxillofacial Surgery. 1992 Feb 1;30(1):2-7.

27. Müller H, Slootweg PJ. Mandibular invasion by oral squamous cell carcinoma: clinical aspects. Journal of Cranio-Maxillofacial Surgery. 1990 Feb 1;18(2):80-4.

28. Slootweg PJ, Müller H. Mandibular invasion by oral squamous cell carcinoma. Journal of Cranio-Maxillofacial Surgery. 1989 Feb 1;17(2):69-74.

29. Brown JS, Browne RM. Factors influencing the patterns of invasion of the mandible by oral squamous cell carcinoma. International journal of oral and maxillofacial surgery. 1995 Dec 1;24(6):417-26.

30. Schwartz S, Shklar G. Reaction of alveolar bone to invasion of oral carcinoma. Oral Surgery, Oral Medicine, Oral Pathology. 1967 Jul 1;24(1):33-7.

31. McGregor IA, Gordon Macdonald D. Spread of squamous cell carcinoma to the nonirradiated edentulous mandible—a preliminary report. Head & neck surgery. 1987 Jan;9(3):157-61.

32. Kushraj T, Chatra L, Shenai P, Rao PK. Bone invasion in oral cancer patients: A comparison between Orthopantamograph, conventional computed tomography, and single positron emission computed tomography. Journal of cancer research and therapeutics. 2011 Oct 1;7(4):438-41.

33. Kalavrezos ND, Grätz KW, Saller HF, Stahel WA. Correlation of imaging and clinical features in the assessment of mandibular invasion of oral carcinomas. International journal of oral and maxillofacial surgery. 1996 Dec 1;25(6):439-45.

34. Brown JS, Lewis-Jones H. Evidence for imaging the mandible in the management of oral squamouscell carcinoma: a review. British Journal of Oral and Maxillofacial Surgery. 2001 Dec 1;39(6):411-8.

35. Crile G. EXCISION OF CANCER OF THE HEAD AND NECK. WITH SPECIAL REFERENCE TO THE PLAN OF DISSECTION BASED ON ONE HUNDRED AND THIRTY-TWO OPERATIONS. Journal of the American Medical Association. 1906 Dec 1;47(22):1780-6.

36. Dubner S, Heller KS. Local control of squamous cell carcinoma following marginal and segmental mandibulectomy. Head & neck. 1993 Jan;15(1):29-32.

37. Tsue TT, McCulloch TM, Girod DA, Couper DJ, Weymuller Jr EA, Glenn MG. Predictors of carcinomatous invasion of the mandible. Head & neck. 1994 Mar;16(2):116-26.

38. Vidiri A, Guerrisi A, Pellini R, Manciocco V, Covello R, Mattioni O, Guerrisi I, Di Giovanni S, Spriano G, Crecco M. Multi-detector 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. Journal of Experimental & Clinical Cancer Research. 2010 Dec;29:1-8.

39. Gu DH, Yoon DY, Park CH, Chang SK, Lim KJ, Seo YL, Yun EJ, Choi CS, Bae SH. CT, MR, 18F-FDG PET/CT, and their combined use for the assessment of mandibular invasion by squamous cell carcinomas of the oral cavity. Acta Radiologica. 2010 Dec 1;51(10):1111-9.

40. Uribe S, Rojas LA, Rosas CF. Accuracy of imaging methods for detection of bone tissue invasion in patients with oral squamous cell carcinoma. Dentomaxillofacial Radiology. 2013 Jun 1;42(6):20120346.

41. Hong SX, Cha IH, Lee EW, Kim J. Mandibular invasion of lower gingival carcinoma in the molar region: its clinical implications on the surgical management. International journal of oral and maxillofacial surgery. 2001 Apr 1;30(2):130-8.