Abstract: The purpose of the present study was to predict inferior alveolar nerve (IAN) exposure and associated neurosensory deficits after mandibular cyst surgery based on imaging findings. The study includes 193 sites in 184 consecutive patients who underwent enucleation of cystic lesions around a mandibular third molar (MM3) and extraction of the associated MM3. Absence/presence of white lines on panoramic radiographs (PR) and absence/presence of cortication surrounding the mandibular canal on computed tomography (CT) are evaluated as predictor variables. Outcome variables are operative IAN exposure and postoperative lower lip and/or chin dysesthesia. There is a significant correlation between interruption of white lines and loss of cortication. The predictor variables are statistically associated with IAN exposure and dysesthesia. Positive predictive values of CT findings (loss of cortication) for each outcome variable are slightly higher than those of PR findings (interruption of white lines). When considering the variables, type IV, with interruption of white lines and loss of cortication, shows a statistically significant difference compared to the other groups.

White lines on PR images and cortication status of the mandibular canal on CT images predict operative IAN exposure and postoperative dysesthesia in mandibular cyst surgery.

Keywords: panoramic radiograph; computed tomography; mandibular cyst; inferior alveolar nerve; dysesthesia.

Introduction

Dentists frequently encounter cystic lesions within jawbones due to the presence of abundant odontogenic epithelial remnants (1). Several different imaging modalities, including panoramic radiography (PR) and computed tomography (CT), have been used for preoperative evaluation of cystic lesions within jawbones (2). In dental practice and oral surgery, PR is used most frequently for diagnosis and treatment planning because of its wide availability and low cost. PR provides two-dimensional information involving anterior-posterior and upper-lower positional relations, but does not yield three-dimensional information, which includes buccolingual data. Alternatively, CT provides three-dimensional and cross-sectional information and multiplanar views, but involves high radiation exposure and high cost.

Among jawbone cysts, those that develop around the mandibular third molar (MM3) are relatively frequent. The usual treatment for such cysts is careful enucleation together with removal of the associated MM3. In many such cases, the cysts and/or MM3s are in contact with or in immediate proximity to the inferior alveolar nerve.
IAN). Therefore, IAN injury and associated neurosensory deficits are serious complications associated with surgical removal of the cyst and the MM3. Complications associated with extraction of MM3s have been discussed previously (3-10). IAN injury is the third most reported complication of MM3 surgery (3). However, reports of complications associated with cysts that develop around the MM3 are rare.

The purpose of this study was to estimate the frequency of IAN exposure and associated neurosensory deficits during and after surgical removal of mandibular cysts and MM3s, and assessed the value of preoperative PR and CT in predicting IAN exposure and associated neurosensory deficits. In particular, the white lines on PR images and cortication surrounding the mandibular canal on CT images were focused on as predictor variables and operative IAN exposure and postoperative lower lip and/or chin dysesthesia as complications. The relationships between these image variables and complications were analyzed.

Materials and Methods

Subjects
The study included 193 sites in 184 consecutive patients who underwent simultaneous surgical removal of cystic lesions around the MM3 and MM3 extraction at the dental hospital of Tokyo Medical and Dental University between January 2009 and March 2016. The incidence of lower lip and/or chin dysesthesia after extraction of a MM3 without a cyst or other pathologies at the dental hospital of Tokyo Medical and Dental University was used as a reference. Cases receiving local anesthesia were treated during year 2012, and those receiving general anesthesia were treated between 2012 and 2014. The study was approved by the institutional review board of the Faculty of Dentistry, Tokyo Medical and Dental University (No. D2017-038).

Imaging
All digital panoramic images were obtained using a Veraviewpocs (Morita Corp., Kyoto, Japan) instrument operated at 79-80 kVp and 9-10 mA with a photostimulated phosphor plate (ST-IV; Fuji Film Medical Co., Ltd, Tokyo, Japan). This apparatus provided panoramic images with uniform magnification in horizontal and vertical dimensions. CT examinations were performed using a 64-slice multidetector CT (MDCT) instrument (Somatom Sensation 64; Siemens AG, Erlangen, Germany) with parameters of tube voltage 120 kV, effective mAs 140 mAs, and collimation 64 × 0.6 mm. Cross-sectional CT images 1-mm thick at 2-mm intervals were acquired using a CT work station (Syngo Acquisition Workplace: Siemens AG, Erlangen, Germany).

Study variables
Imaging findings on PR and CT images as mentioned below were evaluated by an oral surgeon (R.H.) and an oral radiologist (A.T.), with each observer blind to the other’s results. When disagreement existed, another blinded observer (S.Y; oral surgeon) evaluated the images, and the findings were judged by majority decision.

Visualization and assessment of the mandibular canal via PR
Two radiopaque lines, known as “white lines,” found on PR images constituted the superior and inferior borders of the mandibular canal. Visibility of the white lines was used to assess the mandibular canal on PR images. When white lines were clearly and continuously visible, the image was classified as “presence (+)” (Fig. 1A). Alternatively, when either or both white lines were discontinuous because of interruption due to a cyst or MM3, the image status was defined as “absence (−)” (Fig. 1B).

Visualization and assessment of the mandibular canal via CT
The features of the mandibular canal were assessed on reconstructed cross-sectional CT images, and cortication status was defined as an important evaluation parameter.
The cortical lining surrounding the mandibular canal was observed on cross-sectional CT images. When the cortical lining was clearly and continuously visible, the image status was defined as “presence (+)” (Fig. 1C). Alternatively, when the cortical lining was lost because of interruption due to a cyst or MM3, the image was classified as “absence (−)” (Fig. 1D).

**Outcome variables**

Enucleation of the cyst, together with removal of the associated MM3, was performed by qualified oral surgeons with the patient under general or local anesthesia. In each cyst and tooth position, the outcome variables were IAN exposure and the occurrence of lower lip and/or chin dysesthesia.

IAN exposure was defined as direct visualization of the IAN at surgical sites during the operation. As part of usual practice, surgeons examined the operating field for the presence or absence of an exposed IAN. If the IAN was visualized following removal of the cyst and tooth, the finding was recorded in the operative note. Lower lip and/or chin dysesthesia was evaluated by self-reported sensation of the patients on the day after surgery.

**Classification of cases based on the combination of white lines on PR images and cortication status on CT images**

Four categories were defined based on presence (+) or absence (−) of the white lines of the mandibular canal wall on PR images and that of the cortical bone on CT images: Type I = white line (+), cortication (+); Type II = white line (+), cortication (−); Type III = white line (−), cortication (+); and Type IV = white line (−), cortication (−). The relationships of these groups to IAN exposure at the surgical site and lower lip and/or chin dysesthesia in each cyst and tooth position were analyzed.

**Statistical analysis**

Absence of the white lines on PR images and of cortication on CT images suggested contact between the mandibular canal and cystic lesion or tooth. Therefore, the hypothesis was proposed that absence of the white lines and/or cortication are positive predictors for operative IAN exposure and postoperative dysesthesia. Statistical analysis was performed based on this hypothesis. The relationships between predictor and outcome variables were analyzed using cross-tabulations and the χ² test. The κ coefficient was used to check agreement rate between white lines on PR images and cortication status on CT images. Logistic regression analysis was used to assess the relationship between explanatory variables (type, sex, and age) and outcomes (IAN exposure and dysesthesia). Multicollinearity was assessed using the variance inflation factors (VIF). Results were presented as odds ratios (ORs) with 95% confidence intervals (CIs). \( P < 0.05 \) was considered statistically significant. All analyses were performed using the IBM SPSS statistics 19.0 software (Chicago, IL, USA).

**Results**

This series included 115 men (62.5%) and 69 women (37.5%; male:female ratio, 1.67:1; mean age at first visit, 45.9 ± 12.0 years; range, 11-73 years). A summary of descriptive statistics is shown in Table 1. Histologically, the most commonly encountered cysts were dentigerous cysts (165 cases), followed by inflammatory granulation tissue (10), lateral periodontal cysts (4), odontogenic keratocysts (2), radicular cysts (2), ameloblastoma (cystic type, 1), a simple bone cyst (1), and an orthokeratinized odontogenic cyst (1; data not shown). The incidence of lower lip and/or chin dysesthesia after MM3 extraction without a cyst or other pathologies at the dental hospital of the Tokyo Medical and Dental University is shown in Table 2 as a reference. The total incidence of dysesthesia after MM3 extraction, and incidences in cases receiving local and general anesthesia were 1.4%, 0.8%, and 11.3%, respectively (Table 2).
Assessment of visibility of the mandibular canal on PR and CT images
Of 193 cases studied, the white lines were absent on PR images in 135 (69.9%) and cortication was absent on CT images in 118 (61.1%; Table 1). Among the latter 118 cases, white lines were not visible in 107 (90.7%). Conversely, 107 (79.3%) of the former 135 cases lost cortical lining. There was a significant correlation between absence of white lines on PR and of cortication on CT images ($P < 0.001$; Table 3). The $\kappa$ coefficient between those two predictors was 0.567, showing moderate agreement (11).

Relationship between white lines on PR images, and IAN exposure (Table 4) and dysesthesia (Table 5)
The frequency of presence and absence of white lines on PR images was 58 (30.0%) and 135 (70.0%), respectively. White lines were absent in 69 of 84 cases in which IAN was exposed at the surgical site (sensitivity, 0.821; 95% CI, 0.749-0.881) and were present in 43 of 109 in which IAN was not exposed at the surgical site (specificity, 0.394; 95% CI, 0.339-0.441). The Positive (PPV) and negative (NPV) predictive values were 0.511 (95% CI, 0.466-0.548) and 0.741 (95% CI, 0.637-0.828), respectively. Interruption of white lines on PR images also was statistically associated with dysesthesia ($P = 0.005$).

The relationship between cortication on CT images, and IAN exposure (Table 6) and dysesthesia (Table 7)
The frequencies of retention and loss of cortical lining surrounding the mandibular canal were 75 (38.9%) and 118 (61.1%), respectively. Cortical lining was lost in 69 of 84 cases in which the IAN was exposed at the surgical site (sensitivity, 0.821; 95% CI, 0.749-0.881) and was retained in 60 of 109 cases in which the IAN was not exposed at the surgical site (specificity, 0.550; 95% CI, 0.494-0.597). The PPV and NPV were 0.585 (95% CI, 0.532-0.627) and 0.800 (95% CI, 0.717-0.867), respectively. Loss of cortical lining on CT was statistically associated with IAN exposure ($P = 0.001$). Interruption of white lines on PR images also was statistically associated with IAN exposure ($P = 0.001$).
Relationship between IAN exposure and dysesthesia
Postoperative dysesthesia usually occurs upon IAN exposure at the surgical site. Therefore, the relationship between IAN exposure and dysesthesia was analyzed (Table 8). IAN exposure at surgical sites was observed in 84 (43.5%) cases and dysesthesia occurred in 61 (31.6%). The IAN was exposed in 40 of 61 cases in which dysesthesia occurred (sensitivity, 0.656; 95% CI, 0.553-0.747) and was not exposed in 88 of 132 in which dysesthesia did not occur (specificity, 0.667; 95% CI, 0.619-0.709). The PPV and NPV were 0.476 (95% CI, 0.402-0.543) and 0.807 (95% CI, 0.750-0.859), respectively. There was a significant correlation between IAN exposure at surgical sites and lower lip and/or chin dysesthesia ($P < 0.001$).

The statistical parameters (sensitivity, specificity, PPV, NPV, and $P$ value) are summarized in Table 9.

Combination of white lines on PR images and cortication on CT images, and their relationship to IAN exposures and dysesthesia
For further analysis, all cases were categorized into the aforementioned four groups according to the combination of white lines on PR and cortication on CT images. Of the total, 47 cases (24.4%) were Type I, 11 (5.7%) Type II, 28 (14.5%) Type III, and 107 (55.4%) Type IV. The relationship between combination types and IAN exposure and dysesthesia is shown in Tables 10 and 11. The hypothesis was that IAN exposure and dysesthesia would occur most frequently in Type IV (white line [−], cortication [−]) cases. The Type IV incidence in IAN-exposed cases ($n = 84$) and dysesthesia cases ($n = 61$) was 76.2% ($n = 64$) and 75.4% ($n = 61$), respectively. Among the Type IV cases, the incidence of IAN exposure was 59.8% (Table 9) and the incidence of dysesthesia

<table>
<thead>
<tr>
<th>Table 6</th>
<th>The relationship between cortication on CT and IAN exposure</th>
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<tr>
<td>IAN exposure</td>
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<tr>
<td>Cortex</td>
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<td>Presence</td>
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<tr>
<td>Absence</td>
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IAN: inferior alveolar nerve

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<tr>
<th>Table 7</th>
<th>The relationship between cortication on CT and dysesthesia</th>
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<td>Dysesthesia</td>
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<tr>
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<th>Table 8</th>
<th>The relationship between IAN exposure and dysesthesia</th>
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<tr>
<td>IAN exposure</td>
<td></td>
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<tr>
<td>Dysesthesia</td>
<td>Presence</td>
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<tr>
<td>Absence</td>
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IAN: inferior alveolar nerve

<table>
<thead>
<tr>
<th>Table 9</th>
<th>Summary of statistics values</th>
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<tr>
<th>IAN exposure</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>$P$ value</th>
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<tbody>
<tr>
<td>White line</td>
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<td>0.394</td>
<td>0.511</td>
<td>0.741</td>
<td>0.001</td>
</tr>
<tr>
<td>Cortication</td>
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<td>0.550</td>
<td>0.585</td>
<td>0.800</td>
<td>&lt;0.001</td>
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</table>

<table>
<thead>
<tr>
<th>Dysesthesia</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>White line</td>
<td>0.836</td>
<td>0.364</td>
<td>0.378</td>
<td>0.828</td>
<td>0.005</td>
</tr>
<tr>
<td>Cortication</td>
<td>0.787</td>
<td>0.470</td>
<td>0.407</td>
<td>0.827</td>
<td>0.001</td>
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<tr>
<td>IAN exposure</td>
<td>0.656</td>
<td>0.667</td>
<td>0.476</td>
<td>0.807</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

IAN: inferior alveolar nerve; PPV: positive predictive value; NPV: negative predictive value
Logistic regression analysis was performed to assess the relationship between predictor variables (age, sex, and type) and outcomes (IAN exposure and dysesthesia). The VIFs of age, sex, and type were 1.004, 1.004, and 1.000, respectively. Therefore, multicollinearity among predictor variables could be ignored. Based on the results of forward selection (likelihood ratio), age and sex were removed as predictor variables from further analysis. Based on the ORs obtained through logistic regression analysis, Type IV was the most reliable predictor of IAN exposure and dysesthesia among the four types (Table 12). The data from Type II were unreliable in terms of $P$ value ($>0.05$). The high $P$ value may have been due to the small sample size of the Type II group.

### Discussion

The overall incidence of lower lip and/or chin dysesthesia after surgical treatment for cysts associated with MM3 was 31.6% in this study. The incidence of dysesthesia after extraction of the MM3 was 0.8% and 11.3% in cases receiving local and general anesthesia, respectively (Table 2). As the procedure for extracting a deeply impacted MM3 is highly invasive, it was performed with the patient under general anesthesia. Even so, the incidence of dysesthesia after mandibular cyst surgery was higher compared to that after MM3 extraction. The main reason for this observation may be that since these cysts originated and developed around an MM3, there was a higher likelihood of invasion into the IAN. The sites of interruption of white line and cortical lining were not divided into cyst and MM3 sites in this study. Similarly, the sites of IAN exposure also were not divided. Therefore, the effect of MM3 extraction on IAN exposure and dysesthesia in mandibular cyst surgery could not be discussed clearly, although it was an important point. Postoperative lower lip and/or chin dysesthesia is a significantly serious complication. Therefore, patients must be sufficiently informed and educated about the risk of this complication preoperatively.

Radiological images provide valuable preoperative information to predict postoperative dysesthesia. Thus, PR and CT are invaluable tools for diagnosis and surgical treatment of mandibular cysts, and provide three-dimensional data about positional relationships of the cysts with teeth and the extent of disease. Presence/absence of white
lines of the mandibular canal on PR images and presence/absence of cortication surrounding the mandibular canal on CT images were analyzed as predictor variables for IAN exposure and postoperative dysesthesia in this study. These two factors have been suggested to indicate a relationship of MM3 extraction with IAN exposure and dysesthesia (5-7,12,13). Absence of white lines on PR images was related to the absence of cortication on CT images in this study \( (P < 0.001) \), although the agreement rate \( (\kappa \text{ coefficient}, 0.567) \) between these two predictors was moderate. The findings from PR and CT images did not correspond completely. CT provided higher-contrast images and allowed for better identification of the mandibular canal than did PR \( (14) \). In fact, the false-positive ratio for PR (absence of white line, 60.6%; Table 4) for IAN exposure was higher than that for CT (absence of cortication, 45.0%; Table 6). A previous report showed that interruption of the white lines on PR images did not correlate with absence of cortication on CT images, in cases of MM3 surgery \( (15) \). A possible cause for this observation is that the visibility of the mandibular canal on PR and CT images in cases of mandibular cysts differs from that in cases of MM3 surgery. Radiographically, a cyst presents as a well-defined radiolucency with corticated margins. Alternatively, the MM3 shape, especially that of the root close to the mandibular canal, is so varied that images showing the relationship between the MM3 and mandibular canal are complex. Therefore, absence of white lines on PR images and cortication on CT images is easier to detect in cases of cysts compared to that in cases of MM3 surgery.

Absence of white lines \( (P = 0.005) \) and cortication \( (P = 0.001) \) were statistically significantly related to lower lip and/or chin dysesthesia, and, hence, may be reliable predictive markers of dysesthesia after mandibular cyst surgery. The sensitivities of white lines and cortication were 0.836 and 0.787, respectively, which meant that the incidence of cases with white line interruption or loss of cortication was high among those with dysesthesia. However, it is noteworthy that this was a retrospective study aiming to predict IAN exposure and dysesthesia from preoperative images. In this respect, PPV is a parameter of considerable significance. The PPVs of white lines and cortication, for dysesthesia after mandibular cyst surgery. Generally, predictor variables tend to have a low PPV and high NPV when the prevalence of the outcome variables is low, even if sensitivity and specificity are high. The prevalence of dysesthesia was 31.6%, and the NPV of white lines and cortication for dysesthesia was high (0.828 and 0.827, respectively) in this study. In previous studies on MM3 surgery, the PPV of white lines as the radiographic markers of IAN injury was 0.12 (NPV = 0.98), assuming a 1% prevalence of IAN injury \( (5) \). Thus, it is unreasonable to compare the PPV of white lines and cortication in this study with that in MM3 surgery, even for the same predictive parameters and outcome variables, owing to differences in the prevalence of outcome variables.

Though conventionally not considered to be a preoperative predictor of dysesthesia, IAN exposure at the surgical sites during surgery was examined as a predictive factor for dysesthesia, and it was likely to be a good predictor. The PPV of IAN exposure for dysesthesia, however, was not high \( (0.476; \text{ sensitivity}, 0.656; \text{ specificity}, 0.667) \). This value also was affected by the prevalence of dysesthesia \( (31.6\%) \), as mentioned above. The possible reason for this observation may be that the cyst and associated MM3 were removed with great care in cases with a high risk for IAN exposure. Furthermore, the exposed IAN at surgical sites were protected using a cotton-type oxidized regenerated cellulose to prevent damage to the IAN, which may have effectively prevented any subsequent lower lip and/or chin dysesthesia.

We hypothesized that CT images were superior to those of PR to predict IAN exposure and dysesthesia at the outset. In concrete terms, we speculated that the loss of cortical lining surrounding the mandibular canal on CT was a better predictor than interruption of the white line on PR. In this study, the PPVs for IAN exposure and dysesthesia of CT images \( (0.585 \text{ and } 0.407, \text{ respectively}) \) were slightly higher than those of PR images \( (0.511 \text{ and } 0.378, \text{ respectively}) \). This result showed that PR was not to be outdone by CT. Previous studies also have shown that cone-beam CT was not better than PR in predicting postoperative IAN sensory disturbance \( (10,16,17) \). However, cone-beam CT revealed the number and divergence of roots more reliably than did PR \( (10) \), and was superior in predicting IAN exposure \( (16) \). PR is performed routinely and is an important tool for diagnosis and treatment-planning. It also is the standard technique for assessing risk of IAN injury after MM3 extraction. Our results show that PR had an important role even in mandibular cyst surgery, and reaffirmed the usefulness of PR in dental practice.

In case of mandibular cyst surgeries, PR and CT must be performed to ascertain the extent of the cyst and positional relationship between the tooth and cyst. Therefore, the combination variables consisting of interruption of the white lines on PR images and loss of cortical lining
surrounding the mandibular canal on CT images were setas predictors of IAN exposure and dysesthesia. Type IV cases, having interruption of the white lines and loss of cortical lining, were encountered most frequently. This result reflected the significant relationship between interruption of the white lines and loss of cortical lining. Statistical analysis showed that Type IV status was the most effective predictor for IAN exposure and dysesthesia among the four types, as predicted.

In conclusion, the frequencies of operative IAN exposure and postoperative lower lip and/or chin dysesthesia as complications of mandibular cyst surgery were 43.5% and 31.6%, respectively. Interruption of the white lines on PR images and loss of cortical lining surrounding the mandibular canal on CT images may be reliable preoperative predictors for these complications. The results of the present study may be used to improve outcomes and prevent postoperative complications in patients undergoing mandibular cyst surgery.

**Acknowledgments**
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**Conflict of interest**
The authors have no conflict of interest to declare.

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