Value of cone beam computed tomography for detecting bone invasion in squamous cell carcinoma of the maxilla

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Objective. To determine the diagnostic value of cone beam computed tomography (CBCT) in detecting bone invasion in maxillary squamous cell carcinoma (MSCC).

Study Design. In this retrospective cohort study, preoperative CBCT scans were independently assessed by a single surgeon in imaging assessment 1 (IA 1) and by 1 surgeon with 2 dentists in consensus (IA 2) for the presence of bone invasion in MSCC. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, area under the receiver operating characteristic curve (AUC), and Cohen's κ were calculated. Histopathologic results of resection specimens served as the reference standard.

Results. Of 27 patients, 19 (70%) had proven bone invasion. IA 1 yielded 68.4% sensitivity, 75.0% specificity, 86.7% PPV, 50.0% NPV, 70.4% accuracy, and 0.717 AUC. All results of IA 2 were true-positive and true-negative, resulting in 100% sensitivity, specificity, PPV, NPV, accuracy, and AUC. The assessments differed in 6 cases. Interobserver κ was fair (0.38, 95% CI 0.04-0.72, $P = .038$). There was a significant association between CBCT detection of bone invasion and extent of surgical treatment ($P = .006$)

Conclusions. The diagnostic accuracy of CBCT was high but observer-dependent. CBCT examination may be useful in surgical treatment planning. (Oral Surg Oral Med Oral Pathol Oral Radiol 2022;134:102−109)

Maxillary squamous cell carcinoma (MSCC) usually originates from the mucosa of the alveolar process or hard palate. It can invade the adjacent bone and grow into the maxillary sinus or nasal cavity.[1] The preferred treatment is complete surgical removal of the tumor.[2,3] The preoperative extent of bone invasion involving the maxilla may be challenging to predict. Therefore, a reliable imaging method for preoperatively detecting invasion is important in order to limit the resection size. Preoperative computed tomography (CT) is often used for detecting maxillary bone invasion.[4-6]

Cone beam computed tomography (CBCT) is an alternative to conventional spiral CT imaging. A conical X-ray beam captures the image in 1 exposure and requires less time, produces lower radiation dosage to the patient, and generates images with higher spatial resolution than CT.[7,8] Furthermore, patients are not required to lie down but can sit with their head in the natural position during the scanning procedure.[8] Because of these advantages, CBCT has gained popularity over the last 2 decades in multiple fields of dentistry and oral and maxillofacial surgery. Detecting mandibular bone invasion with CBCT has been examined,[9,10] but, to the best of our knowledge, no studies have focused on the maxilla. Therefore, the potential value of CBCT to detect maxillary bone invasion by oral cancer is a subject of interest.[8]

The objective of this study was to determine the diagnostic value of CBCT for detecting bone invasion by MSCC. We hypothesized that the diagnostic value of CBCT would be high and that interobserver agreement would be good.

METHODS

This retrospective cohort study was exempted from ethical review by the Institutional Review Board Utrecht. The guidelines of the Declaration of Helsinki were followed. The research findings were written in accordance with the Standards for the Reporting of Diagnostic Accuracy Studies (STARD) criteria[11] and Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[12]

Statement of Clinical Relevance

This study demonstrates that cone beam computed tomography can accurately detect bone invasion of the maxilla, which might be beneficial during preoperative assessment of oral squamous cell carcinoma of the maxilla. However, the results are observer-dependent.

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Consecutive patients surgically treated for MSCC between September 2013 and August 2018 and who had had a preoperative CBCT scan were identified from the departmental database. To be included, the MSCC had to originate from the mucosa of the alveolar process or the hard palate. Exclusion criteria were sinonasal tumors, histopathologic tumor types other than squamous cell carcinoma, and imaging artifacts on the CBCT scan.

Preoperative evaluation

The standardized preoperative diagnostic work-up included physical examination, radiologic imaging, and ultrasonography of the neck with fine-needle aspiration cytology when examination results indicated possible metastasis. Orthopantomogram radiographs and CBCT were performed if the tumor was localized near or attached to the maxilla. Magnetic resonance imaging (MRI) was acquired for staging of the neck, s but spiral CT of the head and neck area was performed instead if MRI was contraindicated because of claustrophobia or the presence of metallic dental restorations that could cause imaging artefacts.

CBCT

CBCT was performed with the classic i-CAT scanner (Imaging Sciences International, Inc, Hatfield, PA, USA) using i-CAT vision software version 1.9.314. The scanning parameters were standardized at 120 kVp, 8.2 mA, and scan time of 15.1 seconds, with exposure time of 1.8 seconds. The field of view (FOV) was 10 × 5 cm for small- and medium-sized tumors and 12 × 8 cm for large lesions. Scans were performed with the patients seated and in the natural head position.

Tumor staging

The American Joint Committee on Cancer tumor and node metastasis staging classification was used.[13] The clinical examination, imaging, and histopathologic findings were discussed in a weekly multidisciplinary team meeting to ascertain the clinical tumor and node metastasis staging and determine the optimal treatment plan according to national guidelines.[14]

Surgical treatment

Surgical procedures comprised local soft tissue resection, partial maxillectomy, hemimaxillectomy, or (sub) total maxillectomy. Patients were treated within 3 weeks of preoperative staging. When histopathologic analysis demonstrated tumor cells less than 1 mm from the surgical margin, re-resection of the relevant margin was performed if feasible. If re-resection was not feasible, adjuvant radiotherapy was administered.

Histopathologic evaluation

Standardized histopathologic examination of the resection specimens was performed. The resection specimens were cut into 3-mm-thick buccopalatal slices with a water-cooled, engine-driven, circular diamond-coated saw blade. The slices were decalcified in 10% formic acid and processed in paraffin wax. The formalin-fixed, paraffin-embedded tissue was sectioned at 5 μm and stained with hematoxylin and eosin. A head and neck pathologist examined the slides and reported the findings in a standardized histopathologic report.

Imaging assessment 1

Imaging assessment 1 (IA 1) was performed by a single surgeon (J.T.M.V.G.) who assessed the CBCT scans. The reviewer was blinded to the original imaging reports and the histopathologic results but was informed of the tumor location. Bone invasion was defined as any disruption of the cortical bone adjacent to the abnormal soft tissue mass and categorized as present or absent.

Imaging assessment 2

Imaging assessment 2 (IA 2) was performed by 1 surgeon (E.M.V.C.) and 2 dentists (M.G.S. and S.F.) who assessed the CBCT scans, similar to a clinical scenario in which colleagues assess CBCT images together. The reviewers in IA 2 were blinded to the original imaging reports and the histopathologic results, but they were informed of the tumor location. To investigate whether additional diagnostic criteria would improve the interpretation of the CBCT images, bone invasion was categorized as the presence of cortical interruption, the presence of cortical interruption and invasion into the maxillary sinus and/or nasal cavity, or absent. Disagreements between the surgeon and dentists were resolved by discussion until consensus was reached.

The results of IA 1 and IA 2 were used to calculate the diagnostic test efficacies of CBCT. The predictor variable was the presence of bone invasion on the CBCT images. For IA 1, the results were dichotomized as the presence or absence of bone invasion. The results from IA 2 were dichotomized as the presence of bone invasion (i.e., cortical interruption or cortical interruption with invasion into the maxillary sinus and/ or nasal cavity) or the absence of bone invasion (no cortical interruption).

The outcome variable was the presence or absence of bone invasion on histopathologic examination of the resection specimens. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, and 95% CI were calculated with cross-tabulations.

For each imaging assessment, receiver operating characteristic (ROC) curves were computed, and the area under the curve (AUC) was calculated. The AUC was considered excellent if ≥0.91, very good if 0.81 to 0.90, good if 0.71 to 0.80, sufficient if 0.61 to 0.70, and bad if 0.51 to 0.60.[15]

The sensitivity, specificity, PPV, NPV, accuracy, and AUC results of IA 1 were compared with IA 2. Fisher's exact test was used to examine the association between bone invasion and surgical treatment type. The association was considered statistically significant at $P < .05$.[16]

Agreement between the results of IA 1 and IA 2 was calculated with Cohen's kappa (κ). IA 1 had 1 rater as the consequent observer. IA 2 had 3 raters working in consensus serving as the consequent observer, which required a variant application of Cohen's κ analysis.[17-20] Agreement was considered very good if κ was 0.81 to 1.00, good if κ was 0.61 to 0.80, moderate if κ was 0.41 to 0.60, fair if κ was 0.21 to 0.40, and poor if κ was ≤0.20.[21]

Kaplan-Meier survival analysis was performed to calculate the 2-year local control rate, the 2-year regional recurrence rate, and the 2-year disease-specific survival rate of patients with MSCC. The 2-year local control rate was defined as the proportion of patients without local recurrence 2 years after surgery. The 2-year regional recurrence rate was defined as the proportion of patients with regional recurrence within 2 years after surgery. The 2-year disease-specific survival rate was defined as the proportion of patients who had not died of MSCC within 2 years after surgery. The log-rank test ($\alpha = 0.05$) was used to analyze statistical differences between patients with and without bone invasion in relation to the local control rate, the regional recurrence rate, and the disease-specific survival rate. The log-rank test was considered statistically significant at $P < .05$.[22] Missing or indeterminate data were handled by pairwise deletion.

Sample size calculation

The study aimed to determine interobserver agreement for CBCT imaging assessments. The hypothesis was that the minimum value for Cohen's κ coefficient would be 0.6 (K2 = 0.6), vs the null hypothesis of no agreement (K1 = 0). Twenty cases were required to detect a 0.6 κ minimum value. The power and alpha were prespecified at 80.0% and 0.05, respectively. It was assumed that the proportion of ratings in agreement by both raters in each category would be considered directly proportional to one another.[23] IBM SPSS Statistics version 25.0 for Windows (IBM Corp., Armonk, NY, USA) was used for statistical analysis.

RESULTS

Sixty patients were potentially eligible for inclusion. Of these patients, 12 were excluded because they had histologic tumor types other than squamous cell carcinoma and 21 had no preoperative CBCT scan. In total, 27 patients were included (Figure 1).

Table I shows the baseline characteristics of the study population. There were 7 male patients (26%) and 20 female patients (74%). Age at the time of surgery ranged from 38 to 92 years. The most frequent tumor location was the alveolar process (82%). There were 11 pT1 tumors (41%), 5 pT2 tumors (19%), 2 pT3 tumors (7%), and 9 pT4 tumors (33%). The tumor diameters ranged from 1 to 68 mm. Five patients had cervical lymph node metastasis (19%), but there were no patients with distant metastases. Additional information about the patients and tumor properties is included in Supplementary Table SI.

The results of IA 1 and IA 2 are listed in Table II. Histopathologic examination of the resection specimens revealed bone invasion in 19 patients (70.4%). IA 1 yielded 13 true-positive (TP), 2 false-positive (FP), 6 true-negative (TN), and 6 false-negative (FN) results, which indicated 68.4% sensitivity, 75.0% specificity, 86.7% PPV, 50.0% NPV, and 70.4% accuracy. Figure 2 shows CBCT images with TP, FP, TN, and FN cases based on IA 1. In contrast, IA 2 yielded only TP and TN results, which indicated 100% sensitivity, 100% specificity, 100% PPV, 100% NPV, and 100% accuracy. ROC curves were computed for IA 1 and IA 2 (Figure 3). AUC of IA 1 was good (.717), and AUC of IA 2 was excellent (1.000).

Of the 19 patients diagnosed with bone invasion, 12 had a partial maxillectomy and 7 had a hemimaxillectomy. Of the 8 patients without bone invasion, 3 had a local soft tissue resection, and 5 had a partial maxillectomy. According to Fisher's exact test, there was a statistically significant association between bone invasion and the surgical treatment type ($P = .006$).

The results of IA 1 and IA 2 were different in 6 cases. Consequently, the κ for interobserver agreement was .38 (95% CI 0.04-0.72; $P = .038$). The interobserver agreement was therefore deemed fair, with statistically significant differences between the 2 imaging assessments.

Two years after surgery, 1 patient was diagnosed with local recurrence, which resulted in a 2-year local control rate of 96.3%. The patient with local recurrence had been diagnosed with bone invasion. According to the local control rate log-rank test, bone invasion was not statistically significant in local recurrence ($P = .516$) (Figure 4A). Four patients were diagnosed with regional recurrence (3 with bone invasion, 1 without bone invasion) 2 years after surgery, which resulted in a 2-year regional recurrence rate of 14.8%. The regional recurrence rate log-rank test showed that bone invasion was not statistically significant ($P = .760$) (Figure 4B). Five patients, all with bone invasion, died

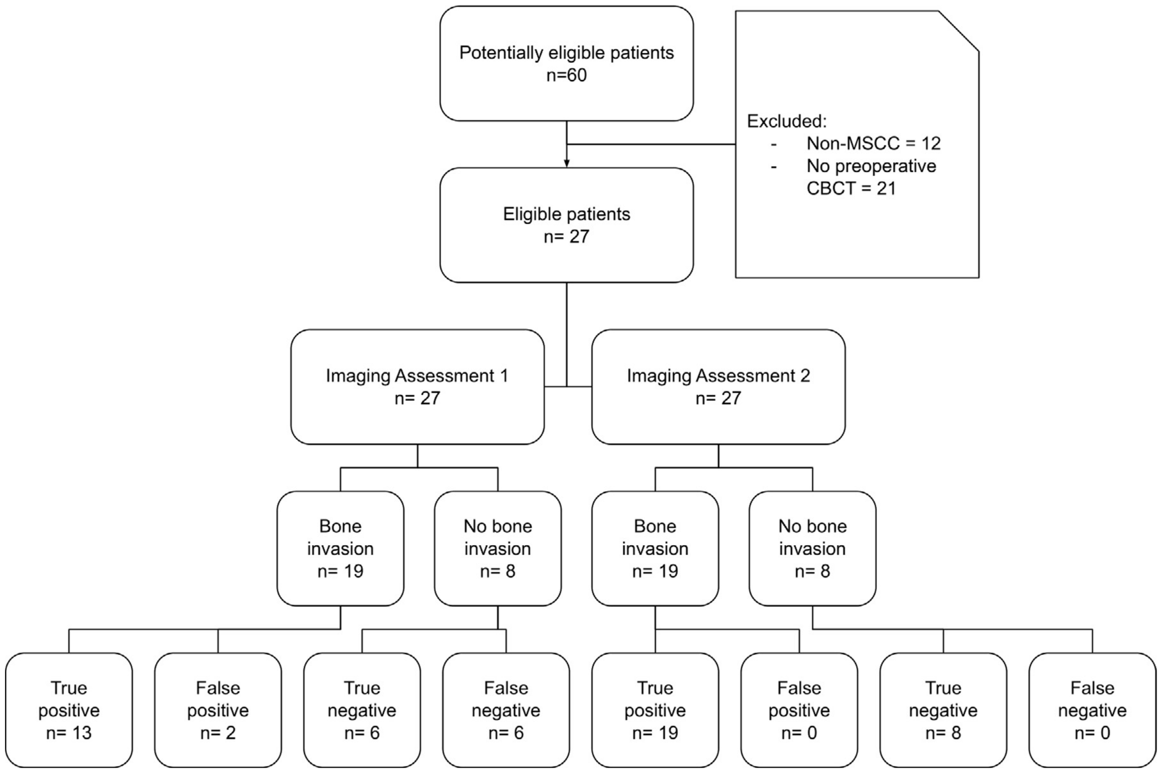

Fig. 1. Flowchart of the patients and imaging assessments 1 and 2. *MSCC*, maxillary squamous cell carcinoma; *CBCT*, cone beam computed tomography.

of MSCC within 2 years after surgery. The 2-year disease-specific survival rate was 81.5%. According to the log-rank test of the disease-specific survival rate, bone invasion was not statistically significant (P = .123) (Figure 4C).

Table I. Patient demographic information and tumor characteristics

Sex	
Male	7 (26%)
Female	20 (74%)
Age (yrs)	38-92
Tumor Location	
Alveolar process	22 (82%)
Hard palate	3 (11%)
Alveolar process and hard palate	2 (7%)
Tumor Stage	
T1	11 (41%)
T2	5 (19%)
T3	2 (7%)
T4	9 (33%)
Tumor Diameter (mm)	1-68
Cervical Lymph Node Metastasis	
Present	5 (19%)
Absent	22 (81%)
Distant Metastasis	
Present	0 (0%)
Absent	27 (100%)

DISCUSSION

A recent systematic review compared the accuracy of CBCT with CT, MRI, single-photon emission CT, multislice computed tomography (MSCT) with contrast, and panoramic radiography (PR).[8] Two studies mentioned in this systematic review reported on detection of bone invasion by CBCT. The first investigation assessed bone invasion of the mandible by squamous cell carcinoma, for which CBCT had 93% sensitivity, 62% specificity, and 78% accuracy.[10] The second study assessed bone invasion of the mandible by oral tumors located in the floor of the mouth, retromolar area, and mandibular alveolar process, for which CBCT had 90.9% sensitivity, 100% specificity, and 95.7% accuracy.[9] The systematic review concluded that the NPV of CBCT (89.83%) and single-photon emission CT (95.53%) for detecting bone invasion of the mandible were much higher than the NPV of CT, MRI, MSCT, and panoramic radiography. Scanning the patient in the natural head position and the higher spatial resolution of CBCT scans might have contributed to the favorable test results for this imaging modality.[8]

In our investigation, the assessment of CBCT for bone invasion by 1 observer (IA 1) yielded good results (sensitivity 68.4%, specificity 75.0%, PPV 86.7%, NPV 50.0%, accuracy 70.4%, AUC 0.717). However, assessment by 3 observers in consensus

Table II. Diagnostic results of the imaging assessments.

Imaging Assessment 1		*Imaging Assessment 2*	
Sensitivity	68.4% (95% CI 43.5-87.4%)	Sensitivity	100% (95% CI 82.4-100%)
Specificity	75.0% (95% CI 35.0-96.8%)	Specificity	100% (95% CI 63.1-100%)
PPV	86.7% (95% CI 65.3-95.7%)	PPV	100%
NPV	50.0% (95% CI 31.6-68.4%)	NPV	100%
Accuracy	70.4% (95% CI 50.0-86.3%)	Accuracy	100% (95% CI 87.2-100%)
AUC	.717 (95% CI .501-.933)	AUC	1

PPV, positive predictive value; *NPV*, negative predictive value; *AUC*, area under the curve.

(IA 2) yielded perfect results (sensitivity, specificity, PPV, NPV, and accuracy all 100%, with an AUC value of 1). These results indicate that CBCT was of value for detecting maxillary bone invasion by MSCC. However, the results were observer-dependent. The κ value for interobserver agreement between IA 1 and IA 2 was only fair (0.38), with a significant difference in agreement (P = .038) between the imaging assessments.

Observer dependence may have been caused by differences in training and experience of the observers.[24-26] However, we think this is unlikely because all observers in this study had been trained and were experienced in interpreting CBCT scans. It is more probable that IA 2 yielded perfect outcomes because the 3 observers shared their expertise in the process of coming to consensus. This suggests that joint evaluation of the scans and discussion can improve the diagnostic efficacy of CBCT.

Observer-dependent results may have been caused by the lack of scoring criteria. Standardized scoring and reporting have been shown to improve the interpretation of scans of the appendix, pulmonary edema, and adnexal masses.[27-29] Standardized reporting helps with the correct interpretation of imaging in general.[30] To the best of our knowledge, there are no studies on the value of standardized scoring and reporting of CBCT scans for oral cancer. This study reached the highest accuracy when the scans were assessed with the more specifically defined categories in IA 2. Our findings suggest, therefore, that the use of specific criteria improves the interpretation of CBCT imaging for bone invasion by MSCC.

Formats for structured reporting of CT and MRI scans have been widely adopted to describe the location of the primary tumor, the extent of soft tissue and bony involvement, and nodal status.[31] Similar formats

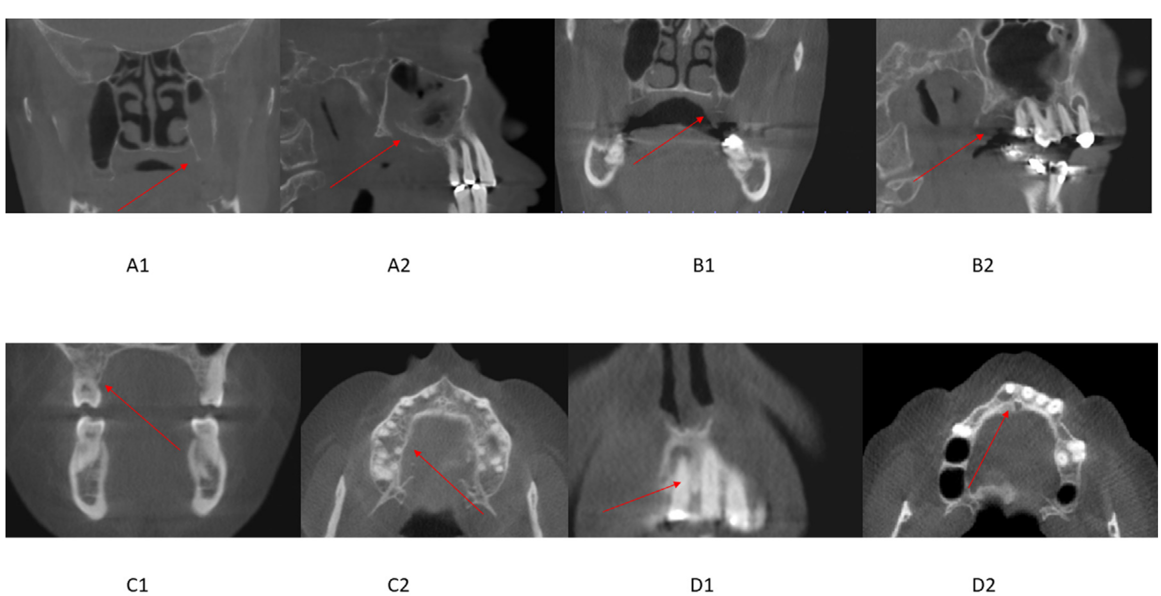

Fig. 2. **(A)** Cone beam computed tomography (CBCT) images of a true-positive case of bone invasion. Coronal **(A1)** and sagittal **(A2)** sections reveal invasion of the tumor into the alveolar process (*arrows*). **(B)** CBCT images of a false-positive case of bone invasion. The *arrows* on the coronal **(B1)** and sagittal **(B2)** sections indicate apparent invasion of the tumor into the alveolar process, but histopathologic examination revealed no invasion. **(C)** CBCT images of a true-negative case of bone invasion. The *arrows* on the coronal **(C1)** and axial **(C2)** sections indicate the area of maxillary squamous cell carcinoma, with no radiographic or histopathologic evidence of bone invasion. **(D)** CBCT images of a false-negative case of bone invasion. The *arrows* on the coronal **(D1)** and axial **(D2)** sections indicate no apparent invasion of bone, but histopathologic examination revealed invasion.

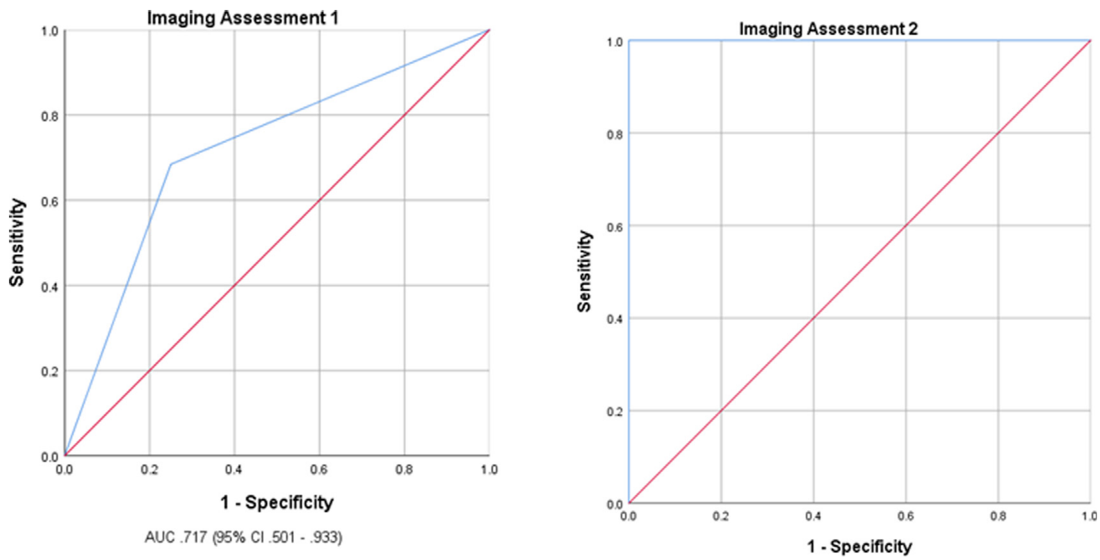

Fig. 3. Receiver operating characteristic curves and area under the curve results.

for CBCT reports are not now in place. Clear, peer-reviewed guidelines are lacking for interpreting and reporting CBCT images of oral cancer. High-quality imaging reports should be accurate, clear, complete, and timely.[32] A CBCT report format has been proposed in general practice that mentions all anatomic subheadings that may be depicted on a CBCT scan: paranasal sinuses, nasal cavity, airway, cervical spine, temporomandibular joint, dental findings, other non-dental findings, and recommendations.[33] In this way, the observer is forced to analyze every section of the CBCT image and report findings in a standardized manner without completing inefficient and time-costly formats.

The accuracy of CBCT for detecting bone invasion in MSCC and the interobserver agreement may improve by incorporating the essential CT/MRI reporting requirements of oral tumors (primary tumor dimensions, soft tissue involvement, bony involvement, and nodal status)[31] into the CBCT report format as proposed by Miles and Danforth.[33] Whether standardized reporting helps to improve the accuracy and interobserver agreement of CBCT in detecting bone invasion needs to be evaluated in the future.

If bone invasion is present, it is often necessary to increase the resection size so that complete surgical removal of the tumor might be achieved.[2,3] Our results indicated that CBCT was helpful for surgical planning because the depiction of bone invasion on CBCT appeared significantly associated with wider surgical resection of the primary tumor (P = .006).

In this study, bone invasion diagnosed on the basis of preoperative CBCT was not significantly associated with the 2-year local control rate (P = .516), the 2-year regional recurrence rate (P = .760), or the 2-year disease-specific survival rate (P = .123). In 2003, Ogura et al.[34] showed that bone invasion diagnosed on the basis of preoperative spiral CT was significantly predictive for the presence of cervical metastases (P < .05). The case mix may explain the difference in the prognostic value of bone invasion on the preoperative scan. Approximately 60% of our study population had T1-2 tumors, whereas Ogura et al. reported that 85.7% of their patients had a hemimaxillectomy, which might indicate larger tumors in their study population.

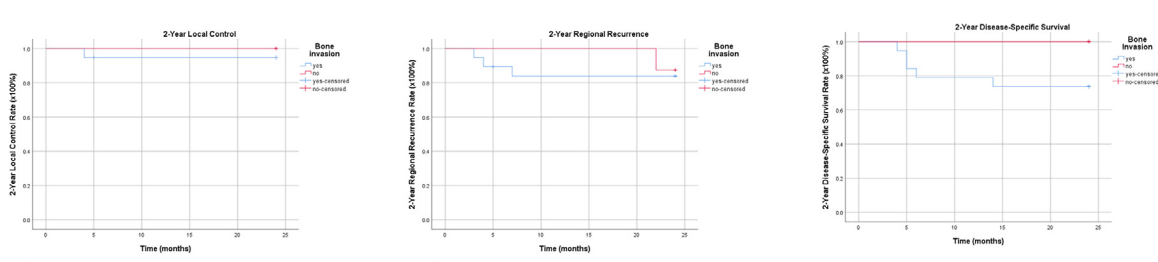

Fig. 4. (A) Kaplan-Meier survival analysis curve of 2-year local control. (B) Kaplan-Meier survival analysis curve of 2-year regional recurrence. (C) Kaplan-Meier survival analysis curve of 2-year disease-specific survival.

Moreover, the clinical importance of bone invasion was corroborated in a study conducted by Slieker et al. in 2019,[35] in which bone invasion was correlated with 5-year overall survival in a Cox multivariate regression analysis.

Limitations

This study was limited by its relatively small sample size due to the very low incidence of MSCC, the retrospective design, and the small number of patients who had received preoperative CBCT scans. Out of 60 potentially eligible patients, 21 patients were not examined with CBCT because they had either spiral CT or MRI or a combination of the two. Nevertheless, for this study, the sample size was deemed sufficient.

CONCLUSION

CBCT is of value for detecting bone invasion in maxillary squamous cell carcinoma (MSCC). The accuracy of CBCT was high but observer-dependent. CBCT examination may be useful in surgical treatment planning.

DECLARATION OF COMPETING INTEREST

None.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.oooo.2022.01.020.

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