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

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Objective. The aim of this study was to compare the performance of cone-beam computerized tomography (CBCT) with multislice CT (MSCT) and single photon emission CT (SPECT) in the detection of bone invasion from oral malignancies.

Study design. In this prospective investigation, 77 patients with histologically proven malignancy of the oral cavity received MSCT, CBCT, and SPECT imaging of the head presurgically. Radiologic evaluations were compared with histopathologic examinations of the resected tumor specimens. Receiver operating characteristic (ROC) analysis as well as the sensitivity, specificity, and positive and negative predictive values were calculated.

Results. The sensitivity, specificity, positive predictive value, and negative predictive value for MSCT were 0.8, 1.0, 1.0, and 0.75, respectively; for CBCT 0.92, 0.965, 0.98, and 0.875; and for SPECT 0.91, 0.4, 0.7, and 0.75. ROC analysis showed area under the curve values of 0.894 (95% confidence interval [CI] 0.806-0.982) for MSCT; 0.931 (95% CI 0.835-1.000) for CBCT, and 0.716 (95% CI 0.566-0.866) for SPECT.

Conclusion. CBCT is accurate in predicting malignancies’ bone involvement and can compete with MSCT and SPECT in detecting bone invasion in patients with oral malignancies. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;112:367-374)
resonance imaging (MRI), panoramic tomography (PT), positron emission tomography (PET), and single photon emission computerized tomography (SPECT), are available to address this question. Because none of these imaging modalities alone is 100% accurate, their optimal combination is crucial in the preoperative assessment of local bone invasion. There is still controversy as to how these imaging modalities should become combined for optimal staging results, even though a combination of preoperative examination methods has been determined to optimally predict a malignancy’s mandibular bone invasion. In our department, the standard protocol for staging oral cavity malignancies includes MSCT and MRI of head and neck, PT, full-body scintigraphy, SPECT of the head, conventional 2-plane x-ray of the chest, and abdominal ultrasound. Results from MSCT, MRI, PT, and SPECT are reviewed to determine if local bone invasion has occurred.

In 1998, cone-beam computerized tomographic (CBCT) technology was clinically introduced, which allows for 3-dimensional (3D) diagnosis of the hard tissues of the face and jaws, third molars, and salivary calculi. There is also evidence that CBCT is a potential tool in the assessment of facial skull bone invasion form oral cavity malignancies. Based on a comparison of the sensitivity and specificity, it can be concluded that CBCT is superior to PT and MRI in the assessment of tumors’ bone invasion. Further advantages of CBCT imaging are lower radiation doses than MSCT and its ability to substitute for PT regarding anatomic assessment of the stomatognathic system. Based on these findings we hypothesized that CBCT should be able to substitute for MSCT and PT in preoperative assessment of bone invasion from oral cavity malignancies. Therefore, we performed a prospective direct comparison between MSCT and CBCT in the assessment of malignant osseous invasion. Additionally, findings of MSCT and CBCT were compared with SPECT analysis.

**MATERIAL AND METHODS**

**Patients**

Permission for this prospective clinical trial from the ethic committee at the University of Cologne was requested and approved beforehand. Patient inclusion criteria were admittance to our department in the period from January 2005 to September 2009 and histologically proven oral cavity malignancy clinically suspect for primary surgical treatment. From all potential patients, 100 individuals were randomly selected to receive an alternative preoperative tumor-staging protocol in which CBCT imaging replaced PT. In particular, patients received MSCT and MRI of the head and neck, CBCT, full-body scintigraphy, SPECT of the head, conventional 2-plane x-ray of the chest, and abdominal ultrasound investigation. According to the cTNM classification after tumor staging, 77 patients qualified for primary surgical treatment and were included in the present study, whereas 23 patients were excluded and referred for neoadjuvant radiochemotherapy. Fifty-eight (75.3%) of the tumors were located in the mandible, 19 (24.7%) in the maxilla. See Table I for patient age and gender distribution as well as histologic tumor classification.

**Image data acquisition**

From the abovementioned preoperative staging investigations, CBCT, MSCT, and SPECT analyses were included in the study.

CBCT scans were taken with the Galileos device (Sirona, Bensheim, Germany). This CBCT device corresponds to the principal setup described elsewhere. Constant scanning parameters were 85 kV and 28 mA. Within 14 seconds, 200 single x-ray raw projections per scan were gathered. The reconstructed 3D volumes had a size of 15 cm in all 3 dimensions. Reformating (secondary reconstruction) allowed the cross sectional

### Table I. Specifications of the patient and tumor cohort

<table>
<thead>
<tr>
<th>n</th>
<th>Patients’ average age (y)</th>
<th>Patients’ age range (y)</th>
<th>Patients’ gender distribution</th>
<th>Tumor sites</th>
<th>Tumors bone invasion</th>
<th>Tumor entities</th>
</tr>
</thead>
<tbody>
<tr>
<td>77</td>
<td>61.04 ± 11.25</td>
<td>32-81</td>
<td>52 (68%) male; 25 (32%) female</td>
<td>19 (24.7%) maxilla; 58 (75.3%) mandible</td>
<td>48 (62%) positive; 29 (38%) negative</td>
<td>67 (87%) SCC; 3 (4%) ACC; 2 (3%) AC; 2 (3%) OSS; 1 (1%) CCC; 1 (1%) Meta; 1 (1%) ND</td>
</tr>
</tbody>
</table>

ACC, Adenoid cystic carcinoma; CCC, clear cell carcinoma; SCC, squamous cell carcinoma; AC, adenocarcinoma; OSS, osteosarcoma; Meta, metastasis of an undifferentiated tumor; ND, not differentiable/not determined.
and panoramic views to be imaged. Visualization were performed with 512 pixels, and a resolution of 300 μm, or 2.5 line pairs per mm. All scans were performed by the same well instructed radiologic technical assistant. Patients were positioned upright, a light localizer was aligned with the midsagittal plane, and contact was made between the patient and the standardized forehead and chin rest. Two senior oral and maxillofacial surgeons assessed the CBCT scans for the presence or absence of bone invasion based on either cortical erosion or complete cortical bone disappearance adjacent to the abnormal tumor’s soft tissue mass. Investigators were aware of the clinical location of the tumor but unaware of the findings from the MSCT and SPECT. Consensus was reached regarding the findings.

MSCT examinations were obtained with 2 state-of-the-art 16-detector-row CT devices: MX8000 IDT or Brilliance 16 (both from Philips Healthcare, Hamburg, Germany). Patients were intravenously injected with 150 ml iohexol (Omnipaque®) 350 mg/ml. MSCT examinations were carried out by using either the NNH (maxillary sinuses) imaging protocol or the CAS (computer-assisted surgery) imaging protocol. The NNH protocol used a slice thickness of 0.8 mm and a reconstruction interval of 0.4 mm, resulting in a voxel size of 0.49 × 0.49 × 0.4 mm. The CAS protocol provided images with a slice thickness of 1 mm and a reconstruction interval of 1 mm, with a voxel size of 0.49 × 0.49 × 1.0 mm. Bone invasion was defined as the erosion or absence of cortical bone adjacent to the abnormal tumor’s soft tissue mass. Two senior radiologists, specialized in head and neck oncology, assessed the MSCT scans for the presence or absence of bone invasion. Investigators were aware of the clinical location of the tumor but unaware of the findings from CBCT and SPECT investigations. Consensus was reached regarding the findings.

Skeletal scintigraphy and SPECT images were performed after intravenous injection of 700 MBq Tc-99m–hydroxyethylene diphosphonate. Three hours after injection, anterior and posterior whole-body images, planar images of the head in 4 views (right-ventral left, left-dorsal right, right lateral, and left lateral) and SPECT images of the head were routinely performed. SPECT of the head and neck area was performed with either a dual-head or a triple-head gamma camera equipped with low-energy high-resolution parallel-hole collimators. The 140 keV photopeak with a 15% window was used with a 128 × 128 matrix and 20 seconds per step for the SPECT acquisition. After reconstruction of the images with a Butterworth filter, the transverse sections were reoriented in the plane parallel to the plane of the jaws and displayed as axial, coronal, and sagittal images. Two nuclear medicine physicians assessed the scans for any increased tracer uptake at the tumor site. Observers were informed of the clinical location of the tumor, but unaware of the findings of MSCT and CBCT. Consensus was reached regarding the findings.

**Image analysis**

For all CBCT, MSCT, and SPECT investigations, the presence or absence of bone involvement in the primary tumor site was assessed by 2 experienced investigators as specified for each imaging modality above. Observers were aware of the patient’s clinically diagnosed tumor site and evaluated the x-ray examinations prospectively to the planned surgical procedure. For CBCT and MSCT, tumor invasion of the bone was considered to be present if the cortical bone in the primary tumor site showed strictly local signs of erosion or degradation (Figs. 1-3) as differentiation criteria for general periodontal disease where multiple cortical erosion sites are present. For SPECT analysis, any increased tracer uptake at the tumor site was considered to be a sign of tumor invasion. Tumor involvement of the bone had to be rated as present or absent as a consensus decision from both of the investigators.

Whereas SPECT examinations were visualized on film-based printed images, as described above, CBCT and MSCT examinations were visualized on a radiology workstation consisting of a monitor and a computer. The monitor (Captiva E1701; Berkgirchenfeldgeding, Germany) had a 43.2-cm-diagonal display, a resolution of 1,280 × 1,024 pixels, a contrast of 700:1, and an image refresh rate of 75 Hz. The computer possessed a 3.4 GHz CPU and a graphic card with 256 MB card memory, 400 MHz clock speed, and 128-bit memory interface.

Evaluation took place in a room equipped with window shades and dimmable light for a standardized low-lit ambience illumination.

CBCT data processing and visualization was performed with the visualization software Galaxis (Sirona, Bensheim, Germany) accompanying the CBCT device.

MSCT images were processed with visualization software accompanying the Philips CT devices after being imported in DICOM 3.0 format. The windowing was adapted to optimal bone illustration by choosing the “bone window” from the software’s presets. Soft tissue visualization was not considered in the present study.

Common software features for the applications used were controls to adjust contrast and brightness as well as zoom. Reconstructed orthogonal (sagittal, coronal, and axial) planes of the tumor sites from CBCT and MSCT data sets were intensively investigated by the observers before a consensus decision was made re-
Regarding the presence or absence of malignancies bone invasion.

**Histopathologic assessment**

Surgical specimens were fixed in 4% buffered formalin and cut coronally into 3-mm-thick slices. For decalcification of bone structures, specimens were submerged into EDTA solution (34 g/L Tris amine and 100 g/L Titriplex) at room temperature with constant stirring. The exposure time varied depending on bone type and density and was checked routinely until bone was dissectible with a knife. After routine paraffin embedding, 3-mm-thick sections were cut and stained with hematoxylin and eosin. Microscopic analysis was performed by an experienced pathologist who was unaware of the preoperative imaging results (Fig. 1, C).

**Statistical analysis**

The pathologists’ histopathologic findings regarding the presence or absence of bone invasion by tumor were considered to be the criterion standard. This was then correlated with the preoperatively assessed findings from CBCT, MSCT, and SPECT visualizations. For evaluation and comparison of CBCT, MSCT, and SPECT, the receiver operating characteristic (ROC) curve and a descriptive statistical analysis were applied to determine each image modality’s sensitivity, specificity, and positive and negative predictive values. Results were calculated with SPSS 17.0 software for Windows (SPSS, Chicago, IL, USA).

**RESULTS**

Seventy-seven patients with histologically proven malignancy were included in the present prospective study. The patients’ cohort and histopathologic specifications of the resected tumor specimens are summarized in Table I.

The calculated sensitivity, specificity, positive predictive value, and negative predictive value for bone malignancies, which were derived from an analysis of the preoperatively assessed imaging modalities, are presented in Table II.

MSCT showed a sensitivity, specificity, positive predictive value, and negative predictive value of 0.8, 1.0, 1.0, and 0.75, respectively. For CBCT examination, a sensitivity of 0.92, a specificity of 0.965, a positive predictive value of 0.98, and a negative predictive value of 0.875 were calculated. Results for the preoperatively

the tumor mass on the lower left and lower right. Tumor cells are separated from the normal bone in the picture’s center.
assessed SPECT investigations were sensitivity 0.91, specificity 0.4, positive predictive value 0.7, and negative predictive value 0.75.

The results of ROC analysis are illustrated in Fig. 4 and Table II. The area under the curve (AUC) value for CBCT was 0.931 (95% confidence interval [CI] 0.835-1.000), which was superior to MSCT [0.894 (95% CI 0.806-0.982)] and SPECT [0.716 (95% CI 0.566-0.866)]. However, because of the overlap from the 95% CI of the ROC analysis, the investigated differences cannot be classified as significant between CBCT, MSCT, and SPECT.

DISCUSSION
At present, no single imaging technique is sufficiently accurate to predict the presence of bone invasion from oral malignancies. Several studies recommend a combination of various imaging techniques to combine their distinct advantages for the achievement of relatively reliable preoperative tumor staging results. The value of MSCT and MRI is still being discussed. For the assessment of mandibular invasion, the currently preferred diagnostic algorithm consists of either MSCT or MRI followed by bone SPECT in cases in which the first scan shows no signs of mandibular invasion. Such combinations predict mandibular invasion equally accurately in 85% of patients, without yielding false negative results. However, the cited study did not include consideration of CBCT technology.

In 1998, CBCT technology was clinically introduced and showed promising results for its diagnostic value. In particular, CBCT data sets achieve similar information and visualization quality for high-contrast structures, such as bone, compared with MSCT investigations. Additionally, CBCT had substantially better sensitivity and specificity rates in the assessment of tumoral bone invasion than MRI. Based on these considerations, the present study was performed to clarify the question of whether CBCT can replace MSCT in preoperative assessment of malignant bone invasion of the jaw. Results were also compared with SPECT results.

CBCT scanners provide adequate image quality for dentomaxillofacial examinations. However, it must be kept in mind that there are large variations in patient dose, displayed field of view (FOV), resolution, artifact influence, and image quality. These differences are mainly based on imaging parameters and applied detector technologies, such as image intensifiers and flat-panel detectors, as well as on reconstruction algorithms. The CBCT device of the present study proved MSCT-like diagnostic potential for high-contrast structures, such as bone or salivary calculi, and shows one of the lowest radiation dosages compared with 7 other...
CBCT devices. The FOV size is sufficient to visualize all important anatomic structures for the assessment of tumor invasion in both jaws and additionally enables secondary panoramic view reconstructions with similar or even higher diagnostic value than conventional PT visualizations.

MSCT, MRI, and SPECT are error prone in cases of periapical and periodontal diseases or remodeling procedures after trauma, such as tooth extraction, which easily can be misinterpreted as bone invasion by an oral cavity tumor. PT can display the stomatognathic systems in a way that is easily extrapolated to the clinical situation and allows for reliable safeguarding of periodontal lesions and extraction sockets. PT in addition to MSCT or MRI therefore can help to reduce false-positive misinterpretations and is additionally useful for the planning and implementation of surgical modifications (Fig. 3) of the bone in tumor surgery. The applied CBCT system from the present study routinely displays PT-like views. These secondary reconstructed PT views have similar or even higher diagnostic value than conventional PT visualizations.

Results from the present investigation showed similar sensitivity rates for CBCT and SPECT, whereas MSCT showed a lower sensitivity rate. Although specificity was unreliable for SPECT investigations, MSCT

Table II. Results overview for the 3 investigated imaging modalities in the evaluation of bone invasion from oral cavity malignancies

<table>
<thead>
<tr>
<th>Imaging modality</th>
<th>Descriptive analysis</th>
<th>ROC analysis</th>
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<tbody>
<tr>
<td></td>
<td>Sensitivity</td>
<td>Specificity</td>
</tr>
<tr>
<td>CBCT</td>
<td>0.92</td>
<td>0.965</td>
</tr>
<tr>
<td>MSCT</td>
<td>0.8</td>
<td>1</td>
</tr>
<tr>
<td>SPECT</td>
<td>0.91</td>
<td>0.4</td>
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</table>

Although the AUC level for CBCT was favorable compared with MSCT and SPECT, the observed differences here did not reach significance level, owing to the overlap of the 95% CIs.

ROC, receiver operating characteristic; PPV, positive predictive value; NPV, negative predictive value; AUC, area under ROC curve; CI, confidence interval.

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showed a slightly superior specificity rate than CBCT. ROC analysis showed a slightly superior overall diagnostic reliability for the assessment of malignancies’ bone infiltration to CBCT compared with MSCT and SPECT. However, because of the overlap of the 95% CI, the observed differences did not reach significance level.

CBCT also could not be used to correctly classify all cases with present bone invasion, especially when only subtle bone invasion of small portions from the alveolar crest was present or metal-dense restorations and image noise hampered image quality. For CBCT the present study’s sensitivity rate of 92% was slightly higher but similar to the 89% from Momin et al. (2009)12 or the 91% from Hendrikx et al. (2010).11 In contrast to this, specificity values vary widely: 60% from Momin et al.12 and 100% from Hendrikx et al.11 The difficulty in distinguishing tumor invasion from periodontal disease was suggested as a reason for the large amount of false positive results found by Momin et al.,12 because both diseases lead to radiologically detectable local erosion of cortical bone. Possible explanations for the observed CBCT specificity differences in the assessment of tumor invasion therefore have to be discussed here. Momin et al. calculated their specificity as a mean value from the results of 5 different observers ranging from 29% to 86%. These data indicate a higher observer dependency than Momin et al. reported, which might have been triggered by observers’ different experience levels. Contrasting the specificity rate of 97% from the present study and the 100% specificity rate found by Hendrikx et al., one can assume that the 60% of Momin et al. are presumably underestimated. Another possible explanation for the observed specificity differences might by higher periodontal disease rates among the patient cohort investigated by Momin et al., which therefore led to more false positive diagnoses. In the present study, tumor invasion of the bone was considered to be present if the cortical bone at the primary tumor site showed strictly local signs of erosion or disappearance as differentiation criteria against general periodontal disease (Fig. 2). With these differentiation criteria, a relatively high specificity rate could be achieved for CBCT. Therefore, the specificity rate of CBCT for local tumor invasion with the abovementioned criteria is still error-prone in the relatively unlikely situation in which isolated periodontal disease is present only at a patient’s primary tumor site. In such cases bone invasion could be false-positively diagnosed, biasing the present study’s results.

MSCT tends to underestimate the extent of bone invasion. This is supported by the restricted sensitivity rate of 0.8, which demonstrates that smaller bone invasions are especially not easily detected in MSCT. Proper diagnosis in MSCT also can be hampered by metal-dense structures in the occlusion plane resulting in beam hardening, blur outs, and streak artifacts potentially obscuring important areas. For MSCT, potential influence factors on the image quality are even more abundant than for CBCT and can result from the amount of rows from the detector, the applied imaging protocol, and scanning parameters. Whereas the radiation dose is generally higher for MSCT than for CBCT, it must not be neglected that the application of different low-dose protocols can significantly reduce the radiation from MSCT examinations. On the other hand, these protocols are sometimes accompanied by reduced image quality and small FOVs. Another noteworthy disadvantage of MSCT examinations is the potential induction of severe anaphylactic reactions if intravenous contrast dye is injected.

An important aspect of the present study is the comparison based on 2 different MSCT machines and 2 different MSCT imaging protocols. However, both MSCT scanners were equipped with 16-row detectors that use the same provider’s technology, so image quality differences can be neglected. The imaging protocols were chosen because of their broad application for routine diagnosis of the facial skeleton, assuming that both protocols generate images at a quality level that allows for a comparison with CBCT scans. The CAS protocol was applied in only 2 of the 77 cases and therefore had only minor contribution to the present study results. Predominantly, the NNH protocol with its slice thickness of 0.8 mm and a reconstruction interval of 0.4 mm was applied here. In this context, the literature shows that reconstruction intervals of 1 mm are sufficient for the assessment of tumoral bone invasion in the mandible, and our NNH protocol exceeded this demand by far. Despite our MSCT data’s relatively narrow reconstruction interval of 0.4 mm, the CBCT device still operates at a lower isotropic voxel size of $0.3 \times 0.3 \times 0.3$ mm. This better spatial resolution might be a reason for the superior sensitivity rate observed for CBCT in contrast to MSCT, because smaller tumor erosions of the cortical bone in the submillimeter range could also be displayed.

For SPECT, the exact delineation of bone invasion can be hampered by extended tracer uptake beyond the area of actual bone invasion and a limited spatial resolution of the gamma camera. Also, increased tracer uptakes at the tumor site in the SPECT analysis was considered to be a sign of tumor invasion; our results suggest a relatively high false positive rate. An explanation for this could be that increased tracer uptake is not only specific for a tumor’s jaw-bone infiltration, but may also be provoked by nonspecific tracer uptake originating from periodontal inflammation reactions or
bone formation after tooth extraction. Furthermore, the SPECT images were evaluated as film prints, which do not support visualizations aids, such as zoom and adaptation of contrast and brightness, as were available with the workstation-based analyses of CBCT and MSCT data sets. All of these reasons can explain why the investigated SPECT’s specificity value here is fairly restricted.

In conclusion, although not reaching significance level, CBCT showed slightly preferable results for the preoperative staging diagnosis of malignancies’ bone invasion of the jaws in contrast to MSCT and SPECT. Owing to the abovementioned advantages for diagnosis, FOV-to–radiation dose ratio, easy panoramic view reconstruction, and clinical accessibility, we prefer CBCT diagnosis over MSCT for preoperative maxillofacial assessment of tumor invasion into the bone. The previously published preferred diagnostic algorithm for the assessment of carcinoimal bone invasion should become expanded by CBCT in the following manner: primarily performance of either MSCT, CBCT, or MRI, followed by bone SPECT in cases in which the first scan shows no signs of bone invasion.

REFERENCES

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