



# Remaining tooth sizes in persons with congenitally missing upper lateral incisor (ULI)

Hiroyuki Yamada

Department of Anatomy, School of Dentistry, Aichi-Gakuin University, Nagoya, Japan. E-mail: ymd\_20hiro4@yahoo.co.jp.

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## ABSTRACT

**An investigation was conducted on Japanese males to determine how the size of the remaining teeth is affected in individuals with a congenital absence of an upper lateral incisor (ULI). The material used was 18 persons with missing ULI out of 83 persons with congenitally missing teeth (other than M3). Compared to the control group with 32 teeth, the ULI missing group had larger teeth for all measurements, especially for the central incisor ( $P < 0.01$  for the absence side;  $P < 0.05$  for the presence side) and first molar ( $P < 0.05$  for the absence side), except for the ULI on the presence side. In the ULI deficient group, the compensatory effect of tooth size is strong within a particular tooth type and not only do the teeth become larger, but the entire dentition is also affected and increases in size. Only the ULI on the presence side is affected by the defect, resulting in a reduction in tooth size. The presence or absence of M3 and ULI was unrelated to the frequency of congenitally missing teeth. There was no significant difference in the variation in tooth size of the ULI between the ULI missing group and the control group.**

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## INTRODUCTION

As hominines have evolved, tooth size has decreased and the number of teeth has gradually reduced (Bolk, 1916; Sofaer et al., 1971a, b). The third molar (M3) is the most delayed erupting tooth in the dentition, susceptible to environmental influences, and likely to be absent. According to Hellman (1928), in some populations, the frequency of congenital missing of M3 reaches up to 50%. In modern Japanese, a congenitally missing incidence of M3 is reported to be about 30% (Yamada and Hanamura, 1993). Garn and his colleagues, who studied M3 defects in American Caucasians, commented on the reduction in crown size, residual tooth morphology, and developmental timing as compared to controls. (Garn et al., 1963; Garn and Lewis, 1970; Le Bot and Salmon, 1977).

On the other hand, in the absence of upper lateral incisor (ULI), the size of adjacent teeth is said to increase compensatory to fill the space (Sofaer et al., 1971a,b). There is also an increase in remaining teeth in the group without all M3s and a significant difference in remaining molars in both jaws (Yamada and Tagaya, 2018). It was thought that these two conflicting results of remaining teeth degenerating or increasing were due to differences in the

materials used (Yamada and Tagaya, 2018). This study reports on the maxillary lateral incisors, where congenitally missing teeth are relatively frequent, and how the congenital missing of ULI affects the size of the remaining teeth.

## MATERIALS AND METHODS

Individuals suspected of having congenitally missing teeth were collected for boys 20 years of age and older, and panoramic and intraoral dental radiographs were performed to ascertain whether they had congenitally missing teeth. Patients with cleft palate and cleft lip were excluded from the study. There were 83 persons with congenitally missing teeth, 18 of whom had unilateral or bilateral ULI agenesis. From the central incisor to the second molar of both jaws were measured on the dental casts following the method of Fujita (1949) using sliding calipers (manufactured by Mitutoyo). The side with an absence of ULI was analyzed as the absence side, and the side with a presence ULI as the presence side. If the ULI

was absent on both sides, the right side was considered the absence side.

As a control group, a group with 32 teeth (Yamada and Tagaya, 2018) was used. The presence of congenitally missing teeth other than the third molars (M3s) was treated as hypodontia. Basic statistics were calculated for the mesiodistal crown measurements. The size of the teeth on an absence and a presence sides relative to the control group was expressed as a percentage difference. That is, percentage difference (%) = (mean of absence side – mean of control group) / mean of control group. A t-test was used to test the significance of the difference in means, and the F-test was used to test the variance. The chi-square test of independence was used in a 2x2 table.

## RESULTS

Of the 83 males with congenital absence of teeth studied, the number of missing teeth was 128 teeth, 103 teeth with M3 absence, and 18 persons with congenital absence of ULI. Table 1 shows the mesiodistal crown diameters for the presence and absence sides of the ULI missing group (except for M3) and compares them to the control group. In the ULI missing group, there was no significant side difference in any of the measurements between the absence and presence sides. Compared to the control group with 32 teeth, the ULI missing group had larger teeth for all of the measurements except for ULI, especially for the central incisor ( $P < 0.01$  for the absence side;  $P < 0.05$  for the presence side) and first molar ( $P < 0.05$  for the absence side) (Figure 1, Table 1).

The relationship between the presence or absence of ULI and the presence or absence of M3 among the 83 Hypodontia was compared. Of the 18 persons in the ULI missing group, 10 were in the M3 presence group and 8 in the missing group, and of the 65 persons in the non-ULI missing group, 26 were in the M3 presence group and 39 in the missing group. There is no significant relationship between the two groups ( $\chi^2 = 0.8276$ ).

Table 2 compares the size of the teeth on the presence and absence sides of the ULI in the M3 missing and all M3s presence groups. The size of the other teeth tended to increase more in the M3 missing group than in all M3s presence group, and more on the absence side of ULI than on the presence side of ULI. However, there was no significant difference between the absence and the presence groups of M3s regardless of the presence or absence of ULI (Table 2).

Table 3 shows the coefficients of variation for the absence and presence sides in the ULI missing group. The coefficients of variation ranged from 3.8% to 6.0% for all tooth measurements. In particular, ULI was 7.2% in the control group (Table 2), whereas it was 5.1% on the presence side in the ULI missing group (Table 3).

## DISCUSSION

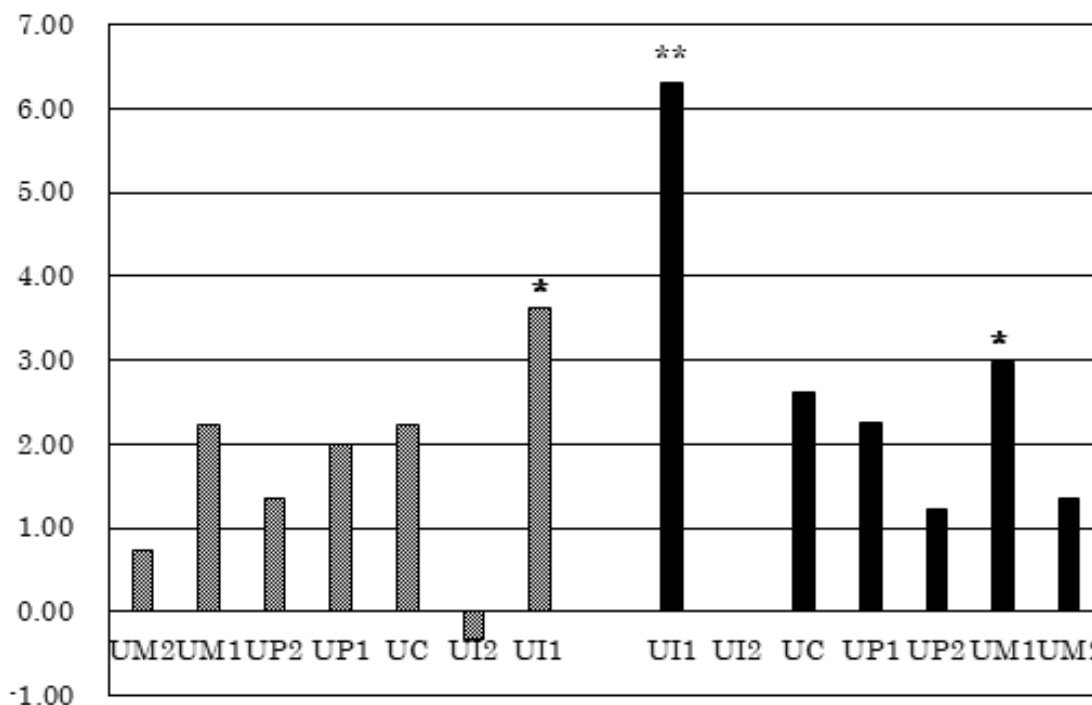
The genetic mechanism that alters tooth morphology affects all teeth, but the influence of degeneration is stronger in teeth that are further away from the key teeth (Dahlberg, 1945). It is an obvious fact that tooth size tends to decrease progressively during hominin evolution (Garn et al., 1963; Garn and Rohmann, 1966; Yamada et al., 2022). Among congenitally missing teeth (Brothwell et al., 1963), M3 congenital absence is the most common, with Pedersen (1949) reporting 29.5% in South-West Greenlanders, Campbell (1925) 1.5% in Australian aboriginals, Grahnen (1956) 25.0% in Swedes, Thomson and Popovich (1974) 22.3% among American Caucasians, and Chagula (1960) 1.6% among East African residents. In Japanese, Takahama and Otawa (1982) reported 25.8%, and Yamada and Hanamura (1993) 28.7%. In ULI, which tends to be relatively degenerate, the incidence of missing ULI is 1.9% in French (Le Bot and Salmon, 1977), 1.5%–3.4% in Caucasian Europeans (Haavikko, 1971; Brekhus, 1944; Werther and Rothenberg, 1939; Dolder, 1936), and 1.3%–2.6% in Japanese (Terasaki and Shiota, 1954; Yamasaki et al., 2010). Therefore, the incidence between ULI deficiency and M3 deficiency differs considerably in many populations.

### Influence of congenitally missing third molar

Garn and his colleagues have reported that the persons with congenitally missing third molar in European-Americans has smaller teeth, being associated with degeneration of the size of the remaining teeth, that with congenitally missing teeth other than M3s also has smaller teeth (Garn et al. 1963; Baum and Cohen, 1970), and that the remaining teeth were even smaller in those with multiple missing teeth including M3s (Garn and Lewis, 1962). In contrast, Japanese data comparing the size of the remaining teeth in the M3 missing and all M3s presence groups (Asakura, 1975) reported that the missing group had larger the remaining teeth than all M3s presence group. Furthermore, when M3 was missing, the mesiodistal crown diameters of the remaining teeth except for ULI were larger in many measurements, and there was a significant difference in the size of M1 and M2 in the maxilla and mandible of all M3s missing groups compared to the control group (Yamada et al., 2005). Yamada et al. (2010), who studied the relationships between the number of missing teeth and the size of remaining teeth in hypodontia, reported that the remaining teeth were enlarged in those with one or two teeth missing, but reduced in those with three or more teeth missing.

### Influence of degeneration and missing ULI

When the ULI degenerated or was missing, the size of the



**Figure 1.** Percentage differences between presence and absence sides of mesiodistal crown diameters in ULI missing group based on the control group. Gray color: presence side, Black color: ULI absence side. \*: P<0.05, \*\*: P<0.01.

**Table 1.** Statistics of mesiodistal diameters in presence and absence sides of ULI missing group (except for M3), and in control group.

	Presence side	Absence side	Control
UI1	8.87 (0.41, 16)*	9.10 (0.48, 17)**	8.56 (0.40, 48)
UI2	7.21 (0.37, 11)		7.23 (0.52, 48)
UC	8.24 (0.48, 16)	8.27 (0.41, 17)	8.06 (0.33, 49)
UP1	7.64 (0.29, 15)	7.66 (0.33, 18)	7.49 (0.39, 49)
UP2	7.20 (0.31, 15)	7.19 (0.43, 18)	7.10 (0.36, 49)
UM1	10.90 (0.52, 15)	10.98 (0.53, 18)*	10.66 (0.40, 49)
UM2	10.17 (0.58, 16)	10.23 (0.56, 17)	10.09 (0.47, 49)

**Table 2.** Comparisons of tooth size on presence and absence sides in the M3 missing and all M3s presence groups due to presence or absence of ULI.

	10 persons with all M3s presence		8 persons with M3 absence	
	ULI presence side	ULI absence side	ULI presence side	ULI absence side
UI1	8.90	9.01	8.83	9.18
UI2	7.04		7.36	
UC	8.19	8.25	8.30	8.29
UP1	7.58	7.60	7.74	7.74
UP2	7.18	7.13	7.22	7.26
UM1	10.66	10.84	11.18	11.16
UM2	10.11	10.12	10.26	10.36

**Table 3.** Coefficients of variation for the absence and presence sides in ULI missing group.

	Presence side	Absence side
UI1	4.7%	5.3%
UI2	5.1%	
UC	5.8%	5.0%
UP1	3.8%	4.3%
UP2	4.3%	6.0%
UM1	4.8%	4.9%
UM2	5.7%	5.4%

remaining teeth also decreased, but the reduction in size was more pronounced in the degenerate group than in the missing group (Le Bot et al., 1977). In morphology, the effects of degeneration also showed in the cusp number of molars and the groove pattern of mandibular molars (Le Bot et al., 1980). Hanihara et al. (1965) and Hanihara (1970) studied the ULI of Pima Indians and stated that the size of the ULI plays a role in determining the size of the entire dentition because when the ULI is degenerated, the other teeth are also smaller. In general, M3 absence and ULI degeneration were phenomena that occurred because the entire dentition showed a degenerative tendency (Garn et al., 1963; Baum and Cohen, 1970; Garn and Lewis, 1962; Le Bot and Salmon, 1977, 1980), and congenitally missing tooth was considered to be final arrivals of degeneration. However, Le Bot and Salmon (1977) questioned the conventional view that tooth degeneration is intermediate between presence and absence: although the absence of ULI is related to the absence of the other teeth, the teeth are smaller in the degenerate group than in the missing group in terms of tooth size.

On the other hand, Sofaer et al. (1971a, b) and Sofaer (1973) argued in a study of high school students in Hawaii that when an upper lateral incisor is unilaterally missing, the central incisor on the absence side is significantly larger than the central incisor in the normal, suggesting compensatory interaction in the incisal tooth class. Bishara et al. (1989) showed for residents of Iowa, Egypt and Mexico that in the incisor and premolar classes, groups with earlier onset and larger teeth had slower onset and relatively smaller teeth, indicating that compensatory effects were observed not only in the incisal class but also in the premolar class.

In the present study, the mesiodistal crown diameters in the lacking ULI group was found to be larger than that of the control group, except for the ULI on the presence side (Fig. 1). Especially in the central incisor (absence side:  $P < 0.01$ ; presence side:  $P < 0.05$ ) and first molar (absence side:  $P < 0.05$ ), a significant difference from the control group was observed. In short, it was thought that when there were missing teeth, the other teeth increased in size

to compensate for the entire dentition (Sofaer et al., 1971a, b; Yamada et al., 2005; Kondo and Hanamura, 2010).

### Relationship between M3 absence and ULI absence

When comparing the presence or absence of M3 with the presence or absence of ULI in Japanese population, there is no significant relationship between the two in terms of frequency of missing third molars (Yamada and Hanamura, 1993). Again, there was no significant relationship in frequency between M3 and ULI deficiencies in this study. However, among the French, those who are ULI deficiencies have significantly more M3 absence teeth (Le Bot et al, 1977).

### Genes contributing to lack of teeth

Recently, the genetic basis of congenital defects in teeth has been explored in terms of embryology.

Kavanagh et al. (2007) found in an experimental mouse that when the tooth embryo of a slow-developing second molar was detached from the dental lamina extending behind the fast-developing first molar and cultured, the tooth embryo of the delayed-developing second molar grew in a speedier manner. In other words, when the first molar is large, the second molar, which is delayed in development, is strongly inhibited and becomes reduced in size, and when the first molar is small, the teeth become larger due to weaker inhibition applied to the second molar (inhibition cascade). They list BMPs, EDA, and Pax9 as molecular candidates to act as this inhibitory cascade. In a study of twins, Kondo, and Hanamura (2010) and Kondo et al. (2014) used an inhibitory cascade model to explain that UI2 was smaller due to the increased inhibitory effect of larger UI1. Their results support the hypothesis of compensatory interaction by Sofaer et al. (1971a, b) and Sofaer (1973) as a model for molecular embryology.

### Geographic differences in genes associated with missing teeth

As described above, Europeans and Japanese differ in the way they deal with the size of the other teeth in the case of congenitally missing teeth. Generally, when Europeans have congenitally missing teeth, the other teeth are smaller, while Japanese are larger. It is possible that there are differences in the genes involved in the lack of tooth in these two opposing phenomena. Recently, genetic factors have been proposed to explain the various phenomena caused by missing teeth, and the MSX1, PAX9, AXIN2, and EDAR genes have been mentioned. Among them, variants of the PAX9 and EDAR genes have been

identified to be associated with third molar absence (Shahid et al., 2017). Abu-Hussein et al. (2015) reviewed genetic studies on tooth agenesis and concluded that mutations in *MSX1*, *PAX9*, and *AXIN2* genes were associated with hypodontia and oligodontia, and mutations in *AXIN2* were implicated only in rare, severer cases.

Yamada and Tagaya (2018) found that MTA (with up to two missing teeth other than M3, with larger remaining teeth and no degeneration) is common in East Asians, including Japanese, and the *PAX9* and *EDAR V370A* mutants are associated with MTA. On the other hand, Europeans were more likely to have DTA (more than three congenitally missing teeth other than M3, and the remaining teeth were smaller and degenerate), and the *MSX1* mutant and *PAX9* mutant were thought to be responsible for DTA.

Regarding tooth size variation, Yamada and Tagaya (2018) found that ULI varied most in the non-M3 dentition, the present results show that the variation in ULI on the presence side of the lacking ULI group was smaller and less variable than that of the controls. Baum and Cohen (1971) studied mesiodistal crown diameters in Caucasian Europeans and found that tooth size variation was significantly greater in hypodontia than in the controls for several measurements, but there was no significant difference with respect to ULI. Yamada et al. (2010) also found no significant difference in tooth size variability of ULI between hypodontia and the controls.

## Conclusion

The author investigated how the remaining tooth size is affected by ULI deficiency in Japanese males. The material used was 18 persons with missing ULI out of 83 persons with congenitally missing teeth (other than M3). Compared to the control group, except for the ULI on the presence side, the ULI missing group had larger teeth for all measurements, especially significant for the central incisor ( $P < 0.01$  for the absence side;  $P < 0.05$  for the presence side) and first molar ( $P < 0.05$  for the absence side). Furthermore, ULI defects not only have a strong compensatory effect on tooth size within a particular dentition, but the entire dentition is affected and teeth are enlarged. In the ULI missing group, only the ULI on the presence side was affected by the tooth reduction, and the tooth size was reduced.

The presence or absence of M3 and ULI was unrelated to the frequency of congenitally missing teeth. There was no significant difference in the variation in tooth size of the ULI between the ULI missing and the control groups. The difference between Europeans and Japanese in the way other teeth respond to congenitally missing teeth was related to the genetic differences between the two populations.

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