



# Comparative evaluation of SPECT/CT and CBCT in patients with mandibular osteomyelitis and osteonecrosis

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## Abstract

**Objectives** Therapy of osteomyelitis and osteonecrosis very often requires surgery. Proper preoperative radiological evaluation of a lesion's localization and extent is a key in planning surgical bone resection. This study aims to assess the differences between single-photon emission computed tomography and cone beam computed tomography when detecting an osteomyelitis/osteonecrosis lesion as well as the lesion's qualitative parameters, extent, and localization.

**Material and methods** Identification of candidates was performed retrospectively following a search for patients with histologically or clinically confirmed osteomyelitis or osteonecrosis. They were matched with a list of patients whose disease extent and localization had been evaluated using single-photon emission computed tomography and cone beam computed tomography in the context of clinical investigations. Subsequently, two experienced examiners for each imaging technique separately performed de novo readings. Detection rate, localization, extent, and qualitative parameters of a lesion were then compared.

**Results** Twenty-one patients with mandibular osteomyelitis and osteonecrotic lesions were included. Cone beam computed tomography detected more lesions than single-photon emission computed tomography (25 vs. 23; 100% vs. 92%). Cone beam computed tomography showed significantly greater depth, area, and volume, whereas length and width did not differ statistically between the two groups.

**Conclusion** Both single-photon emission computed tomography and cone beam computed tomography could sensitively detect osteomyelitis/osteonecrosis lesions. Only single-photon emission computed tomography showed metabolic changes, whereas cone beam computed tomography seemed to display anatomic morphological reactions more accurately. The selection of the most adequate three-dimensional imaging and the correct interpretation of preoperative imaging remains challenging for clinicians.

**Clinical relevance** In daily clinical practice, three-dimensional imaging is an important tool for evaluation of osteomyelitis/osteonecrosis lesions. In this context, clinicians should be aware of differences between single-photon emission computed tomography and cone beam computed tomography when detecting and assessing an osteomyelitis/osteonecrosis lesion, especially if a surgical bone resection is planned.

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## Introduction

Bone tissue is a type of dense connective tissue, and bone quality is a collective term referring to the mechanical properties, architecture (thickness of cortical bone, distribution of trabecular network), degree of mineralization of the bone matrix, and chemistry as well as the remodeling properties of bone. Mandibular osteomyelitis (OM) and septic osteonecrosis (ON) are both infectious bone diseases that affect bone quality [1]. Histologic evaluation is nonspecific and cannot differentiate OM from ON [2, 3]. Various etiologies, such as drugs, radiation, trauma, or extraction of teeth, can cause OM and ON. These conditions modifying the bone can affect the health and quality of life of patients due to infected and painful necrotic jawbone, ulcerated, painful and swollen oral mucosa, speech disorders, and swallowing and eating difficulties. Patients with OM and ON of the jaw require frequent medical and dental treatments [4]. Diagnosis and therapy are complex and challenging and need to be approached by an interdisciplinary team of oral and maxillofacial surgeons, dentists, radio oncologists, infectiologists, pathologists, radiologists, and nuclear medicine physicians. Furthermore, OM and ON represent two of the most complicated infections of the oral and maxillofacial region, not the least because the boundary between the infected or necrotic area and healthy bone is often so ill-defined [5].

Consequently, distinguishing between affected and healthy areas can be difficult [6, 7]. In general, therapy of OM and ON includes surgical curettage, decortication, and bone resection. A key requirement for surgical planning is an exact preoperative evaluation of the extent of the disease [8]. Previous studies have shown that 3D imaging is essential for diagnosis. Moreover, it is important to localize the lesion and evaluate its dimensions to plan the surgery [2, 8–12]. An intraoperative evaluation of the extent of bone resection is no longer sufficient, as a potential bone reconstruction has to be planned before surgery. A clinical examination alone may not be reliable and may underestimate the extent of a lesion [9].

Over the last several decades, technical improvements involving newer three-dimensional imaging techniques such as cone beam computed tomography (CBCT) and single-photon emission computed tomography (SPECT/CT) have led to a range of methods which are valuable for the diagnosis and treatment planning of OM/ON. Meanwhile, SPECT/CT and CBCT have become standard diagnostic modalities used in daily clinical routine. The increasing number of imaging options has proven to be a challenge for clinicians, who must choose the most appropriate method for their patients.

Previous studies have focused on describing imaging findings for OM and ON lesions [13, 14]; however, comparative data for different imaging modes is limited [8]. The prevalence of OM/ON is fairly high and tends to increase further in part due to increases in the life expectancy of cancer patients [15, 16]. Comparisons of imaging methods could help refine the role of different imaging modalities [3, 8].

For example, in a comprehensive evaluation of skeletal lesions, including OM and ON, SPECT/CT proved better at characterization than computed tomography (CT) [11, 17]. It seems that, due to its high sensitivity, SPECT/CT is vastly superior to other diagnostic methods and can reliably predict the extent of the disease [17, 18]. However, based on the literature and our anecdotal experience, CBCT can effectively and reliably diagnose and quantify OM/ON, especially when bone mass has already been lost and morphologic changes have become visible [7, 19, 20].

Each imaging method has its pros and cons. Whereas SPECT/CT allows for *in vivo* visualization of inflammation and bone metabolism, reflecting actual activity of OM/ON, it is associated with relatively higher radiation burden and costs in comparison with CBCT [21–24].

Based on these considerations, the aim of the present study was to analyze patients treated in the Bern University Hospital's Department of Cranio-Maxillofacial Surgery to assess the discrepancies between SPECT/CT and CBCT imaging when identifying an OM/ON lesion. The focus was on comparison of the localization of the lesions and the quantitative and qualitative parameters of the lesions, as well as the determination rates between the two imaging procedures.

## Material and methods

### Patients

The study was approved by the local ethical committee of the State of Bern (permission number 2017-00533).

Candidates were identified in the Department of Cranio-Maxillofacial Surgery's database of patients with clinically and/or histologically confirmed mandibular OM or ON. The selection of candidates was further refined by matching potential candidates with a list of patients who were evaluated within a 3-month period with both SPECT/CT and CBCT imaging. The imaging was performed in the context of clinical investigations for evaluation of the extent and localization of disease.

The main inclusion criterion was confirmed OM or ON based on histopathological findings and/or on clinical assessment by experienced maxillofacial surgeons using guidelines

according to the current literature [25, 26]. Patients were excluded if their biopsy confirmed a pathology other than OM or ON, or if the interval between the two imaging modalities exceeded 3 months. Other exclusion criteria were local treatments, such as a surgical intervention, during this period.

## Image review

The study focused on qualitative and quantitative imaging assessment of mandibular OM/ON lesions identified using SPECT/CT and CBCT. The SPECT/CT images were obtained 3 h after intravenous injection of 700 MBq TechneScan® HDP (Tc-99m-hydroxymethylene diphosphonat (HDP)) with in-line Hybrid-SPECT/CT devices. SPECT reconstruction was performed using an iterative three-dimensional ordered subset expectation maximization (3D-OSEM) algorithm incorporating resolution recovery (Astonish) with a matrix size of  $128 \times 128$  and a zoom factor of 1.85. Imaging settings for CT acquisition were 180mAs 120 kV with a matrix size of  $512 \times 512$  (slice thickness 1 mm) for the multi-slice CT (Precedence 6, Philips Healthcare, Zurich, Switzerland) and 80 mA and 120 kV with a matrix size of  $512 \times 512$  (voxel size 0.33 mm isotropic) for the flat-panel cone beam CT (Bright View XCT, Philips Healthcare, Zurich, Switzerland).

Image analysis was performed using workstations dedicated for medical image reading and a server-based multi-modality reading solution (syngo.via, Siemens Healthcare, Zurich, Switzerland). No algorithm for a standardized OPT-like curved image reconstruction of fused hybrid images was available.

The CBCT images were obtained with a 3D Accuitomo 80 ( $n = 5$ ) or a 3D Accuitomo 170 ( $n = 16$ ) (Morita Corp., Kyoto, Japan) with full scan rotation ( $360^\circ$ ) for all cases, and exposure settings of 5.0 mA/80 kV ( $n = 5$ ), 5.0 mA/90 kV ( $n = 11$ ) and 7.0 mA/90 kV ( $n = 5$ ). The devices were used by an experienced team within the section of dental radiology at the Department of Oral Surgery and Stomatology, School of Dental Medicine, University of Bern, Bern, Switzerland. The fields of view (FOV) and respective voxel sizes were  $4 \times 4$  cm/125  $\mu\text{m}$  ( $n = 1$ ),  $6 \times 4$  cm/125  $\mu\text{m}$  ( $n = 1$ ),  $6 \times 6$  cm/125  $\mu\text{m}$  ( $n = 5$ ),  $8 \times 8$  cm/160  $\mu\text{m}$  ( $n = 2$ ),  $8 \times 5$  cm/160  $\mu\text{m}$  ( $n = 2$ ),  $10 \times 10$  cm/250  $\mu\text{m}$  ( $n = 1$ ),  $10 \times 5$  cm/250  $\mu\text{m}$  ( $n = 2$ ),  $14 \times 10$  cm/250  $\mu\text{m}$  ( $n = 4$ ),  $14 \times 5$  cm/250  $\mu\text{m}$  ( $n = 2$ ),  $17 \times 12$  cm/250  $\mu\text{m}$  ( $n = 1$ ). Cases were excluded if artifact formation did not allow proper evaluation. The images were examined on a Dell 380 precision work station (Dell SA, Geneva, Switzerland) and a 19-in. Eizo Flexscan monitor with a resolution of  $1280 \times 1024$  pixels (Eizo Nanao AG, Wädenswil, Switzerland), using a specialized computer software (i-Dixel Version 2.2.1.2, Morita Corp., Kyoto, Japan).

A total of four experts experienced in maxillofacial radiology performed individual de novo readings of the images. They knew the diagnosis of OM/ON but were blinded to further clinical or radiological information. Two nuclear

medicine physicians evaluated each separately the SPECT/CT scans (BK and BV). Since the primary focus of this study was the extent of radiographically determined bone involvement, each visible lesion was scored for length, depth, width, surface area, and volume. Inter-observer agreement was determined. Furthermore, the lesion's localization and qualitative parameters were documented. In the same manner, two experienced maxillofacial radiologists individually evaluated CBCT scans (VS and MS). The reviewers used all three individually adapted planes (coronal, transverse, sagittal) for assessing OM/ON lesions.

Only the SPECT/CT software offered integrated volume calculation for each detected lesion. Therefore, the surface area and volume were estimated for each lesion by using the mathematical formulas for calculating the area of an ellipse and the volume of an ellipsoid, respectively.

## Localization

Different areas of the lower jaw (ascending branch, angle, posterior region/body, inferior and anterior region) were defined, and we assessed how frequently each region was affected.

## Qualitative evaluation

Every observer assessed each mandibular lesion for the presence or absence (yes/no) of the following radiological findings: (1) osteolysis (Figs. 1 and 2); (2) sclerosis (Figs. 1 and 2); (3) bone thickening (Figs. 1 and 2); (4) periosteal thickening (Fig. 1); (5) monocortical perforation (Fig. 2); (6) bicortical perforation (Fig. 1); (7) extraneous material; and (8) artifacts. Additionally, in SPECT/CT, early-stage reaction and tracer uptake in the osseous phase was noted.

## Dimensions

To evaluate the dimensions of a mandibular lesion—the primary endpoint of this study—each observer first defined one area exhibiting the widest extent of disease in anteroposterior (a), superoinferior (b), and mediolateral (c) directions and measured it in centimeters. The area of disease extent ( $S$ ) was then calculated and defined in square centimeters using the mathematical formula for the area of an ellipse ( $S = \pi \frac{1}{2} a \frac{1}{2} b$ ). By analogy, the lesion's volume ( $V$ ) was evaluated and specified in cubic centimeters using the formula for the volume of an ellipsoid ( $V = \frac{4}{3} \pi \frac{1}{2} a \frac{1}{2} b \frac{1}{2} c$ ).

## Statistical evaluation

As suggested by Stockmann et al. [8], the detectability of lesions using different imaging techniques was calculated according to this formula:

**Fig. 1** A 26-year-old female patient with SAPHO syndrome. Screenshots of coronal, sagittal, and axial images seen on the CBCT scan (**a**, **b**, and **c**) and with SPECT/CT (**d**, **e**, and **f**), respectively. A lesion in the right mandible exhibiting osteolysis, sclerosis, cortical perforation, and bone and periosteal thickening also shows tracer uptake with SPECT/CT, but active bone metabolism appears smaller than morphological reactions with regard to length measurements (**b** and **e**)



$$\text{Detectability } [\%] = \frac{\text{number of positive detected lesions}}{\text{number of all included lesions}} \times 100$$

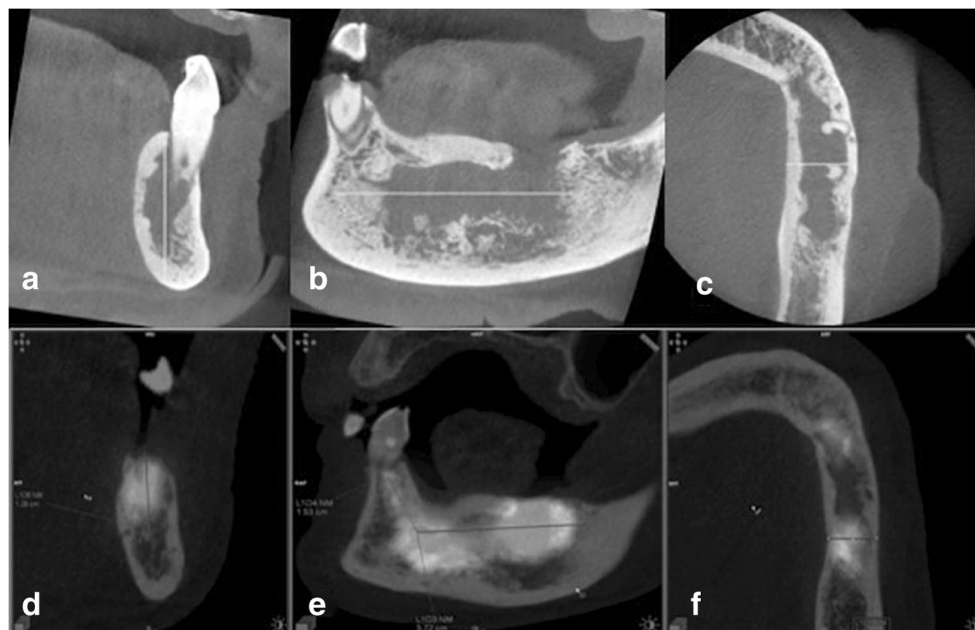
Paired *t* tests were used to compare the two modalities in terms of primary and secondary outcomes. For this purpose, the measurements for each modality were averaged. Some lesions were only visible in one modality or were only evident to a single observer of one or more modalities. Lesions with at

least one measurement in both modalities were included. A *p* value of 0.05 was considered statistically significant.

Additionally, many images showed evidence of multiple lesions, which might have resulted in non-independent samples. Due to this, linear mixed-effect models were also used to compare the modalities.

Concerning the metric analysis, an inter-researcher agreement was assessed by calculating intraclass correlation

**Fig. 2** A 60-year-old male patient with osteoradionecrosis. Screenshots of coronal, sagittal, and axial images seen on the CBCT scan (**a**, **b**, and **c**) and with SPECT/CT (**d**, **e**, and **f**), respectively. Lesions in the right and left mandibles exhibiting osteolysis, sclerosis, cortical perforation, and bone thickening also show tracer uptake with SPECT/CT, but active metabolism appears smaller than morphological reactions regarding depth measurements (**a** and **d**)



coefficients (ICC). ICCs for each imaging modality were calculated from linear mixed models as the ratio between lesion variance and the sum of all variance components (between patients, within patients, and within lesions). Values were then interpreted according to Landis and Koch [27]: < 0 poor, 0 to 0.2 slight, 0.21 to 0.4 fair, 0.41 to 0.6 moderate, 0.61 to 0.8 substantial, and 0.81 to 1 almost perfect.

Bland-Altman plots were also created for each combination of reviewer and mode (e.g., reviewer one using SPECT/CT vs. reviewer one using CBCT, reviewer one using SPECT/CT vs. reviewer two using CBCT, etc.) together with a combined plot following [28], which allows multiple observations per lesion without resulting in overly narrow confidence intervals.

## Results

### Patients

Twenty-one patients (10 women, 11 men) aged between 21 and 87 years (mean age = 58.9 years) and treated at the Bern University Hospital’s Department of Cranio-Maxillofacial Surgery between 2009 and 2017 were included in the study. Histopathologic findings were available for most patients (16 of 21, 76%). In the remaining five patients (5 of 21, 24%) the diagnosis was made clinically by experienced maxillofacial surgeons using guidelines according to the current literature [25, 26].

The majority of the patients included had a basic oncological condition; however, the causes for OM/ON differed. Antiresorptive medication (only bisphosphonates) was causal in 4 patients. Ten patients previously underwent radiotherapy and in 7 patients other reasons were identified, including dental trauma or SAPHO syndrome (Table 1).

**Table 1** Demographics and etiological factors of OM/ON for the 21 included patients

|   | <i>n</i> (%) | mean (sd)   |
|---|--------------|-------------|
| Gender  |              |             |
| Male  | 11 (52)      |             |
| Female  | 10 (48)      |             |
| Age (years)                                   |              | 58.9 (16.5) |
| Diagnosis                                     |              |             |
| Osteomyelitis                                 | 7 (33)       |             |
| Osteonecrosis                                 | 14 (67)      |             |
| Etiology                                      |              |             |
| Antiresorptive medication with bisphosphonate | 4 (19)       |             |
| Radiotherapy                                  | 10 (48)      |             |
| Other   | 7 (33)       |             |

### Detectability

Using SPECT/CT, fewer lesions were identified as metabolically active at the time of the exam than for CBCT, which was based on morphological alterations (23 vs. 25, 92% vs. 100%).

### Localization

Descriptive data of the lesions’ localization refer to the maximum number of lesions identified by the individual reviewer using the respective imaging modality (reviewer 2 with SPECT/CT, 23 lesions; reviewer 1 with CBCT, 25 lesions).

Most lesions were identified within the posterior region/body of the mandible (91% with SPECT/CT and 88% with CBCT) (Table 2). The majority of these lesions appeared not only in the upper area but also in the region below the nerve canal (18 of 21 with SPECT/CT and 22 of 22 with CBCT). Other lesions were mainly detected in the mandibular angle (39% with SPECT/CT and 32% with CBCT) and in the anterior region (39% with SPECT/CT and 32% with CBCT). Few lesions were located in the ascending branch (3 out of 23 with SPECT/CT and 3 of 25 with CBCT).

### Qualitative evaluation

Descriptive data of qualitative evaluation refer to the maximum number of lesions identified by the individual reviewer with the respective imaging modality (reviewer 2 with SPECT/CT, 23 lesions; reviewer 1 with CBCT, 25 lesions). The two most common lesion characteristics were osteosclerosis (96% with SPECT/CT and 84% with CBCT) and osteolysis (61% with SPECT/CT and 100% with CBCT). The incidence of each qualitative feature is demonstrated in Table 3.

### Dimensions

The comparison of reviewer measurements yielded the following results for mean extent of ill-defined bone: OM/ON lesions assessed with SPECT/CT were significantly smaller in depth (1.7 cm vs. 2.2 cm, *p* = 0.004), surface area (6.2 cm vs. 8.5 cm, *p* = 0.025), and volume (4.7 cm vs. 6.8 cm, *p* = 0.038)

**Table 2** Distribution of affected mandible regions as seen with imaging. Inferior region describes the area below the nerve canal

|                  | SPECT/CT ( <i>n</i> = 23)<br><i>n</i> (%) | CBCT ( <i>n</i> = 25)<br><i>n</i> (%) |
|------------------|---|---------------------------------------|
| Ascending branch | 3 (13)                                    | 3 (12)                                |
| Angle            | 9 (39)                                    | 8 (32)                                |
| Body             | 21 (91)                                   | 22 (88)                               |
| Inferior region  | 18 (78)                                   | 22 (88)                               |
| Anterior region  | 9 (39)                                    | 8 (32)                                |

**Table 3** Frequency of different lesions' characteristics detected with the respective imaging method

|                                      | SPECT/CT ( <i>N</i> = 23)<br><i>n</i> (%) | CBCT ( <i>N</i> = 25)<br><i>n</i> (%) |
|--------------------------------------|---|---------------------------------------|
| Osteolysis                           | 14 (61)                                   | 25 (100)                              |
| Osteosclerosis                       | 22 (96)                                   | 21 (84)                               |
| Bone thickening                      | 9 (39)                                    | 7 (28)                                |
| Periosteal thickening                | 8 (35)                                    | 4 (16)                                |
| Monocortical perforation             | 7 (30)                                    | 14 (56)                               |
| Bicortical perforation               | 8 (35)                                    | 9 (36)                                |
| Extraneous material                  | 8 (35)                                    | 3 (12)                                |
| Artifacts                            | 1 (4)                                     | 6 (24)                                |
| Early-stage reaction (only SPECT/CT) | 18 (78)                                   | –                                     |
| Osseous phase (only SPECT/CT)        | 23 (100)                                  | –                                     |

than those assessed with CBCT. There were no statistically significant differences in length and width between the two groups (Table 4).

Bland-Altman plots compared all possible reviewer combinations of each applied imaging technique (e.g., reviewer 1 using SPECT/CT versus reviewer 1 using CBCT and reviewer 1 using SPECT/CT versus reviewer 2 using CBCT) with regard to surface area, length, depth, and width. The plots illustrate the relatively bad agreement between the methods and the slightly greater measurements observed with CBCT compared to SPECT/CT (the mean difference is less than 0) (Fig. 3).

### Inter-rater agreement

Overall inter-rater consistency concerning the metric analysis and within the individual imaging modes was relatively low but still mostly fair to moderate according to Landis and Koch [27] (Table 5).

### Discussion

Proper three-dimensional imaging in severe cases of mandibular OM/ON is mandatory [29]. A key point for

**Table 4** Dimensions of lesions

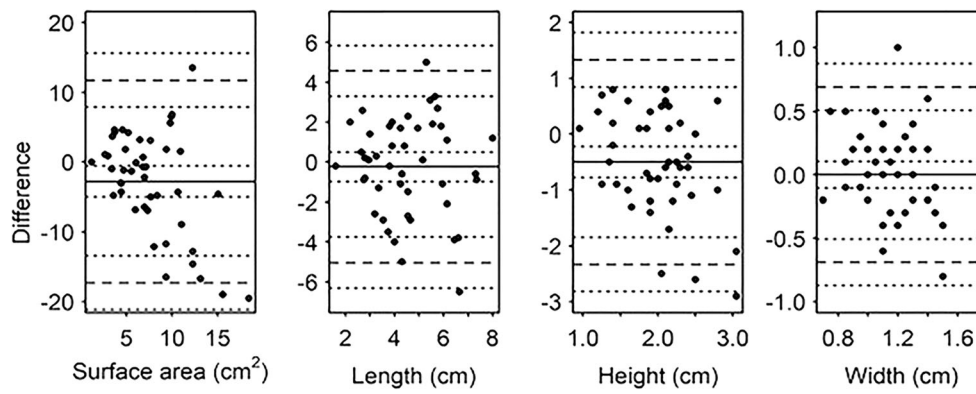
|                                 | SPECT/CT      | CBCT           | <i>p</i> value |
|---------------------------------|---------------|----------------|----------------|
| Length (cm)                     | 4.4 (3.7–5.0) | 4.5 (3.9–5.2)  | 0.534          |
| Depth (cm)                      | 1.7 (1.5–2.0) | 2.2 (2.0–2.4)  | 0.004          |
| Width (cm)                      | 1.2 (1.1–1.3) | 1.1 (1.0–1.2)  | 0.971          |
| Surface area (cm <sup>2</sup> ) | 6.2 (4.5–7.9) | 8.5 (7.0–10.1) | 0.025          |
| Volume (cm <sup>3</sup> )       | 4.7 (3.2–6.2) | 6.8 (5.3–8.2)  | 0.038          |

Mean measurements for the two modalities are provided, together with their respective 95% confidence intervals. With CBCT, larger extents were evident for depth, area, and volume, but length and width did not differ statistically between the two groups.

surgical planning is exact identification of the true extent of the disease. On the one hand, insufficient resection may lead to further proliferation of the lesion, and on the other hand, surgical overtreatment may have a negative impact on the patient's quality of life. Based on these considerations, it is essential to choose the most accurate preoperative 3D assessment for planning the surgery, if necessary with reconstruction, as shown in Fig. 4, and awareness of differences among imaging modalities should be considered when planning the extent of operative treatment [9]. There is only sparse literature regarding which imaging technique should be used, and currently, the imaging modality chosen generally reflects the surgeon's subjective preference [17, 29].

This study was initiated to determine the differences between hybrid-SPECT/CT and CBCT in detecting and evaluating mandibular OM/ON sites. To the best of our knowledge, this is the first study using both qualitative and quantitative data to compare these two imaging modalities. Most previous studies only described qualitative radiological findings which were related to the pathology [2, 3, 8, 10, 12, 13, 17].

In the present study, more OM/ON lesions were identified with CBCT than with SPECT/CT (23 vs. 25, 92% vs. 100%). Previous studies focusing on SPECT/CT have shown that elevated tracer uptake was discernible in all patients and nuclear imaging localized the site of disease in 100% [10, 11, 17]. However, a prospective study conducted by Hakim et al. [18] showed that 6 out of 86 cases of OM/ON were assessed as false negative using 3-phase skeletal scintigraphy. This aligns with the results of Hong et al., who stated that SPECT provides a relatively sensitive means of finding OM/ON lesions and has a detectability 93.8% [30]. An explanation for this was offered by O'Ryan et al. [31], who claimed that OM/ON cannot show a tracer uptake in the necrotic zone, but due to the associated infection, it may be seen. However, it has been argued before that the high resolution of CBCT provides the



**Fig. 3** A Bland-Altman plot using the appropriate method to adjust variance [28]. This demonstrates the difference between two values (*y*-axis) plotted against the mean of the two values (*x*-axis). In this case, the *y*-axis represents SPECT/CT and CBCT, while the *x*-axis represents the mean of the two modalities for each review. Thus, values below 0 mean that lesions measured with CBCT were larger and values above 0 mean that lesions measured with SPECT/CT were larger. The solid line

represents the mean difference (if both methods produce the same value, this would be zero); the dashed lines are two standard deviations from the mean line; the dotted lines are the upper and lower 95% confidence intervals for each of the three other lines. Similar measurements are characterized by a smaller range on the *y*-axis than the *x*-axis

greatest level of detail as well as different radiological signs. Consequently, morphologic changes can be seen in all stages of OM/ON [13, 32].

In this context, it is important to mention that only 16 of the 21 patients included in this study underwent histopathological analysis. For this reason, this result is more a detection rate than a calculation of sensitivity. There are different criteria for the identification of OM/ON based on an evaluation with SPECT/CT, identifying reactive bone metabolism, and CBCT, reflecting OM/ON as well as reactive morphological changes such as osteosclerosis and osteolysis. Furthermore, the sensitivity of each modality may be stage dependent. The results of the current analysis reflect the diagnostic performance of each modality as well as the composition of the study population, e.g., in terms of chronicity, evolution of necrosis, regional bone metabolism, and formation of sclerosis. Consequently, OM/ON detection rates obtained with SPECT/CT and CBCT may vary depending on the patient population studied.

**Table 5** Intraclass correlation coefficients are provided, together with their respective 95% confidence intervals

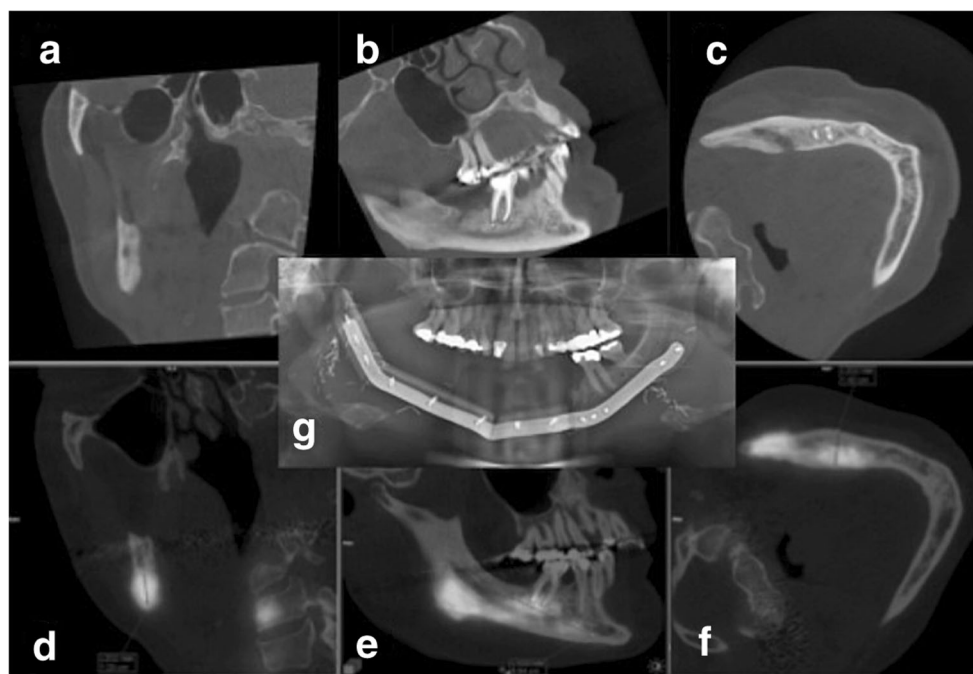
|              | SPECT/CT         | CBCT             |
|--------------|------------------|------------------|
| Length       | 0.55 (0.28–0.80) | 0.35 (0.10–0.70) |
| Depth        | 0.14 (0.01–0.83) | 0.31 (0.08–0.71) |
| Width        | 0.19 (0.02–0.72) | 0.68 (0.45–0.85) |
| Surface area | 0.21 (0.02–0.74) | 0.29 (0.06–0.70) |
| Volume       | 0.35 (0.10–0.73) | 0.40 (0.14–0.73) |

According to Landis and Koch, values < 0, 0 to 0.2, 0.21 to 0.4, 0.41 to 0.6, 0.61 to 0.8, and 0.81 to 1 would indicate poor agreement, slight agreement, fair agreement, moderate agreement, substantial agreement, and almost perfect agreement, respectively [27]

The metric analysis of OM/ON lesions has demonstrated that length measurements were statistically identical for both methods. Concerning depth, surface, and volume, the lesions tended to appear larger with CBCT than with SPECT/CT. Although SPECT/CT may sensitively detect sites of disease and reliably predict their extent [17], an explanation for this may be a limited tracer uptake in the necrotic area in the depth of the lesion [31]. Therefore, it seems to be important not only to focus on metabolic reactions when assessing OM/ON lesions with SPECT/CT, but also to include displayed morphological changes in the evaluation. In a rat model, Cankaya et al. [32] demonstrated that there is a significant correlation between CBCT measurements and intraoperative measurements. On the other hand, intraoperative examination, even fluorescence-guided, is very useful but still not 100% reliable [5, 33, 34]. Furthermore, due to mechanical considerations in certain cases, not all of the necrotic bone that is found during surgery can be resected, and intraoperative quantification may underestimate the true extent of disease to some degree [9]. However, Cankaya et al. [24] are in agreement with Olutayo et al. [14], who demonstrated that CBCT scans allow the identification of the true extent of affected marrow and are able to fully characterize the bony lesions and describe their extent and neighboring structures. Consequently, CBCT may be used as a guide toward planning in all cases. Nevertheless, based on the results of this metric analysis, the question whether metabolic changes displayed in SPECT/CT or anatomic morphological reactions evident in CBCT are more important for the planning of a surgical procedure cannot be answered conclusively.

Additionally, qualitative lesion characteristics detected with SPECT/CT and CBCT were assessed. Osteosclerosis and osteolysis were found most often (as shown in a case description, Fig. 4); they were also the most frequent

**Fig. 4** A 57-year-old female patient with chronic osteomyelitis. Screenshots of coronal, sagittal, and axial images seen on the CBCT scan (**a**, **b**, and **c**) and with SPECT/CT (**d**, **e**, and **f**), respectively. The lesion in the right mandible shows osteosclerosis, osteolysis, and periosteal and bone thickening as well as cortical perforation. SPECT/CT also shows tracer uptake, but active metabolism appears smaller than morphological reactions regarding depth measurements (**a** and **d**). Panoramic radiography obtained after partial resection of the mandible and reconstruction with fibula free flap is shown in (**g**).



qualitative findings in a previous study evaluating CBCTs of 22 patients with OM/ON [19]. These results are consistent with another previous study in which 27 CBCTs of OM/ON sites were examined on the basis of radiological findings. Cancellous bone destruction/osteolysis was the most common finding [13]. However, the role of osteosclerosis in OM/ON sites is controversial in the literature. On the one hand, some authors [14, 35] found a correlation between sclerotic manifestation and the severity of OM/ON, but on the other hand, Wilde et al. [13] did not. Previously, it was demonstrated that 50% of 33 OM/ON patients had radiological evidence of osteosclerosis [2]. The authors also stated that although some investigations consider osteosclerosis a complication of OM/ON, this change could be a result of infection and might represent a reactive process to inflammation. Furthermore, they described it as a hyperactive immunologic reaction to bacterial toxins, or a defensive reaction to a slowly progressive process, such as bacterial biofilms, which have lower metabolic and divisional rates and, moreover, decreased antibiotic penetration. Consequently, osteosclerosis might represent a mechanism to quarantine an infection, but can also contribute to poor wound healing, infection, and sequestrum formation. Fleisher et al. conclude that this common morphological characteristic of OM/ON may present as a double-edge sword.

The majority of lesions were detected in the posterior region/body of the mandible. This is in accordance with a previous study, which demonstrated that the body of the mandible was the predominant clinical site of involvement in all their patients [14]. The authors argued that antiresorptive drugs such as bisphosphonates, which can cause OM/ON, have particularly high concentrations in this region due to

the consistently high mastication rate. It was shown previously with CBCT that the occurrence of cancellous bone destruction, cortical bone erosion, sequestration, and osteosclerosis seems to increase with increasing severity of OM/ON [13].

Several limitations of this study must be kept in mind. First, the sample size was small. Twenty-five lesions were assessed in this study and an initial power analysis has shown that a good 30 lesions are desirable. The study design was retrospective and data were obtained by de novo reading of the imaging without including the clinical correlate. Only the SPECT/CT software provided integrated volume calculation for each detected lesion. No corresponding program was integrated in the CBCT computer software. Therefore, the measurements were carried out in anteroposterior, superoinferior, and mediolateral direction, meaning that surface area and volume could only be estimated for each lesion. This was done using the mathematical formulas for calculating the area of an ellipse and the volume of an ellipsoid, respectively. In this context, it is conceivable that if lesions have an irregular shape, the formula-based volumes might be slightly bigger than the actual sizes. Furthermore, the inter-rater agreement is relatively weak, which is probably due to the varying angulation and adaption of planes between the measuring observers when assessing a lesion (as shown in the case descriptions in Figs. 1 and 2). For SPECT/CT and CBCT, no image-reading software allowing for an automated curved image reconstruction and an OPT-like visualization of the 3D data was available, especially not for hybrid imaging. It cannot be excluded that such software limitations were finally responsible for the low inter-rater agreement of measurements and could limit the intermodality comparison of measurements.



A previous study has demonstrated that CBCT only offers the possibility of estimating the extent of the lesion and depicting the involvement of important anatomical structures, for example, the inferior alveolar nerve. The authors stated that the exact margins of a lesion cannot be determined by any mode of imaging [13]. Based on both the partly contradictory data from the literature and the not entirely homogeneous results of the quantitative analysis in the present study, it may be concluded that the interpretation of the extent of disease is difficult, even if SPECT/CT and CBCT are available, and the choice of imaging should always be made in the individual clinical context. Further prospective comparative studies are necessary to determine the recommended standard radiological examination needed before surgery.

## Conclusion

The present study showed that SPECT/CT and CBCT could sensitively detect OM/ON lesions, but the latter tended to display morphologic reactions more exactly. With regard to quantitative issues, comparison of length and width between the two imaging methods yielded a statistically identical result. However, there was a significant difference between the two when determining depth. Therefore, not only well-defined preoperative 3D evaluation but also exact intraoperative assessment is still recommended.

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## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** This article does not contain any studies with human participants or animals performed by any of the authors.

**Informed consent** For this type of study, formal consent is not required.

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