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REVIEW ARTICLE

Imaging diagnosis for bone invasion by gingival carcinoma of the mandible: The value and the limitation

Eiji Nakayama*

Department of Oral and Maxillofacial Radiology, School of Dentistry, Health Sciences University of Hokkaido, 1757 Kanazawa, Ishikari-Tobetsu, Hokkaido, 061-0293, Japan

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KEYWORDS

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Summary The bone invasion in carcinoma of the mandibular gingiva (CaMG) is one of the important factors to determine the treatment planning and predict the prognosis. Japan Society for Oral Tumors proposed a new criterion of T4 classification of CaMG in 1997 as follows: the tumor is classified as T4 when the tumor spreads into the mandibular canal, and the tumor should not be classified as T4 when the tumor does not invade into the mandibular canal. Thus, the supero-inferior extent of bone invasion is one of the important diagnostic factors on Images.

The accuracy of the supero-inferior extent of bone invasion by diagnostic images is equal between panoramic radiography (PR) and CT, and hence, PR would be suitable for the initial screening modality to survey the bone invasion into the mandibular canal.

However, regarding the pattern of bone invasion by CaMG, the CT pattern of bone invasion is associated with the prognosis, and therefore the pattern should be determined based on the CT findings.

In conclusion, at the present time, CT is suitable for detection of bone invasion in CaMG, although CT cannot detect precisely an early weak bone invasion, or a bone invasion infiltrating through the trabecular bone.

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* Tel.: +81 133 23 2591; fax.: +81 133 23 1410.
E-mail address: enaka@hoku-iryu-u.ac.jp.

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1. Introduction

The bone invasion in carcinoma of the mandibular gingiva (CaMG) is one of the most important factors to determine the treatment planning and the prognosis, because the extent and pattern of bone invasion is associated with the outcome of the patients with CaMG [1,2]. Regarding the extent of bone invasion, the supero-inferior extent should be detected precisely on the diagnostic imaging, because it is one of the determinant factors for the surgeons to choose between a rim or a segmental resection of the mandible as the surgical method [1–3]. The pattern of bone invasion on the diagnostic images is generally classified into two types. One is erosive, and the other is infiltrative [1,2,4], or invasive [5]. Invasive is synonymous with infiltrative. However, we know that more aggressive pattern of bone destruction exists in some cases showing a type of infiltrative bone invasion, and these are called “moth-eaten type” destruction. Therefore, we classified the bone invasion into the three types: erosive, mixed, and invasive with reference to the histologic classification of bone invasion due to the tumor [6,7]. The mixed pattern includes infiltrative pattern but excludes the moth-eaten type, and the invasive pattern in our classification is synonymous with moth-eaten type. Then, we clarified the accuracy of diagnostic imaging including panoramic radiography (PR) and X-ray CT (CT) for the supero-inferior extent of bone invasion due to CaMG. Next, we clarified the association between the pattern of bone destruction based on the diagnostic imaging and the outcome of the patients with CaMG.

In this article, I review some studies including Japanese ones regarding the bone invasion due to CaMG based on the diagnostic imaging together with our own studies related to this theme. Then, the value and the limitation of imaging diagnosis for bone invasion by gingival carcinoma of the mandible are discussed.

2. T classification of CaMG in TNM classification system

2.1. UICC classification

International Union Against Cancer (UICC) defines the TNM classification system of malignant tumor, and T classification is introduced to describe the extent of primary tumor. According to the T classification of UICC, the criteria of T4 for oral cavity in fifth [8] and sixth edition [9], which was published in 1997, and 2002 respectively, is as follows: T4a;

Tumor invades through cortical bone, into deep/extrinsic muscle of tongue, maxillary sinus, or skin of face, T4b; Tumor invades masticator space, pterygoid plates, or skull base, or encases internal carotid artery. In the T classification, a supplementary criterion for gingival cancer is described in footnote as follows: Superficial erosion alone of bone/tooth socket by gingival primary is not sufficient to classify a tumor as T4. This supplementary criterion for gingival carcinoma is important, because gingival carcinoma easily invades the alveolar bone although the tumor is not large and does not spread into the surrounding muscles, and the tumor is classified as T4, even though the tumor does not have an essential feature of T4, if supplementary criterion is not present.

Those T classification criteria for gingival carcinoma are widely used in the world. However, the footnote does not describe the criterion of superficial erosion definitely, and therefore, the judgment of whether the bone destruction is “superficial erosion” or not varies and the judgment is not constant among clinicians. Moreover, according to these T4 criteria, most of gingival carcinomas are classified into T4, and the T classification was poorly correlated with the outcome of the patient with the tumor [10].

2.2. A new criterion of T4 proposed by Japan Society for Oral Tumors

For above-mentioned reason, Japanese clinicians thought that the T classification criteria of UICC should be modified precisely so that all clinicians could define T4 of CaMG in accordance with the same standard and the T classification could be correlated with the prognosis. Hence, in 1990s, the members of Japan Society for Oral Tumors reviewed the validity of TNM classification of UICC by analyzing the relationship between the extent of bone destruction of the mandible due to CaMG and the outcome of the patients with the tumor. Then they discussed the introduction of a new T4 criterion for CaMG by revising the original UICC classification published in 1987 [8] and 1997 [9].

The goal of the new revised T Classification for CaMG was the establishment of the proper criteria by which the T classification is well correlated with the prognosis and the distribution of each T group becomes as nearly equal as possible. To achieve this purpose, the members of the society collected 1187 cases of CaMG from 24 Japanese hospitals that have the department of oral and maxillofacial surgery, and studied a new proper T4 criterion of CaMG based on the clinicopathological database of those cases.

As the result, they found that the outcome of the patients with the tumor invading into the mandibular canal was

significantly different from that of the patients with the tumor invading above the mandibular canal. Moreover, they found that, if the T4-tumor was defined as a tumor spreading into the mandibular canal, the distribution of each T group becomes nearly equal, compared with that classified by the original T classification of UICC [10].

Therefore, the society proposed a new criterion of T4 for CaMG in 1997 as follows: the tumor is classified as T4 when the tumor spreads into the mandibular canal, and the tumor should not be classified as T4 when the tumor does not invade into the mandibular canal, even though the tumor invades deeply more than the alveolar bone.

Now in Japan, many oral and maxillofacial surgeons arrange the T classification of CaMG according to this new criterion. To perform this new T classification precisely, the supero-inferior extent of bone invasion should be accurately diagnosed based on the diagnostic imaging.

3. Accuracy of imaging diagnosis for the supero-inferior extent of bone invasion due to CaMG

3.1. Panoramic radiography, intraoral radiography, and CT

Panoramic radiography (PR), intraoral radiography (IR) with periapical projection, and CT are generally used as imaging methods for detecting the bone invasion due to CaMG in dentistry field. CT clearly represents bony changes of the mandible due to carcinoma, if the CT images fill the following conditions: 1, thin scanning widths are chosen; 2, the scanning plane is selected parallel to the mandibular plane in order to eliminate any artifacts caused by metallic dental restorations; 3, super high resolution CT images of the optimal bone window mode are obtained [6].

Until 1990s, regarding the accuracy of CT for bone invasion due to CaMG, there was little study in which the CT images satisfied those required condition. Thus, in 1999, we investigated which images, PR, IR, or CT, could diagnose the supero-inferior extent of bone invasion due to CaMG accurately by using the CT images that satisfied those required condition [11]. The subjects were 37 patients with CaMG who underwent the PR, IR and CT before surgery. Table 1 shows the distribution of the supero-inferior extent of bone invasion in those patients. Three types of diagnostic imaging (PR, PR + IR, and CT) were evaluated using the receiver operating characteristic (ROC) analysis. The area under ROC curves (Az) was used as the index of diagnostic accuracy in the study [12]. As the result of this study, the accuracy of diagnostic images regarding the detection of a slight bone invasion within the

Table 1 Distribution of the supero-inferior extent of bone invasion in 37 cases of carcinoma of mandibular gingiva.

Grade	Number	Percentage
0: No bone invasion	6	16.2
1: Invasion within the alveolar bone	6	16.2
2: Invasion beyond the alveolar bone	8	21.6
3: Invasion into the mandibular canal	17	46.0
Total	37	100.0

Table 2 ROC curve area as an indicator of the accuracy for the detection of the supero-inferior extent of bone invasion on diagnostic images in each level of bone invasion.

Level of bone invasion	PR	PR + IR	CT
Bone invasion positive or not	0.88	0.77	0.87
Beyond the alveolar bone or not	0.89	0.85	0.83
Into the mandibular canal or not	0.94	0.94	0.91

PR, panoramic radiography; PR + IR, panoramic radiography with intraoral radiography; CT, X-ray CT.

alveolar bone ranged from 77% to 88%, and that accuracy was lower than that of the detection of bone invasion beyond the alveolar bone (83–89%), and that of bone invasion into the mandibular canal (91–94%) (Table 2).

It means that the diagnostic imaging could not detect the weak and early bone invasion within the alveolus accurately. This low detectability for the early bone invasion is considered weak point of the diagnostic images, and the limitation of the diagnostic imaging on the bone invasion in CaMG.

However, Totsuka et al. [13] mentioned that a marginal resection of the mandibular bone was necessary to control CaMG when a bone defect was suspected, whether it was due to the tumor invasion or not, and other investigators have also reported similar findings [2, 14–16]. This fact shows that the low accuracy for the detection of the early bone invasion within the alveolus on diagnostic imaging does not become a large problem in clinical aspect of CaMG.

On the other hand, the supero-inferior extent of bone invasion in the mandible is one of the most important factors for decision of the extent of surgical resection of the mandible affected by the tumor [2, 13–18]. Totsuka et al. [13] mentioned that a marginal resection should be performed for CaMG which radiologically showed no bone defect, an erosive bone defect without extending beyond the inferior alveolar canal, or an invasive bone defect within a superficial area of the alveolar bone. In contrast, they stressed that, if the tumor has spread beyond this area in each pattern, then a segmental resection should be performed to control the tumor. This opinion is accepted among many surgeons including Japanese surgeon who promote bone-preserving surgery [2, 14–19].

It is therefore more important to accurately diagnose the presence of bone invasion beyond the alveolar bone, or into the mandibular canal rather than to accurately diagnose whether or not a slight degree of bone invasion is present based on imaging examinations in order to determine the surgical field.

Moreover, as mentioned above, some Japanese surgeons consider that the presence of bone invasion into the mandibular canal is one of the determinants of T classification in CaMG, and therefore, it is important to detect the bone invasion into the mandibular canal based on the diagnostic images. According to the result of this study, the accuracy of diagnostic imagings ranged from 91% to 94% concerning the detection of bone invasion into the mandibular canal and the accuracy is high (Fig. 1). Thus the imaging diagnosis plays significant roles to detect the bone invasion and decide the new revised T classification of CaMG proposed in Japan.

On the other hand, the accuracy of PR and PR + IR is equal to that of CT regarding the detection of bone invasion into the

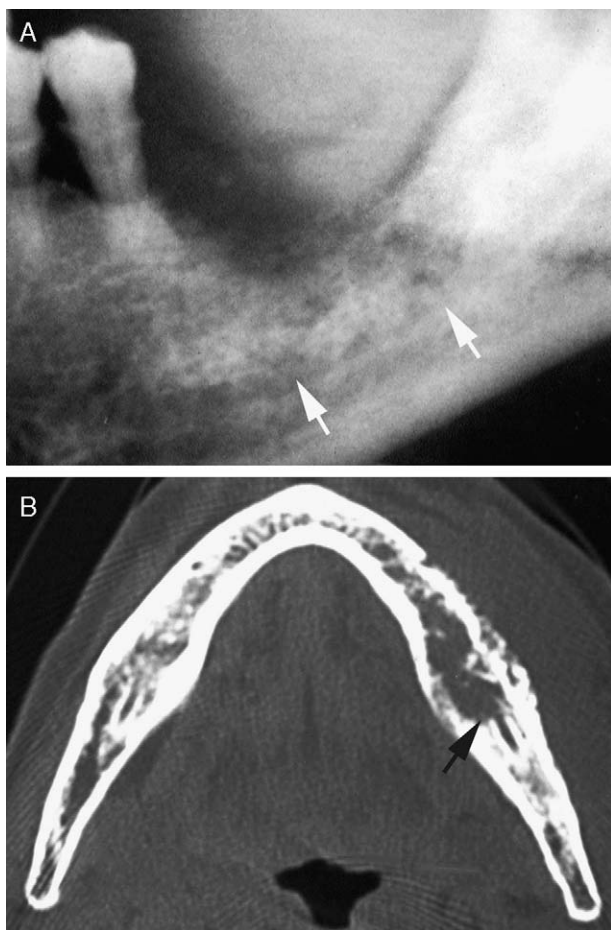


Figure 1 Panoramic radiography (A) and X-ray CT (B) definitely shows the bone invasion into the mandibular canal (arrow) due to carcinoma of the mandibular gingiva. Note that both images show also an invasive pattern of bone destruction.

mandibular canal, and hence, PR would be suitable for the initial screening modality to survey the bone invasion into the mandibular canal and determine the T classification, because it is generally available at most hospitals, and more economical than CT.

Kawano et al. [20] compared the depth of tumor invasion of 21 CaMGs on the cross-sectional (bucco-lingual) decalcified HE stained sections with that on the PR. Then, they concluded that the depth of tumor invasion on PR coincided with that on HE stained section in many cases. However, in some cases with infiltrative bone invasion, the depth of tumor invasion on PR were underestimated compared with that on the HE stained section. In these cases, tumor infiltrated into the deep bone marrow without destroying the bone trabecula, and the fact is the reason of the underestimation on PR. This type of tumor infiltration cannot be detected by any diagnostic imaging modalities, and it is the limits of the diagnostic imaging in the detection of bone invasion of CaMG [21].

In our study, the observers did not refer any clinical information except for the location of the tumor, and therefore, if the observers had been informed of the clinical details, the accuracy of each imaging modality is expected to improve more [14,22].

On the other hand, concerning the method of CT examination, our study in 1999 was performed by using the contiguous axial CT images of 4 mm thickness. At that time, available CT machine is a conventional non-helical one, and thus, we could not but choose the slice thickness of 4 mm to finish the CT in a practical examination time. However, I think the 4 mm thickness of CT is not enough thin to detect a weak bone change of the mandible, and I agree that CT images with less than 1 mm thickness or reconstructed paracoronal CT images is necessary to perform more sophisticated study on the detectability of bone invasion by CT.

3.2. Reconstructed paracoronal CT image

Recently, multidetector-row CT (MDCT) had been developed, and it enable us to collect volumetric CT data and obtain the reformatted image of thickness less than 0.5 mm. By the development of MDCT, the z-axis resolution of CT images has been drastically improved. Therefore, it was expected that this improvement plays an important role in advancing the accuracy for detection of mandibular bone invasion on the reconstructed paracoronal CT images.

Moreover, Dental CT or DantaScan, which can visualize the paracoronal cross sectional reconstructed CT images perpendicular to the dental arch curve, became easily available in combination of MDCT, and it is thought to have potential value to detect the extent of bone invasion of CaMG accurately [23,24].

Brockenbrough et al. [24] reported that, in 36 cases of oral cancer, the bone invasions of 32 cases were diagnosed accurately by the Dentascan and the accuracy of it was 88%. However, this accuracy is similar to the result of our study based on the axial CT images and hence, I consider that the superiority of Dentascan is not proven by their study. The quality of the reconstruction CT images strongly depend on the reconstruction parameter, such as the setting of the field of view, reformatting pitch, reconstruction width, and the type of filtering, etc. Therefore, further study is needed to clarify the significance of DantaScan including the reconstruction images from the MDCT data in the future.

3.3. Cone-beam CT

In the beginning of 2000s, several cone-beam CT (CBCT) machines were developed, and the spatial resolution is generally excellent compared with that of whole body fan beam CT. Moreover, CBCT collects volumetric CT data, and multiplanar reconstruction (MPR) images are displayed by default just after obtaining the data. Therefore, it is expected that the accuracy of CBCT for detection of bone invasion due to CaMG may be superior to that of whole body CT [25].

Momin et al. [26] evaluated the accuracy for cone beam CT on the alveolar bone invasion and the mandibular canal invasion of 50 patients with CaMG using ROC analysis. As the result, the mean Az value for cone-beam CT (0.918 for alveolar bone invasion and 0.977 for the mandibular canal invasion) was significantly higher than that for PR (0.793 and 0.872, respectively), and therefore, they concluded that CBCT was superior to PR in evaluating mandibular invasion. However, they mentioned also that the diagnostic value of CBCT might be limited at the alveolar crest, because its

image quality around the alveolar crest was often hampered by severe dental artifacts and image noise. Thus the significance of CBCT should be clarified by further studies including the comparative study between CBCT and whole body CT in the future.

3.4. Magnetic resonance imaging

Magnetic resonance imaging (MRI) is generally valuable for the diagnosis of malignant tumors, and therefore, it is expected to be useful for assessing bone invasion of the mandible due to CaMG [5,27,28]. Van Cann et al. [29] reported that some parameters of dynamic contrast-enhanced MRI could discriminate the tumor with medullary invasion from the tumor without it in oral cancer. However, several study shows that magnetic resonance imaging had more false positives and frequently overestimated the extent of tumor invasion because of the high intensity due to the edematous or inflammatory changes at the soft tissue adjacent to the tumor, and therefore, the accuracy of MRI is not thought superior to that of CT concerning the bone invasion of oral cancer [5,30–32].

3.5. Positron-emission tomography

Positron-emission tomography (PET) with Fluorine 18 fluorodeoxyglucose (FDG) is also expected to be useful for assessing bone invasion because FDG accumulates well at the malignant tumor. However, Goerres et al. [33] reported that the assessment of cortical erosion with contrast-enhanced CT and the CT information from PET/CT were the most reliable methods for detecting bone invasion, and FDG uptake seen on PET/CT images did not improve identification of bone infiltration. This report indicates that CT is essentially superior to PET alone concerning the detection of bone invasion of CaMG. It is likely, because FDG accumulates well at not only the lesion of malignant tumor but also the inflammatory lesion and the spatial resolution of PET is not high [34].

4. The relationship between the diagnostic imaging pattern of bone invasion and prognosis

The pattern of bone destruction, as well as the extent of the bone invasion, is one of the determinant factors of the choice between rim or segmental resection and the prognosis of patients with CaMG [2,6,7,13,22,35,36]. Therefore, it is important to judge accurately the pattern of bone destruction by diagnostic imaging. Previous studies on the possible association between the pattern of bone destruction and outcome were based on the findings of conventional radiographs [10,13,35–40]. In the previous studies based on the conventional radiography, the pattern of bone destruction has been classified into two types; an erosive and an infiltrative pattern [10,13,35–40]. However, we found it was sometimes difficult to classify certain bone destructions in either of the two patterns. We therefore divided the infiltrative pattern into mixed pattern and invasive pattern, and then, we finally classified the pattern of bone destruction into three types: erosive, mixed, and invasive, with reference to the histological classification described by Brown

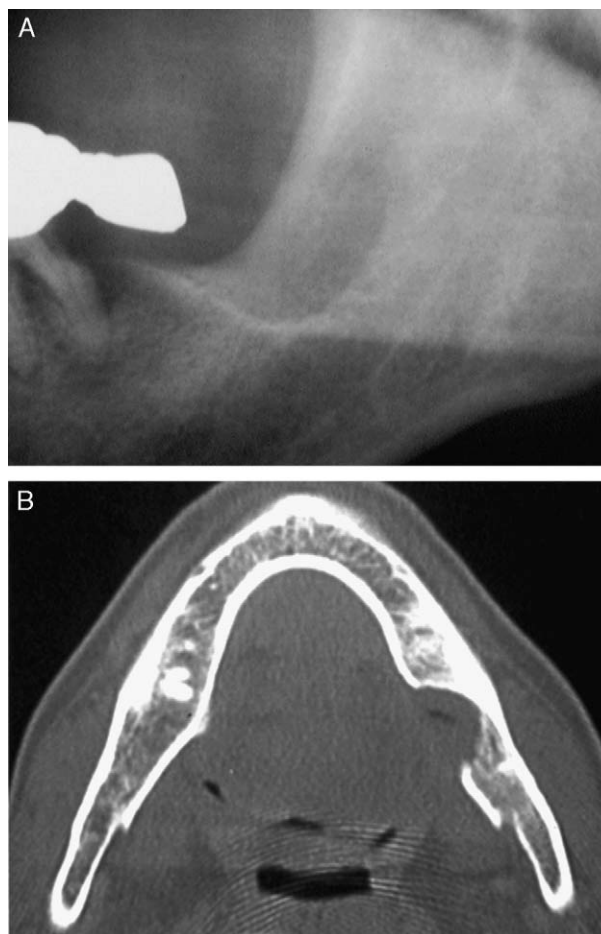


Figure 2 An example of a case classified as the erosive pattern on panoramic radiography (A), and X-ray CT (B).

et al. [6,7]. The invasive pattern was defined as bone destruction with an irregular and ill-defined margin accompanied with bony spicules or isolated fragments (Fig. 1). The erosive pattern showed U-shaped or scalloped bone destruction to the medullary bone with a smooth and well-defined margin, and no isolated bony spicules (Fig. 2). The mixed pattern was defined as bone destruction with an irregular margin and intermediate features between the erosive and invasive patterns (Fig. 3).

On the other hand, previous studies based on the conventional radiographs have reported some discrepancies between the pattern of bone destruction on the images and the histological findings [35,38,40]. Ohba et al. [38] described one case which they classified as moth-eaten on PR findings, but which was shown histologically to be erosive. Reviewing the radiograph, they found that they had misdiagnosed the residual normal trabecular bone around the tumor as bony spicules within it. Totsuka et al. [40] stated that 7 out of 24 cases, which they classified as invasive pattern on the conventional radiographs, histologically showed an erosive pattern, while 2 out of 14 cases, classified as erosive pattern on the conventional radiographs, were histologically invasive. Iwaki [35] also reported a similar discrepancy. I considered that this discrepancy might be caused by the fact that the conventional radiography is two-dimensional superimposed image, and lacks the information about the bone

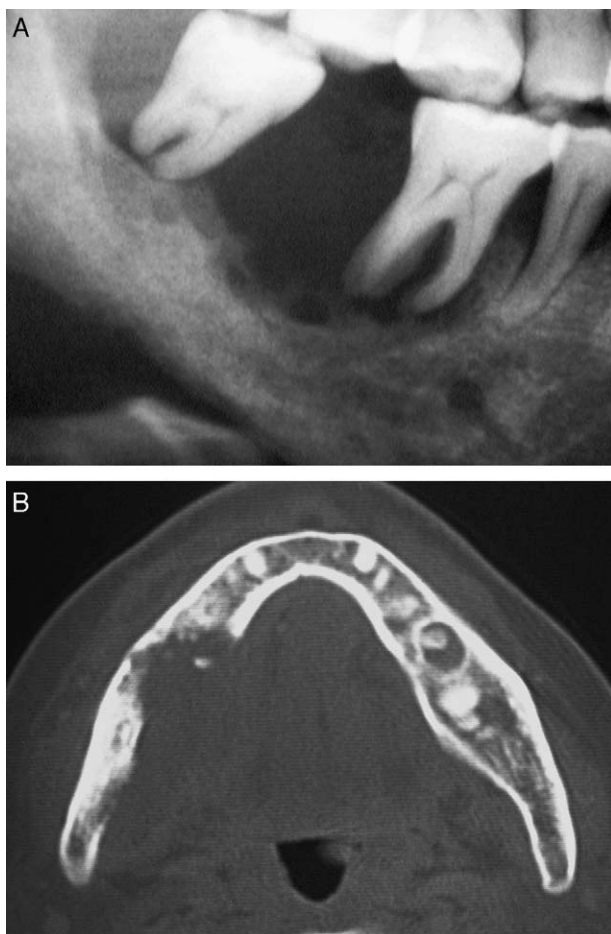


Figure 3 An example of a case classified as the mixed pattern on panoramic radiography (A), and X-ray CT (B).

destruction at the buccal and lingual cortex. If a diagnostic image detects the findings of bone destruction at not only the supero-inferior and medio-distal aspects of the bone, but also the bucco-lingual condition of the bone, the discrepancy might have been solved. Therefore, we have considered that CT is suitable for determining the pattern of bone destruction in CaMG, because the CT image provides three-dimensional information of bone destruction including the buccal and lingual cortex of the mandible [1,22,39].

From the above-mentioned two points of view, we investigated the association between the pattern of bone destruction based on the CT and the outcome of the patients with CaMG compared with the association based on the PR, using our classification into the three patterns of bone destruction [41]. As a result, the pattern of bone destruction based on the CT findings was closely associated (Fig. 4), but in contrast, the pattern of bone destruction based on the PR findings was not associated (Fig. 5) with the cumulative survival rate. In conclusion, the pattern of bone destruction based on the CT is a more important factor in determining the prognosis than that on the PR.

From this result, we considered that the CT findings might reflect the histologic appearance more closely than the PR findings, and that it might be the reason why the pattern of bone destruction based on CT has a better association with the prognosis. Therefore, we next studied the association

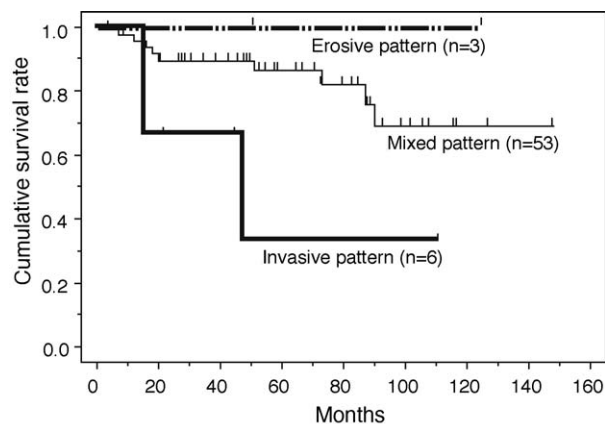


Figure 4 Cumulative survival rate for the pattern of bone destruction based on X-ray CT.

between the CT pattern and histologic pattern of bone destruction by comparing the CT images with the removed specimens [42]. As a result, this study showed that the CT pattern was correlated with the histologic pattern of the bone destruction. However, in this study, the specimens underwent a preoperative radiochemotherapy before resection, and hence the histologic pattern might have altered before and after the therapy [43]. Thus, further strict studies by the specimens receiving no preoperative radiochemotherapy are needed to clarify the association between the CT pattern and histologic pattern of bone destruction in the future.

Our Japanese investigators indicated that the extent and pattern of bone invasion is one of the prognostic factors of CaMG [10,23,41], but in contrast, other investigators mentioned that not only the bone invasion but also the tumor infiltration into the surrounding soft tissues are the determinants of prognosis, on the basis of the fact that the recurrence occurred at the resected margin of not the bone but the soft tissue. I consider that the degree of the tumor infiltration into the adjacent soft tissues and the extent and pattern of bone invasion are not independent, but relate to each other, and therefore, both are important determinants of the prognosis. On that basis, I suspect that the

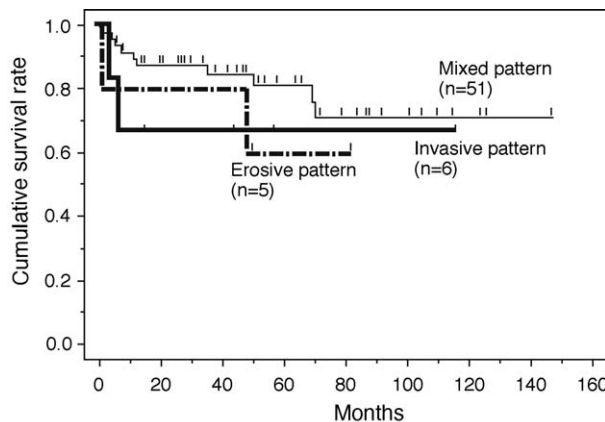


Figure 5 Cumulative survival rate for the pattern of bone destruction based on panoramic radiography.

extent of bone invasion is an indicator of the tumor extent into the adjacent soft tissues. We should clarify the correlation between the two in the future.

In conclusion, the pattern of bone destruction due to CaMG should be classified from the CT rather than the PR findings in order to estimate the prognosis.

5. Summary

Diagnostic imaging has a significant mission to detect precisely the extent and pattern of bone invasion due to CaMG before starting the treatment. Regarding the bone invasion into the mandibular canal, the accuracy of the PR is equal to that of CT, and the both accuracy is not low in comparison with any other imaging modalities. Hence, PR would be suitable for the initial screening modality in order to determine the T classification, especially a Japanese new T classification criteria which is based on the presence of bone invasion into the mandibular canal.

On the other hand, the pattern of bone destruction on the diagnostic images could be classified into three types: erosive, mixed, and invasive. According to this classification, the CT pattern of bone invasion is closely associated with the prognosis, and therefore, the pattern should be determined based on the CT findings.

In conclusion, at the present time, CT is suitable for detection of bone invasion in CaMG, although CT cannot detect precisely an early weak bone invasion, or a bone invasion infiltrating through the trabecular bone.

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