

# Maxillary molar root protrusion into the maxillary sinus: a comparison of cone beam computed tomography and panoramic findings

**S. Themkumkwun<sup>1</sup>,  
J. Kitiskanchana<sup>2</sup>, A. Waikakul<sup>1</sup>,  
K. Boonsiriseth<sup>1</sup>**

<sup>1</sup>Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Mahidol University, Bangkok, Thailand; <sup>2</sup>Department of Oral and Maxillofacial Radiology, Faculty of Dentistry, Mahidol University, Bangkok, Thailand

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**Abstract.** This study aimed to examine the prevalence of molar roots protruding into the maxillary sinus and to determine the panoramic radiographic signs as correlated with cone beam computed tomography (CBCT). CBCT images of 354 roots were assessed and classified into three types, according to the relationship between the root and maxillary sinus. The prevalence of root protrusion into the maxillary sinus was calculated then the panoramic images assessed. After excluding some unidentified roots on the panoramic images, 200 were investigated for panoramic signs, including (i) projection of the root apex into the sinus cavity, (ii) interruption of the maxillary sinus floor's cortex, (iii) absence of periodontal ligament space, (iv) darkening of the involved root region, and (v) upward curving of the sinus floor. The respective correlation between the panoramic signs and CBCT types was assessed. Forty-six percent of roots showed protrusion into the sinus with the palatal root of the first molar having the greatest prevalence (33/200 roots). The panoramic signs 'projection of the root apex in the sinus cavity' and 'darkening of the involved root apical region' both strongly indicated root protrusion into the maxillary sinus ( $P < 0.05$ ).

**Key words:** maxillary sinus; maxillary molar root; panoramic radiograph; CBCT.

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Maxillary sinus is the first paranasal sinus developed in a 10-week-old fetus. The developmental process is called sinus pneumatization<sup>1</sup> and its growth ends at the time of maxillary third molar eruption at the age of 20 years. Pneumatization of the maxillary sinus can, however, be identified after extraction of the maxillary posterior tooth<sup>2</sup>. Previous studies showed that 10.5–34.2% of maxillary molar roots show an intimate relationship to the floor of the maxillary sinus<sup>3–8</sup>. The close relationship can lead to bacterial invasion from infected teeth causing odontogenic sinusitis: a condition found in 12% of all cases of sinusitis<sup>9</sup>. In addition, an oro-antral communication (OAC) following extraction and surgical removal of the maxillary molar may occur due to the proximity between the roots and the maxillary sinus floor.

The most common site of OAC was the maxillary first molar, followed by the maxillary second and third molars<sup>10,11</sup>. Del Rey-Santamaria et al. reported that the incidence of OAC was about 5.1%<sup>12</sup>, which is relatively low, but can lead to serious complications (i.e. orbital abscess, osteomyelitis, cavernous sinus thrombosis, meningitis, subdural empyema, and intracranial abscess). Visscher et al. thus argued that further treatment for OAC closure by an experienced operator is mandatory<sup>13</sup>. We propose that identification of difficult cases – by determining the proximity between the root and the maxillary sinus – would provide a tool for preventing OAC, and would also be useful for endodontic treatment, periodontal treatment, and implant placement.

Radiographic examination is necessary for tooth evaluation prior to surgical procedures, and the panoramic radiograph is the method of choice because it reveals structures in both the maxilla and mandible at a low cost and low radiation dose. The limitations of this two-dimensional technique are (i) superimposition of anatomical structures and (ii) image magnification. Evaluation of the relationship between the maxillary molar root and the maxillary sinus from the panoramic radiograph might be a challenge; however, cone beam computed tomography (CBCT) solves these two limitations. CBCT allows better visualization in three dimensions, thus it plays an important role in the assessment of the relationship between the maxillary molar root and maxillary sinus<sup>14</sup>. Accessibility of CBCT, however, is limited, and the cost and radiation dose from CBCT are higher than panoramic radiography.

There have been few comparative studies of panoramic and CBCT images vis-à-

vis maxillary molar roots invading the maxillary sinus<sup>15</sup>. A systematic review was performed of the accuracy of panoramic imaging compared with CBCT in assessing the relationship between molar roots and the maxillary sinus<sup>16</sup>. According to these prior studies, some of the roots appearing to protrude into the maxillary sinus on panoramic images were actually located laterally or medially to the sinus when observed on CBCT images. Hence, the features of roots protruding into the maxillary sinus as observed on panoramic images might not reflect the invasion into the sinus. Nevertheless, panoramic imaging remains the method of choice for various preoperative procedures; so we aimed (i) to examine the prevalence of roots protruding into the maxillary sinus using CBCT and (ii) to determine the panoramic radiographic signs of maxillary molar root indicating protrusion of the root into the maxillary sinus with respect to CBCT findings.

### Materials and methods

The Institutional Review Board of our university reviewed and approved the study (COA.No.MU-DT/PY-IRB 2017/050.2609). CBCT images – recorded between January and December 2016 – were retrieved from the database. The inclusion criteria were CBCT images of cases prescribed for any dental purposes (e.g., preoperative implant planning, localization of embedded tooth, evaluation of root fracture or root canal morphology) covering the maxillary molar region and floor of the maxillary sinus. The field of view of CBCT images was 6 × 6 cm or 8 × 8 cm resulting in a voxel size of 0.125 mm<sup>3</sup> or 0.16 mm<sup>3</sup>. Thereafter, the availability of panoramic radiographs of these patients was checked in the archive, and the available radiographs were retrieved. The panoramic radiographs of these patients were often taken prior to CBCT for evaluation of any dental problems (e.g., advanced periodontal disease, impacted teeth, prosthetic planning, and cyst or tumor in any area of the jaw). Our study included patients with a normal maxillary sinus and molar teeth showing complete root formation, normal erupting position, and normal apical region. Teeth with root canal treatment or any pathology were excluded.

All CBCT images were captured using a 3D Accuitemo 170 (J. Morita, Kyoto, Japan) with exposure factors of 90 kVp, 5 mA, and 17.5 s. All digital panoramic radiographs were taken in our hospital using a CS 9000 machine (Carestream Health, Inc., Rochester, NY, USA). The exposure

parameters were selected according to the patient characteristics (68–72 kVp, 8–10 mA, 15 s). The time interval between the two imaging modalities was no more than 1 year, and no other intervention was performed in the evaluated region between the two imaging modalities.

An examiner (S.T.) evaluated all panoramic and CBCT images in a random sequence. A 14.0-inch, light-emitting diode, high-definition screen (resolution 1366 × 768 pixels) was used for image assessment. The examiner was allowed to use the zoom tool and to adjust the brightness and contrast of the images. Evaluation of all of the data was repeated at 2-week intervals for intra-examiner reliability. In addition, one-third of the data, on both panoramic and CBCT images, was analysed by two examiners (S.T., J.K.) independently for inter-examiner reliability.

The CBCT images were evaluated with i-Dixel software. The examiners were allowed to view images in all planes. The relationship between the maxillary molar root and maxillary sinus on the CBCT images was classified into three types (Fig. 1): Type 0 – evidence of thick bone between the root and floor of the maxillary sinus; Type 1 – evidence of a thin white line, matching the cortical bone between some part of the root and the floor of the maxillary sinus, with or without its elevation; or, Type 2 – evidence of some part of the root extending beyond the floor of the maxillary sinus, without a cortical bone in between.

Panoramic radiographs were assessed using ImageJ software (NIH, Bethesda, MD, USA; <http://rsb.info.nih.gov/ij>). Radiographic signs of protrusion of the root into the maxillary sinus were modified from the radiographic signs as per Lopes et al.<sup>15</sup> (Fig. 2): Sign 1 – projection of the root apex in the sinus cavity; Sign 2 – interruption of the maxillary sinus floor's cortex; Sign 3 – absence of the periodontal ligament (PDL) space; Sign 4 – darkening of the involved root apical region; and Sign 5 – upward curving of the sinus floor enveloping the root. Each root was evaluated and recorded for the presence of each sign. Accordingly, one root might show no signs or more than one sign.

### Statistical analysis

Kappa analysis was used to evaluate intra- and inter-examiner reliability. The prevalence of each maxillary molar root protruding into the maxillary sinus was calculated as a percentage. Multiple logistic regression was used to evaluate the correlation between CBCT findings and

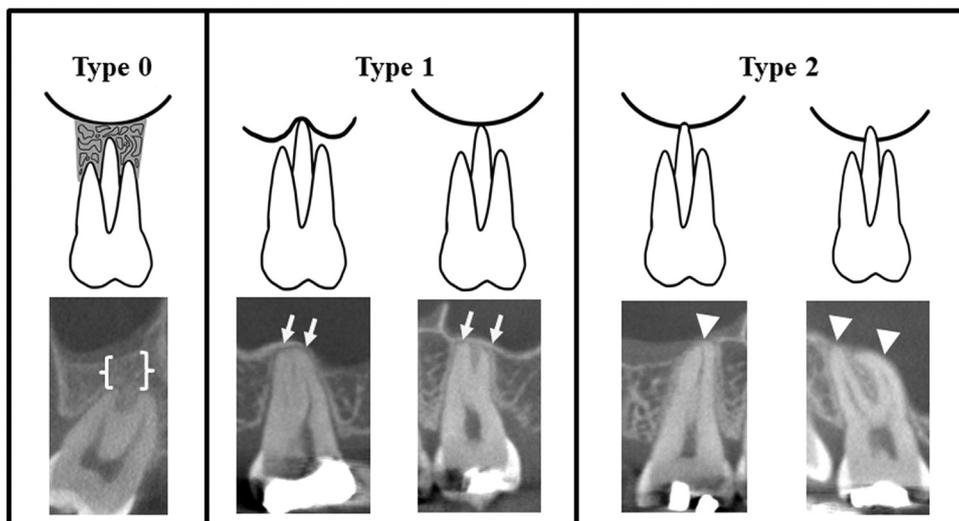


Fig. 1. Classification of CBCT images.

Top row shows schematic images and bottom sagittal CBCT images. From left to right, Type 0, Type 1, and Type 2 are illustrated, respectively. Brackets show thick bone between evaluated roots and the maxillary sinus in Type 0. Arrows indicate white line of sinus floor cortex in Type 1. Arrowheads indicate area showing loss of sinus floor cortex in Type 2.

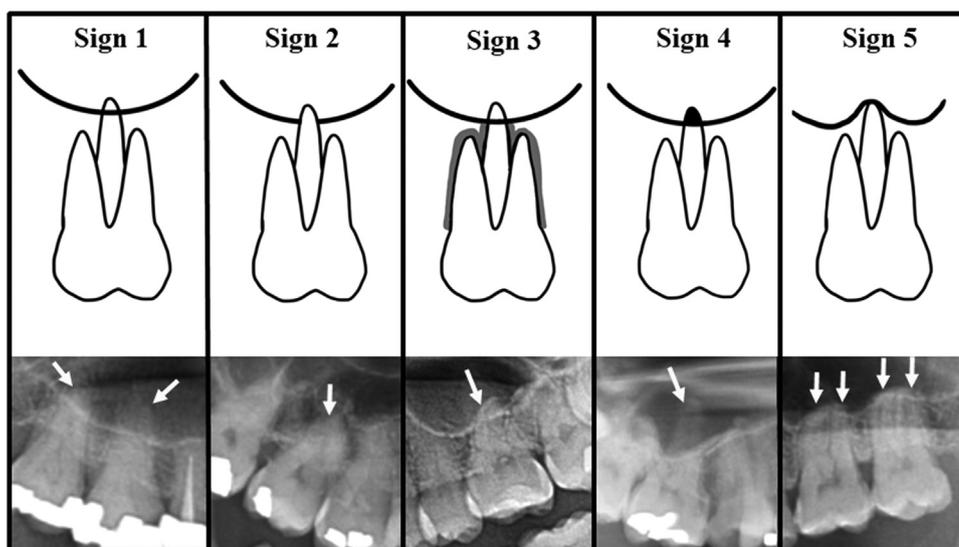


Fig. 2. Radiographic signs on panoramic images.

Top row shows schematic images and bottom panoramic images. From left to right are illustrations of: Sign 1 - Projection of the root apex in the sinus cavity; Sign 2 - Interruption of the maxillary sinus floor's cortex; Sign 3 - Absence of the PDL space; Sign 4 - Darkening of the involved root apical region; and, Sign 5 - Upward curving of the sinus floor enveloping the root. Arrows indicate evaluated roots for each sign.

panoramic radiographic signs. In addition, the positive and negative predictive values of each panoramic sign were calculated.

All statistical analyses were conducted using IBM SPSS Statistics for Windows, version 19.0 (IBM corp., Armonk, NY, USA). Differences were considered significant at  $P < 0.05$ .

### Results

Sixty-five patients (20 males; 45 females) with both CBCT and panoramic images

were included. The mean age of patients was 35 years (range, 13–82). All patients were Thai. In these patients, 126 maxillary molar teeth comprising 61 first molars, 55 second molars, and 10 third molars were included. Conical-shaped roots were found in seven second molars and five third molars. Among these teeth, roots of each tooth were evaluated as one root. A total of 354 roots were analysed on CBCT images.

In the CBCT evaluation, the respective Kappa coefficient for intra- and inter-ex-

aminer reliability was 0.89 and 0.88. In all roots, Type 2 – in which molar roots extend beyond the sinus floor without a cortical bone in between – was the most common type (46%) followed by Type 0 (37.3%) and Type 1 (16.7%). With respect to Type 2 – where roots protrude into the maxillary sinus without a cortical bone of the sinus floor on CBCT images – the palatal root of the first molar had the highest prevalence (9.3%) followed by the mesiobuccal root of the second molar (8.2%) (Table 1).

Table 1. Prevalence of relationship between maxillary molar roots and maxillary sinus according to tooth and root types on cone beam computed tomography (CBCT) images.

Tooth	Root	CBCT (n, %)			Total
		Type 0	Type 1	Type 2	
1 <sup>st</sup> molar	Mesiobuccal root	25, 7.1%	10, 2.8%	26, 7.3%	61, 17.2%
	Distobuccal root	24, 6.8%	11, 3.1%	26, 7.3%	61, 17.2%
	Palatal root	19, 5.4%	9, 2.5%	33, 9.3%	61, 17.2%
2 <sup>nd</sup> molar	Mesiobuccal root	12, 3.4%	7, 2.0%	29, 8.2%	48, 13.6%
	Distobuccal root	15, 4.2%	5, 1.4%	28, 7.9%	48, 13.6%
	Palatal root	19, 5.4%	10, 2.8%	19, 5.4%	48, 13.6%
3 <sup>rd</sup> molar	Conical root	1, 0.3%	5, 1.4%	1, 0.3%	7, 2.0%
	Mesiobuccal root	5, 1.4%	0	0	5, 1.4%
	Distobuccal root	5, 1.4%	0	0	5, 1.4%
	Palatal root	4, 1.1%	1, 0.3%	0	5, 1.4%
	Conical root	3, 0.8%	1, 0.3%	1, 0.3%	5, 1.4%
Total		132, 37.3%	59, 16.7%	163, 46%	354, 100%

n = number of roots.

In the panoramic assessment, 154 roots were excluded due to non-identification because of superimposition of the palatal bone. Finally, panoramic and CBCT images of 200 roots (83 mesiobuccal, 75 distobuccal, 30 palatal, and 12 conical-shaped roots) were analysed for correlation between the five panoramic signs and the three CBCT types. The respective Kappa coefficient for intra- and inter-examiner reliability was 0.73 and 0.78. Table 2 presents the frequency of panoramic radiographic signs on panoramic images. The greater the number of signs found on a panoramic image, the greater the likelihood of finding perforation into the sinus on CBCT images (Table 3). A maximum of four panoramic signs could be detected on five roots with a 100% tendency of root perforation into the sinus. Importantly, 5.8% of roots without any panoramic sign nevertheless showed perforation on CBCT images, suggesting that even if a radiographic sign of protrusion into the maxillary sinus is not apparent on the panoramic image, there remains a

possibility that it is actually protruding into the maxillary sinus. Thus, any surgical procedures related to the maxillary molar root require that surgeons are aware of the potential complications.

The statistical analysis for panoramic signs is presented in Table 4. There were two significant high-risk signs of root perforation into the sinus, including: Sign 1 – projection of the root apex into the sinus cavity ( $P < 0.01$ ) with the highest negative predictive value (0.94); and, Sign 4 – darkening of the involved root region ( $P = 0.013$ ) with the highest positive predictive value (0.92).

**Discussion**

Maxillary molar roots might indicate an intimate relationship with the maxillary sinus. Pathologies of these teeth and supporting structures or various dental procedures in this region could lead to complications related to the sinus. Common complications during oral surgery include OAC and displacement of the root

into the sinus. Other reported complications include (i) orbital abscess arising from odontogenic infection<sup>17,18</sup>, (ii) infection spreading from the periodontal pocket to the nearby maxillary sinus<sup>19</sup>, (iii) risk of pushing root canal material into the sinus cavity<sup>20–22</sup>, and (iv) maxillary sinusitis from impression material being pushed through the OAC undetected<sup>23</sup>.

A preoperative investigation regarding the relationship between molar roots and the maxillary sinus is essential for preventing complications. Panoramic radiography is widely used for evaluation of both teeth and jaws; however, an investigation of root proximity to the maxillary sinus on panoramic images can be difficult because of patient positioning and superimposition of anatomical structures (e.g., palate and maxillary sinus over tooth roots). In addition, the anatomy of roots themselves is also related to the difficulty in identifying roots on panoramic radiographs. Many excluded roots on the panoramic radiographs showed converged roots on the CBCT images; it was difficult to evaluate

Table 2. Frequency of panoramic signs according to tooth and root types (n = 200 roots).

Tooth	Root	Frequency of panoramic signs (n, %)				
		Sign 1	Sign 2	Sign 3	Sign 4	Sign 5
1 <sup>st</sup> molar	Mesiobuccal root	40, 12.7%	6, 1.9%	26, 8.3%	3, 0.9%	4, 1.3%
	Distobuccal root	34, 10.8%	8, 2.5%	17, 5.4%	3, 0.9%	2, 0.6%
	Palatal root	25, 7.9%	7, 2.2%	17, 5.4%	20, 6.3%	3, 0.9%
2 <sup>nd</sup> molar	Mesiobuccal root	23, 7.3%	5, 1.6%	11, 3.5%	2, 0.6%	2, 0.6%
	Distobuccal root	16, 5.1%	2, 0.6%	8, 2.5%	3, 0.9%	2, 0.6%
	Palatal root	3, 0.9%	0	2, 0.6%	1, 0.3%	2, 0.6%
3 <sup>rd</sup> molar	Conical root	7, 2.2%	1, 0.3%	5, 1.6%	1, 0.3%	0
	Mesiobuccal root	0	0	0	0	0
	Distobuccal root	0	0	0	0	0
	Palatal root	0	0	0	0	0
	Conical root	1, 0.3%	1, 0.3%	1, 0.3%	0	1, 0.3%
Total		149	30	87	33	16

n = number of roots.

Table 3. Relationship between number of panoramic signs and percentage of root perforation into maxillary sinus on cone beam computed tomography (CBCT) images ( $n = 200$  roots).

CBCT findings	Number of panoramic sign (%)					Total
	0	1	2	3	4	
No perforation (Type 0, 1)	94.2	48.4	28.2	17.1	0	45.5
Perforation (Type 2)	5.8	51.6	71.8	82.9	100	54.5
Total	100	100	100	100	100	100

Table 4. Statistical analyses vis-à-vis panoramic signs.

Panoramic sign	$P^a$	Adjusted OR	95% CI		PPV	NPV
			Lower	Upper		
Sign 1	<0.01*	23.49	6.15	89.74	0.73	0.94
Sign 2	0.544	1.35	0.51	3.57	0.76	0.49
Sign 3	0.138	1.81	0.83	3.98	0.76	0.63
Sign 4	0.013*	5.49	1.43	20.99	0.92	0.52
Sign 5	0.833	0.84	0.17	4.08	0.60	0.45

Sign 1: projection of root apex into the sinus cavity. Sign 2: interruption of maxillary sinus floor's cortex. Sign 3: absence of periodontal ligament space. Sign 4: darkening of the involved root apical region. Sign 5: upward curving of the sinus floor enveloping the root. CI, confidence interval; NPV, negative predictive value; OR, odds ratio; PPV, positive predictive value.

<sup>a</sup>Multiple logistic regression. Significant at  $*P < 0.05$ .

these converged roots as a distinct root on the panoramic radiographs. We thus excluded them from the evaluation to avoid an error in the analysis. Three-dimensional visualization using CBCT is the method used for complete evaluation of teeth and related structures; however, due to limited accessibility, higher costs, and radiation dose, CBCT is not prescribed in every case. In the present study, we investigated the correlation between panoramic signs of root protrusion into the maxillary sinus with CBCT findings.

Lopes et al.<sup>15</sup> performed a similar comparison of panoramic and CBCT findings for identification of maxillary posterior roots invading the maxillary sinus in 330 teeth. They classified the panoramic signs of roots protruding into the maxillary sinus into five signs (viz. projection of the root apices, interruption of the maxillary sinus floor, absence of lamina dura, darkening in the root apices, and superiorly curving sinus floor enveloping the associated tooth root). Our study modified one of the panoramic radiographic signs from their study: instead of evaluating the lamina dura, we investigated the PDL space. We did this due to the difficulty identifying the radiopaque line of the lamina dura on panoramic images and the radiopaque line at the root apical region close to the maxillary sinus floor, which – observed on panoramic images – might actually be the cortex of the sinus floor. We, therefore, evaluated the presence of a uniform thin black line of the PDL space parallel to the root surface. We believe that the absence

of the PDL space might be a radiographic sign indicating protrusion of the root into the maxillary sinus. As for indicating root protrusion into the sinus, the current study showed a higher odds ratio for the absence of the PDL space (1.81) over against the lamina dura as reported by Lopes et al. (0.85). Consequently, the observation of the radiolucent line along the root surface might be more practical in clinical situation.

Another difference between our study and that by Lopes et al.<sup>15</sup> is the method of evaluating panoramic images. We evaluated the presence of each sign in each root instead of in each tooth because each root of the same tooth might show different features. As with the results from Lopes et al.<sup>15</sup>, our study showed that 'projection of the root apex into the sinus cavity' was a significant high-risk sign of root protrusion into the maxillary sinus. By contrast, we found that the 'presence of darkening of the involved root at the apical region' was another significant high-risk sign, while Lopes et al.<sup>15</sup> reported that 'interruption of the maxillary sinus floor' was another sign highly correlated with CBCT findings of roots invading into the maxillary sinus.

In our study, the predictive values of each panoramic sign were calculated. The positive predictive value was highest for 'darkening of the involved root at the apical region' (0.92); suggesting that roots presenting with this sign on panoramic images have a high tendency to actually perforate into the maxillary sinus. Not-

withstanding, the negative predictive value of this sign was low (0.52), indicating that a root actually perforating into the maxillary sinus might not show this sign on a panoramic image, although that root could show other signs. Meanwhile, the negative predictive value was highest for 'projection of the root apex in the sinus cavity' (0.94). Thus, if a root is not projecting into the sinus cavity on panoramic images, that root should actually not protrude into the maxillary sinus. The predictive values aligned with the odds ratio. According to the odds ratio, projection of the root apex in the sinus cavity was the most significant sign followed by darkening of the involved root apical region, absence of PDL space, interruption of the maxillary sinus floor's cortex, and upward curving of the sinus floor enveloping the root, respectively.

Previous studies about the prevalence of roots protruding into the maxillary sinus have been conducted and the results vary. Details of each study are shown in Table 5. In our study, the prevalence of maxillary molar roots protruding into the sinus was highest among all studies and the palatal root of the first maxillary molar was the most frequent root protruding into maxillary sinus, followed by the mesiobuccal root of the second maxillary molar. The difference in results might be due to ethnicity, study methods, and/or classifications of the relationship between root and sinus. Most studies classified the relationship using the level between the maxillary sinus floor and the root apex<sup>2,4,7</sup>.

Table 5. Previous studies on maxillary molar roots protruded into maxillary sinus.

Study (year)	Number		Type of evaluated tooth	Nationality	Method	Prevalence of tooth root protruded into maxillary sinus (%)	The most protruded root/ tooth
	Patient	Tooth					
This study (2019)	65	126	Root			46	Pa of 1 <sup>st</sup> molar
Sharan and Madjar <sup>2</sup> (2008)	80	—	354	Thai	CBCT	30.09	—
Eberhardt et al. <sup>3</sup> (1992)	38	—	422	Israel	CBCT	—	—
Estrela et al. <sup>4</sup> (2016)	202	300	1 <sup>st</sup> & 2 <sup>nd</sup> P, 1 <sup>st</sup> & 2 <sup>nd</sup> M	American	CBCT	34.17	MB of 2 <sup>nd</sup> molar
Jung and Cho <sup>5</sup> (2012)	83	332	1 <sup>st</sup> & 2 <sup>nd</sup> P, 1 <sup>st</sup> & 2 <sup>nd</sup> M	Brazilian	CBCT	28.1	MB of 2 <sup>nd</sup> molar
Kilic et al. <sup>6</sup> (2010)	92	528	1 <sup>st</sup> & 2 <sup>nd</sup> P, 1 <sup>st</sup> , 2 <sup>nd</sup> & 3 <sup>rd</sup> M	Korean	CBCT	10.5	Rt: DB of 2 <sup>nd</sup> molar
Kwak et al. <sup>7</sup> (2004)	33	43	1 <sup>st</sup> P, 2 <sup>nd</sup> P, 1 <sup>st</sup> M, 2 <sup>nd</sup> M	Korean	Direct measurement	23.1	Lt: DB of 1 <sup>st</sup> molar
Pagin et al. <sup>8</sup> (2013)	50	315	1 <sup>st</sup> & 2 <sup>nd</sup> P, 1 <sup>st</sup> , 2 <sup>nd</sup> & 3 <sup>rd</sup> M	Brazilian	CBCT	14.3	DB of 1 <sup>st</sup> molar
Lopes et al. <sup>15</sup> (2016)	46	330	Maxillary posterior teeth	Brazilian	CBCT	38	MB of 2 <sup>nd</sup> molar
Shahbazian et al. <sup>24</sup> (2014)	157	1084	1 <sup>st</sup> & 2 <sup>nd</sup> M	Belgian	CBCT	46	—

CBCT, cone beam computed tomography; DB, distobuccal root; Lt, left; M, maxillary molar; MB, mesiobuccal root; P, maxillary premolar; Pa, palatal root; Rt, right.

Some researchers used contact or projection of root apex through the sinus cavity<sup>5,6</sup>. Pagin et al.<sup>8</sup> used evidence of bone between the maxillary sinus and the root apex, while others studied the distance between the maxillary molar root and the sinus floor<sup>15,24</sup>. Although a high prevalence of roots protruding into the sinus was encountered in this study, it does not indicate that there must be a high incidence of OAC. Other potential factors include root morphology, periapical lesion, patient's age, experience of surgeon, and surgical technique.

In our study, we hypothesized that evidence of bone between the root and sinus floor and the white line of the cortex of the maxillary sinus floor on CBCT images constitute significant markers of roots not perforating into the sinus. We assumed that absence of the thin white line indicates perforation of the sinus floor. We then assessed various panoramic signs in relation to the CBCT findings in order to evaluate the high-risk signs of root protruded into the maxillary sinus. Differences in inclusion and exclusion criteria with respect to sampling might also affect the results. Our results revealed that the number of roots protruding into the maxillary sinus were higher for roots of the first and second maxillary molar than for those of the third molar. This might be due to the limited number of the third molar in this study because the included teeth for evaluation must show full eruption and complete root formation leading to exclusion of many third molar. In addition, the third molar following the criteria normally located posterior to boundary of maxillary sinus. Further studies focusing on the third maxillary molar should be considered.

In conclusion, 46% of maxillary molar roots showed protrusion into the sinus. Projection of the root apex in the sinus cavity and darkening of the involved root at the apical region on panoramic images were two significant high-risk signs of root protrusion into the maxillary sinus. The tendency of root perforation into the maxillary sinus increased with the number of detected signs in the panoramic radiography. Palatal root of the first maxillary molar root and mesiobuccal root of the second maxillary molar had a high prevalence of root protrusion into the maxillary sinus. According to the high prevalence of maxillary molar roots protruding into the maxillary sinus, panoramic radiographs should be meticulously evaluated prior to dental treatments in this region to help with proper treatment planning. A CBCT for roots in close proximity to the sinus could not be identified on panoramic

radiographs might be considered by the clinician on a case-by-case basis.

### Funding

None.

### Competing interests

There are no conflicts of interest.

### Ethical approval

Ethical approval was provided by The Faculty of Dentistry/ Faculty of Pharmacy, Mahidol University, Institutional Review Board COA.No.MU-DT/PY-IRB 2017/050.2609.

### Patient consent

Not required.

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Address:  
 Jira Kitisubkanchana  
 Department of Oral and Maxillofacial Radiology  
 Faculty of Dentistry  
 Mahidol University  
 No. 6 Yothi Road  
 Ratchathewi District  
 Bangkok 10400  
 Thailand  
 Tel.: +662 200 7837  
 Fax: +662 200 7836  
 E-mail: [jira.kit@mahidol.ac.th](mailto:jira.kit@mahidol.ac.th)