# **Original Article**

# Mesiodistal inclination of the unerupted second premolar in the mandible of Japanese orthodontic patients with incisor agenesis

# Kenichi Kure<sup>a</sup>; Kazuhito Arai<sup>b</sup>

#### ABSTRACT

**Objective:** To elucidate the mesiodistal inclination of the unerupted mandibular second premolar (MnP2) in cases of mandibular incisor (MnIc) agenesis and unilateral MnP2 agenesis.

**Materials and Methods:** Twenty-two cases of unilateral MnP2 agenesis (MnP2 agenesis group) and a control group (control group A) of 22 cases without permanent tooth agenesis excluding third molars were selected. Thirty-six cases of MnIc agenesis (MnIc agenesis group) and another control group (control group B) of 36 subjects were also selected. Mesiodistal inclination of the unerupted MnP2 on the panoramic X-rays was measured according to the distal angle and premolar-molar angle using the methods of Shalish et al. and Baccetti et al., respectively. Differences in mean values of the angular measurements between agenesis groups and corresponding controls were investigated (unpaired *t*-test).

**Results:** In the MnP2 agenesis group, the mean distal angle decreased  $12.3^{\circ}$  and the mean premolar-molar angle increased  $13.3^{\circ}$  for the MnP2 compared with control group A (both *P* < .001). In the MnIc agenesis group, no significant differences in the means of those angles for the MnP2 were found when compared with control group B.

**Conclusion:** In Japanese orthodontic patients, there is a relationship between unilateral MnP2 agenesis and the mesiodistal angulation of the unerupted MnP2. However, no significant relationship was observed between MnIc agenesis (which relationship is often seen in Asian populations) and the position of the unerupted MnP2. These results suggest that different genetic factors are involved in MnP2 agenesis and MnIc agenesis. (*Angle Orthod.* 2015;85:949–954.)

**KEY WORDS:** Mesiodistal angulation of unerupted mandibular second premolar; Mandibular incisor agenesis; Dental anomaly patterns

### INTRODUCTION

Recently, the biological relationship between permanent teeth agenesis and other dental anomalies, including delayed tooth development, anomalies in tooth eruption, and morphological abnormalities of teeth, has received extensive scientific scrutiny.<sup>1</sup>

In a study of children of European ethnicities having unilateral agenesis of the mandibular second premolar (MnP2), Shalish et al.<sup>2</sup> measured the mesiodistal

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inclination of the unerupted contralateral MnP2 using panoramic radiographs of orthodontic patients. They observed a significantly larger distal inclination of the unerupted MnP2 compared with a control group having no agenesis. Similar inclination tendencies have also been reported in other studies of unilateral MnP2 agenesis cases by Garib et al.<sup>3</sup> in Brazil and by Navarro et al.<sup>4</sup> in Spain. However, few studies have investigated this matter in Asian populations, which have different genetic backgrounds.

Polder et al.<sup>5</sup> conducted a meta-analysis of studies from general populations of European ethnicities and statistically analyzed the frequency and site of permanent tooth agenesis. They reported that agenesis of the MnP2 appears with the highest frequency in general populations of European ethnicities. However, in studies of agenesis in Asian populations, a greater prevalence of missing mandibular incisors (Mnlcs) was observed.<sup>6-10</sup>

Wasserstein et al.<sup>11</sup> and Navarro et al.<sup>4</sup> reported that unerupted, distally angulated MnP2s show significantly

delayed formation, which can affect the timing of orthodontic treatment. However, few studies have investigated the association between MnIc agenesis, which is often observed in Asian populations, and unerupted MnP2 positioning.

The aim of this study was to investigate the relationship between agenesis of the MnIcs and MnP2s, which are frequently seen in the Japanese population, and the positioning of the unerupted MnP2s.

# MATERIALS AND METHODS

This study was approved by the Ethics Committee of the School of Life Dentistry at Tokyo, The Nippon Dental University (Approval 07-28).

# **Unilateral MnP2 Agenesis**

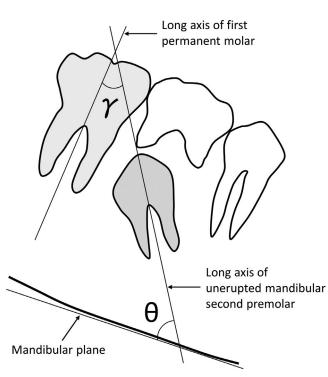
According to the selection criteria of Shalish et al.,<sup>2</sup> subjects were chosen from the records of approximately 5000 patients who attended the Department of Orthodontics of Nippon Dental University Hospital.

Twenty-two children (7 boys and 15 girls; mean age =  $10.5 \pm 1.7$  years; age range = 8.1 to 13.6 years) with unilateral MnP2 agenesis (MnP2 agenesis group) and an age- and gender-matched control group (control group A) comprising 22 children (7 boys and 15 girls; mean age =  $10.5 \pm 1.6$  years; age range = 8.0 to 13.0 years) were selected. Subjects in control group A were age- and gender-matched to individual cases in the MnP2 agenesis group to create fully corresponding subject pairs. Selection criteria for the MnP2 agenesis group were as follows:

- 1. unilateral MnP2 agenesis. MnP2 agenesis was confirmed by examination of follow-up panoramic radiographs made at age 13 years or older,<sup>12</sup>
- 2. no previous orthodontic treatment,
- 3. no history of hereditary diseases often associated with agenesis of permanent teeth (eg, anhidrotic ectodermal dysplasia, Down syndrome, cleft lip and palate),
- 4. existence of radiographic images suitable for analysis,
- 5. tooth germs of the permanent teeth to be studied were between stage D and stage G of tooth formation according to Koch's classification.<sup>13</sup> If multiple panoramic radiographs were present for the same case, we selected the latest radiograph.

Control group A (no agenesis) selection criteria:

- 1. no agenesis of permanent teeth (excluding third molars),
- 2-5. same as for the MnP2 agenesis group,



**Figure 1.** Measurement of mesiodistal inclination of unerupted MnP2 in panoramic radiograph.

- 6. sex composition of the group matched the MnP2 agenesis group,
- age of any given control group subject was close to that of a subject in the MnP2 agenesis group (difference in age from the paired subject was within 0.5 years).

The mesiodistal inclination of the unerupted MnP2s in each MnP2 agenesis subject and the corresponding side of control group A was measured on the panoramic radiographs according to two angular measurements (distal angle  $\theta$  and premolar-molar angle  $\gamma$ ) using the method of Shalish et al.<sup>2</sup> and Baccetti et al.<sup>14</sup> (Figure 1). Measurements were made by an independent evaluator using tracing paper (TR-150, SOMAR, Tokyo, Japan) and a 0.3-mm diameter mechanical pencil. These angles were measured again more than week later and the mean value was used in the analysis.

The mean and standard deviation (SD) of the mesiodistal inclination of the unerupted MnP2 in both groups were calculated. The difference between the means of the two groups was statistically analyzed using an F-test followed by an unpaired t-test at a 5% significance level.

Furthermore, the mean and SD of the mesiodistal inclination of the left and right unerupted MnP2 teeth in control group A were calculated and the difference between the bilateral measurements were statistically analyzed using a paired *t*-test at a 5% significance level.

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Variable	Unilateral MnP2 Agenesis Group	MnIc Agenesis Group	Statistical Analysis
Gender	Boys, 7; girls, 15	Boys, 10; girls, 26	$\chi^2$ value = .11 <i>P value</i> = .74 <sup>NS</sup>
Affected side (MnP2)	Right, 11; left, 11	Right, 36; left, 36	$\chi^2$ value =. 00 <i>P</i> value = 1.00 <sup>NS</sup>
Chronological age (years)	10.5 ± 1.7	8.8 ±1.3	<i>t</i> value = 4.32 <i>P</i> value = <.001***

Table 1. Homogeneity of the Sample Groups

<sup>NS</sup> indicates not significant; \*\*\* P < .001.

#### **Mnlc Agenesis**

Thirty-six children (10 boys and 26 girls; mean age =  $8.8 \pm 1.6$  years; age range = 7.0 to 12.1 years) with mandibular incisor agenesis (MnIc agenesis group) and 36 children (10 boys and 26 girls; mean age =  $9.0 \pm 1.2$  years; age range = 7.1 to 12.0 years) without tooth agenesis excluding the third molars (control group B) were also selected to create age- and gender-matched fully corresponding subject pairs. The selection criteria for the MnIc agenesis group were as follows:

1. agenesis of one or two MnIcs,

2-5. same as for the MnP2 agenesis group.

Control group B (no agenesis) selection criteria:

#### 1-5. same as for control group A,

- 6. sex composition of the group matched the MnIc agenesis group,
- age of any given control group subject was close to that of a subject with MnIc agenesis (difference in age from the paired subject was within 0.5 years).

The mesiodistal inclination of the unerupted MnP2 in the subjects of both groups were measured on the panoramic radiographs using the method of Shalish et al.<sup>2</sup> and Baccetti et al.,<sup>14</sup> as mentioned above.

The mean and SD of the mesiodistal inclination of the left and right unerupted MnP2s were calculated for the 36 subjects in both groups, and the differences were statistically analyzed using an F-test followed by unpaired *t*-tests at the 5% significance level.

Furthermore, the mean values of the mesiodistal inclination between left and right unerupted MnP2 were compared for both groups and statistically analyzed using a paired *t*-test at the 5% significance level.

A power analysis performed using the statistical package R (version 3.1.0; http://www.r-project.org) revealed that a total sample size of 12 subjects was required to detect the effect with 80% power at the 5% significance level.

#### **Evaluation of the Sample**

The homogeneity of the sample groups was statistically evaluated by the chi-square test and unpaired *t*-test.

#### **Test for Measurement Error**

To evaluate errors in measuring the mesiodistal inclination of unerupted MnP2s, intraevaluator errors were calculated according to the method of Shalish et al.<sup>2</sup> Double measurements of 10 randomly selected panoramic radiographs were carried out at an interval of at least 1 month by one of the authors; intraevaluator error was defined as the SD of the difference between the pair of measurements of the same film. For interevaluator error, measurements of 10 randomly selected panoramic radiographs were made by two evaluators. The SD of the difference between the measurements of the same film by the two evaluators was defined as the interevaluator error. Intraevaluator error was 1.0° for both the  $\theta$  and  $\gamma$ angles in measuring the mesiodistal inclination of the unerupted MnP2s. Interevaluator error was  $1.2^\circ$  for both the  $\theta$  and  $\gamma$  angles. The intra- and interevaluator errors were similar to values reported by Shalish et al.,<sup>2</sup> so we determined that the measurement error had little effect on the experimental results.

#### RESULTS

#### **Evaluation of the Sample**

No significant differences between the MnP2 agenesis and MnIc agenesis groups were found in the gender prevalence and affected side for the unerupted MnP2s (Table 1).

Mean chronological age for the MnP2 agenesis group was higher than that of the MnIc agenesis group.

#### **Unilateral MnP2 Agenesis**

A significantly smaller  $\theta$  angle and a larger  $\gamma$  angle were observed in the MnP2 agenesis group compared with control group A (*P* < .001; Table 2).

No significant difference in the mean of the  $\theta$  angle and  $\gamma$  angle were observed between the right and left sides in control group A (P = .97 and P = .56, respectively; Table 2).

#### **Mnlc Agenesis**

No significant difference in the mean mesiodistal inclination of either angle  $\theta$  or  $\gamma$  of the unerupted MnP2

	MnP2 Mesiodistal Inclination (Mean $\pm$ SD)						
	Ν	$\theta$ Angle, $^\circ$	t Value	P Value	$\gamma$ Angle, $^\circ$	t Value	P Value
Unilateral MnP2 agenesis group	22	62.3 ± 13.2	3.83	<.001***	22.7 ± 8.9	5.11	<.001***
Control	22	74.7 ± 7.4			$9.4~\pm~8.3$		
Control (right side)	22	$74.3 \pm 7.8$	0.03	.97 <sup>NS</sup>	$10.8\pm7.7$	0.58	.56 <sup>NS</sup>
Control (left side)	22	$74.4\pm8.7$			$9.3\pm8.8$		

 Table 2.
 Comparison of Mesiodistal Inclination of the MnP2 Between the Unilateral MnP2 Agenesis and Control Groups

<sup>NS</sup> indicates not significant; \*\*\* P < .001.

was observed between the two groups (P = .40 and P = .15, respectively; Table 3).

No significant difference in the mean mesiodistal inclination of either angle  $\theta$  or  $\gamma$  were observed between the left and right unerupted MnP2 in the MnIc agenesis group (P = .42 and P = .61, respectively; Table 3).

Nor was there a significant difference in the mean mesiodistal inclination of either angle  $\theta$  or  $\gamma$  observed between the left and right unerupted MnP2 in control group B (P = .48 and P = .98, respectively; Table 3).

# DISCUSSION

Abnormalities such as developmental delay,<sup>4,11,15</sup> malposed erupting teeth,<sup>2,3,16–18</sup> and agenesis<sup>5</sup> of MnP2 occur more frequently among ethnic European populations than do other teeth. Shalish et al.<sup>2,17,18</sup> noted that among populations of European ethnicities, significant distal inclination of the unerupted MnP2 is found not only in cases of unilateral MnP2 agenesis, but also among individuals having cleft lip/palate and palatally displaced canines.

Garib et al.<sup>3</sup> and Baccetti<sup>19</sup> reported that compared with controls, cases of second premolar agenesis showed significantly more frequent agenesis of other teeth, reduced size of maxillary lateral incisors, infraocclusion of deciduous molars, and palatally displaced maxillary canines. These findings suggest that there is a reciprocal association between second premolar agenesis and other dental abnormalities.<sup>1</sup>

As a cause of malposition of the MnP2, Wasserstein et al.<sup>20</sup> noted that the presence or absence of the mandibular deciduous second molar, the precursor of the MnP2, causes no significant difference in the unerupted MnP2 mesiodistal inclination. Therefore, these authors<sup>20</sup> proposed that genetic factors have a greater influence than do environmental factors on changes in the mesiodistal inclination of the unerupted MnP2. In contrast, Matteason et al.<sup>16</sup> reported that environmental factors, such as early shedding of the mandibular primary first molar, greatly influence the tendency toward mesiodistal inclination of the uner-upted MnP2. Therefore, no consensus has been reached.

The present results suggest that, in cases of unilateral MnP2 agenesis in the Japanese population, the unerupted contralateral MnP2 shows a significant tendency to incline distally, similar to the findings of Shalish et al.<sup>2</sup> Garib et al.<sup>3</sup> and Navarro et al.<sup>4</sup> This finding is likely to affect the drafting of orthodontic treatment plans for Japanese patients with unilateral MnP2 agenesis. As distally inclined, unerupted MnP2s tend to show delayed tooth formation,<sup>4,11</sup> it may be necessary to modify the starting time of orthodontic treatment for these patients.

Previous studies have reported distal inclination and delayed eruption of the unerupted contralateral MnP2 in cases of unilateral MnP2 agenesis.<sup>2–4</sup> In the present study as well, the mean age of the MnP2 agenesis group was 10.5 years. This is 1.7 years more than the mean age of the MnIc agenesis group (8.8 years), which was selected according to the same criteria (Table 1). Furthermore, in 8 of the 22 cases of unilateral MnP2 agenesis and 2 of the 36 cases of MnIc agenesis, the MnP2 was found to be impacted in the alveolar bone when the child had passed the mean age for MnP2 eruption in Japanese children (11.3 years in boys and 10.8 years in girls).<sup>21</sup>

Table 3. Comparison of Mesiodistal Inclination of the MnP2 Between the MnIc Agenesis and Control Groups

			MnP2 Mesiodistal Inclination (Mean $\pm$ SD)				
	Ν	$\theta$ Angle, $^\circ$	t Value	P Value	$\gamma$ Angle, $^\circ$	t Value	P Value
MnIc agenesis group	72	74.0 ± 11.5	0.84	.40 <sup>NS</sup>	13.8 ± 10.8	1.46	.15 <sup>№</sup>
Control	72	$75.3 \pm 7.0$			$11.6 \pm 6.9$		
MnIc agenesis group (right side)	36	73.3 ± 10.5	0.81	.42 <sup>NS</sup>	14.3 ± 9.8	0.51	.61 <sup>NS</sup>
Mnlc agenesis group (left side)	36	74.8 ± 12.5			13.4 ± 11.8		
Control (right side)	36	$74.9 \pm 7.8$	0.72	.48 <sup>NS</sup>	11.6 ± 7.4	0.02	.98 <sup>NS</sup>
Control (left side)	36	$75.8\pm6.1$			$11.6\pm6.4$		

<sup>NS</sup> indicates not significant.

#### SECOND PREMOLAR INCLINITION WITH INCISOR AGENESIS

The results of the present study also showed no significant difference in mesiodistal inclination of unerupted MnP2s between cases of MnIc agenesis and controls among the Japanese orthodontic population. This finding suggests that, compared with cases of unilateral MnP2 agenesis, there is less need to be concerned about the timing of MnP2 eruption in Japanese orthodontic patients having MnIc agenesis.

The male-to-female ratio in the MnP2 agenesis group was approximately the same as in previous studies.<sup>2,4</sup> In this study, no significant differences were found in gender prevalence between MnP2 agenesis and MnIc agenesis groups, although the proportion of women was higher in both groups. The higher percentage of female patients in this study might be due to the possibility that females have a generally higher rate of tooth agenesis.<sup>5,7</sup>

The present study examined MnIc agenesis and unilateral MnP2 agenesis, which are the most common types of dental agenesis in the Japanese population.<sup>6,7</sup> A tendency toward distal inclination of the unerupted contralateral MnP2 was found in cases of unilateral MnP2 agenesis, suggesting that common genetic factors are involved in MnP2 agenesis and positioning of the unerupted MnP2. In contrast, no similar tendency was observed in cases of MnIc agenesis. Endo et al.<sup>22</sup> reported that there was no association between mandibular lateral incisor agenesis and anomalies in tooth shape or position such as pegshaped maxillary lateral incisor, palatal or labial displacement of the maxillary canine, or transposed teeth. MnIc agenesis is frequently observed in other Asian populations, such as Chinese,<sup>8</sup> Korean,<sup>9</sup> and Malaysian.<sup>10</sup> If the present results are considered in conjunction with the fact that MnIc agenesis is commonly seen among Japanese and other Asian populations, it is possible that different factors are responsible for MnIc and MnP2 agenesis.

However, in the present study, both agenesis groups showed relatively greater individual variation in the mesiodistal angulation of the unerupted MnP2 compared with the corresponding control groups. Larger SDs were also observed in unerupted MnP2s of unilateral MnP2 agenesis cases in previous studies.<sup>2,4</sup> This tendency suggests that MnIc agenesis and MnP2 agenesis have a similar biological effect on the position of the MnP2 during development.

The results of the present study are probably insufficient to support Fujita's<sup>23</sup> hypothesis that Mnlc agenesis is caused by a mechanism different from that of agenesis of other teeth. Therefore, to more fully elucidate the reciprocal relationship between dental abnormalities, it will be necessary for future studies to survey the association between dental abnormalities that are expressed with relatively high frequency in both Japanese and populations of European ethnicities, such as maxillary lateral incisor agenesis, maxillary second premolar agenesis, and unerupted MnP2 position.

#### CONCLUSIONS

- According to panoramic radiographs, the mesiodistal inclination of unerupted, contralateral MnP2s in cases of unilateral MnP2 agenesis showed a significant tendency toward distal inclination compared with the control group.
- The mesiodistal inclination of unerupted MnP2s in cases of MnIc agenesis showed no statistically significant difference from the control group.
- Thus, while an association was found between unilateral MnP2 agenesis and the position of unerupted MnP2s, no association was found between agenesis of the MnIc (which is often seen in the Japanese population) and the position of unerupted MnP2s. These results suggest that different genetic factors are involved in MnP2 agenesis and MnIc agenesis.

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