### **Original Article**

# Characterization of dental phenotype in patients with cleidocranial dysplasia using longitudinal data

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#### ABSTRACT

**Objective:** To investigate the characteristics of the dental phenotype in patients with cleidocranial dysplasia (CCD) using longitudinal data.

**Materials and Methods:** Twelve unrelated Korean CCD patients were observed using a longitudinal series of radiographs and clinical photographs. Statistical analysis was performed on the dental phenotypic data.

**Results:** Although dysplasia of the clavicles, open fontanelle, and wormian bone were observed in all 12 patients, delayed fusion of the mandibular symphysis was found in four patients. One patient did not have a supernumerary tooth (ST). However, 62 STs were found in 11 patients (mean, 5.6 per patient; range of ST emergence, 5 years 6 months–14 years 8 months; developing position, occlusal to the permanent incisors, canines, and premolars and distal and apical to the permanent molars). The mandibular premolar region was the most frequent area of ST development (50.0%, *P* < .001). All 12 patients showed impacted permanent teeth (IPT), including one patient without ST (mean, 17.8 per patient). Impaction occurred most frequently in the mandibular premolar region and least frequently in the maxillary molar region (93.8% vs 39.6%, *P* < .01). The ratio of spontaneous eruption of IPT after removal of retained deciduous teeth and/or ST was highest for the maxillary and mandibular incisors (all 54.6%) and lowest for the mandibular canines and premolars (26.7% and 28.9%, respectively); however, the difference was not significant.

**Conclusions:** The emergence time and development position of ST and the root development of IPT should be considered to determine the timing for the removal of ST and forced eruption of IPT. (*Angle Orthod.* 2018;88:416–424.)

**KEY WORDS:** Cleidocranial dysplasia; Dental phenotype; Supernumerary tooth; Impacted permanent teeth

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#### INTRODUCTION

Cleidocranial dysplasia (CCD; OMIM 119600) is known to be caused by mutations in the *RUNX2* gene and inherited in an autosomal dominant pattern.<sup>1,2</sup> The *RUNX2* gene encodes a transcription factor required in osteoblast differentiation, chondrocyte maturation, and skeletal morphogenesis.<sup>1–3</sup>

CCD is characterized by skeletal abnormalities including dysplasia (aplasia or hypoplasia) of the clavicles, patent sutures and fontanelles, formation of wormian bone, short stature, brachycephaly, or a depressed nasal bridge.<sup>2,4</sup> In addition to the skeletal abnormalities, CCD typically involves dental complications such as multiple supernumerary teeth and impaction or delayed eruption of permanent teeth.<sup>2,4</sup> However, the spectrum of CCD phenotypes ranges from mild dental issues to severe skeletal malformation.<sup>2–6</sup> Therefore, the severity of skeletal abnormalities is not necessarily directly related to that of the dental

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complications. As a result, Baumert et al.<sup>7</sup> described four groups of CCD patients showing significant differences in phenotypic expression.

Several theories have been proposed to explain the causes of supernumerary teeth; for example, phylogenetic reversion (atavism), dichotomy of tooth germ, hyperactivity of the dental lamina, and incomplete or markedly delayed resorption of the dental lamina.<sup>8</sup> Various factors can contribute to the impaction or delayed eruption of permanent teeth: (1) presence of multiple supernumerary teeth, (2) malformed roots of the permanent teeth with a lack of cellular cementum, (3) high alveolar bone density, and (4) abnormal resorption of the alveolar bone and the deciduous teeth.<sup>4,9,10</sup> In addition, children with CCD exhibited a 2-to 3-year delay in development of the permanent teeth and an additional 1.5-year delay in development of supernumerary teeth.<sup>11,12</sup>

Although several studies have shown a wide variation in the dental phenotype of CCD,<sup>5,13–15</sup> there is a lack of longitudinal studies on dental phenotype. Furthermore, since previous studies have focused only on somatic development or dental age,<sup>16,17</sup> a longitudinal study on phenotypes is needed. Therefore, the purpose of this study was to investigate the characteristics of the dental phenotype in CCD patients using longitudinal data.

#### MATERIALS AND METHODS

The subjects included 12 unrelated Korean CCD patients, who were diagnosed and treated at the Department of Orthodontics, Seoul National University Dental Hospital, Seoul, Republic of Korea. This study was approved by the institutional review board at Seoul National University School of Dentistry (S-D20160028). Written consent was received from each subject or their parents before inclusion in the study.

After oral epithelial cells were obtained using a mouthwash technique (50 mL water, gargled for 1 minute and then repeated a second time for 1 minute), genomic DNA was extracted with a Labopass Tissue DNA Extraction kit (Cosmogenetech, Seoul, Korea).<sup>2</sup> Amplification of exons 1–8 of the *RUNX2* gene was performed by polymerase chain reaction (PCR), and the PCR product was directly sequenced. *RUNX2* mutations were identified using the BioEdit program (Carlsbad, Calif) and DNA Star software (Madison, Wis) at Cosmo Genetech Co. (Seoul, Korea).<sup>2</sup>

The skeletal and dental phenotypes of CCD patients were investigated using a longitudinal series of orthopantomograms, three-dimensional computed tomograms (3D-CT), lateral and posteroanterior cephalograms, posteroanterior chest x-rays, and clinical photographs. Lateral and posteroanterior cephalograms were used to identify delayed closure of the cranial sutures, open fontanelle, and wormian bone. Posteroanterior chest x-rays were used to identify aplasia or hypoplasia of the clavicles. Orthopantomograms and 3D-CTs were used to investigate the number, distribution, emergence time, and location of the supernumerary teeth, impaction or delayed eruption of permanent teeth, and spontaneous eruption of the impacted permanent teeth after removal of retained deciduous teeth and/or supernumerary teeth. If a permanent tooth did not erupt until 95th percentile of mean eruption age range in Koreans,<sup>18</sup> it was considered as impaction or delayed eruption.

The number, distribution, emergence time, and location of the supernumerary teeth; the ratio of impaction or delayed eruption of permanent teeth; and the ratio of spontaneous eruption of impacted permanent teeth after removal of retained deciduous teeth and/or supernumerary teeth were recorded or obtained. Since there was no statistically significant difference in the findings between the left and right sides, the data from both sides were combined for further statistical analysis. Statistical analysis was performed using the Kruskal-Wallis test and Bonferroni correction.

#### RESULTS

#### **Genotype of CCD Patients**

In total, five kinds of *RUNX2* mutations were identified in eight patients (Table 1), while four patients did not contain a mutation in the *RUNX2* coding region (Table 1).

#### **Skeletal Phenotype of CCD Patients**

Aplasia or hypoplasia of the clavicles, delayed closure of the cranial sutures, open fontanelles, and wormian bone were observed in all 12 patients (Table 1; Figures 1 and 2), while delayed fusion of the mandibular symphysis was found in four patients (range, 10 years 3 months–14 years 3 months; Table 1; Figures 3 and 4).

#### **Dental Phenotype of CCD Patients**

Although one patient did not have a supernumerary tooth, 62 supernumerary teeth were found in 11 patients (91.7%; mean, 5.6  $\pm$  2.5 per patient; range, 1–9 per patient; Table 2). There was a significant difference in the prevalence of supernumerary teeth by region (mandibular incisor [Man-I] region, 0%; maxillary molar [Max-M] region, 1.6%; maxillary incisor [Max-I] region, 4.8%; mandibular molar [Man-M] region, 4.8%; maxillary canine [Max-C] region, 6.5%; maxillary premolar [Max-

Table 1.	Demographic	Data of	Patients	With	Cleidocranial	Dysplasia
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						Phenotype						
		-				Skeletal				Dental		
No.	<i>RUNX2</i> Mutation	Sex	Age at Initial Visitª	Stage	Follow-up Durationª	Delayed Closure of the Cranial Suture and Open Fontanel	Wormian Bone	Aplasia or Hypoplasia of the Clavicle	Delayed Symphysis Fusion	Super- numerary Tooth (ST)	Impacted Permanent Tooth (IPT)	Spontaneous Eruption of IPT After Removal of Retained Deciduous Teeth or ST
1	R225Q	F	23Y 6M	Adult	6Y 1M	Yes	Yes	Yes	No	7	20	0
2	Not found	Μ	28Y 6M		4Y 6M	Yes	Yes	Yes	No	6	3	0
3	M175R	F	20Y 6M		2Y 11M	Yes	Yes	Yes	No	7	2	0
4	R190Q	Μ	17Y 11M	Adolescence	10Y 2M	Yes	Yes	Yes	No	5	18	5
5	Not found	Μ	18Y 3M		3Y 8M	Yes	Yes	Yes	Yes (fused at 14Y 3M)	2	23	19
6	G462X	Μ	14Y		3Y 1M	Yes	Yes	Yes	No	9	17	7
7	R391X	Μ	11Y10M	Childhood	9Y 7M	Yes	Yes	Yes	Yes (fused at 12Y 1M)	9	28	10
8	Not found	F	5Y 7M		9Y 8M	Yes	Yes	Yes	No	0	28	10
9	Not found	F	8Y 2M		13Y 8M	Yes	Yes	Yes	No	5	17	4
10	R190Q	Μ	5Y 6M		16Y 1M	Yes	Yes	Yes	Yes (fused at 14Y)	1	22	18
11	M175R	Μ	8Y 5M		8Y 2M	Yes	Yes	Yes	No	7	12	12
12	R225Q	F	10Y 8M		1Y 7M	Yes	Yes	Yes	Yes (fused at 10Y 3M)	4	24	4

<sup>a</sup> Y indicates years; M, months.

P] region, 25.8%, mandibular premolar [Man-P] region, 50.0%; Table 2). The mandibular premolar region was the most frequent area of supernumerary teeth development ([Man-I, Max-M, Max-I, Man-M, Max-C, Man-C] < [Max-I, Man-M, Max-C, Max-P] < [Max-P, Man-P]; P < .001, Table 2).

The longitudinal series of orthopantomograms since childhood were available for five patients. Development of a total of 26 supernumerary tooth germs could be identified in these five patients (mean,  $5.2 \pm 2.8$  per patient; range, 1–9 per patient; Table 3). The emergence time of the supernumerary tooth germ varied (mean emergence time by region: maxillary incisor region, 5 years 6 months; maxillary canine region, 8 years 9 months; mandibular canine region, 7 years 3 months; maxillary premolar region, 10 years 7 months; maxillary molar region, 14 years 8 months; range, 5 years 6 months; Table 3), Thus, supernumerary teeth

can develop at a later age than normal permanent teeth.<sup>19</sup> The supernumerary tooth germ developed in the occlusal positions of the permanent incisors, canines, and premolars and in the distal and apical positions of the permanent molars (Figure 5).

All 12 patients showed impaction or delayed eruption of permanent teeth, even in one patient without a supernumerary tooth (n = 214/336; 63.7%; mean, 17.8  $\pm$  8.2 per patient; range, 2–28 per patient; Table 4). There was a significant difference in impaction or delayed eruption of the permanent teeth by region (maxillary molar, 39.6%; mandibular incisor, 45.8%; mandibular molar, 50.0%; mandibular canine, 62.5%; maxillary incisor, 68.8%; maxillary premolar, 75.0%; maxillary canine, 83.3%; mandibular premolar, 93.8%; Table 4). Impaction or delayed eruption occurred most frequently in the mandibular premolar region and least frequently in the mandibular incisor region ([Max-M, Man-M, Man-I, Man-C, Max-I] < [Man-M, Man-I, Man-



Figure 1. Chest posteroanterior radiograph and clinical photograph of case 9 (8 years 2 months). Because of aplasia of the clavicles, this patient can bring both shoulders closer together than normal individuals.

Figure 2. Lateral and posteroanterior cephalograms of case 8 (5 years 7 months). Delayed closure of the cranial sutures, open fontanel, and wormian bones are shown.

C, Max-I, Max-P] < [Man-I, Man-C, Max-I, Max-P, Max-C] < [Max-I, Max-P, Max-C, Man-P]; P < .01; Table 4).

Among the 214 impacted permanent teeth, 89 spontaneously erupted after removal of retained deciduous teeth and/or supernumerary teeth (41.6%; Table 5). Although spontaneous eruption of impacted permanent teeth was highest at the maxillary and mandibular incisors and lowest at the mandibular canine and premolars, the difference was not significant (maxillary incisor, 54.6%; mandibular incisor, 54.6%; mandibular molar, 50.0%; maxillary molar, 42.1%; maxillary canine, 40.0%; maxillary premolar, 38.9%; mandibular premolar, 28.9%; mandibular canine, 26.7%; P > .05; Table 5).

#### DISCUSSION

This study was the first to investigate the characteristics of dental phenotype in 12 unrelated Korean CCD patients using longitudinal data. Although the number of patients in the present study was relatively small, the very low prevalence of CCD should be taken into account (prevalence, 1:1,000,000).<sup>1,2</sup>

#### **Genotype of CCD Patients**

In the present study, a clear genotype-to-phenotype correlation was not identified (Table 1). The finding that dental phenotypes showed wide variation regardless of mutational status (Table 1) is in agreement



**Figure 3.** Orthopantomogram of case 7 (10 years 5 months). Delayed fusion of the mandibular symphysis is shown (white rectangle). There are two supernumerary teeth in the premolar region of the mandible (dotted circle). A total of 15 impaction or delayed eruption of permanent teeth were observed (gray arrow).

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Figure 4. Orthopantomogram of case 7. (A) There are eight supernumerary teeth germs in the maxillary and mandibular premolar regions (gray arrow, 11 years 10 months). Delayed fusion of the mandibular symphysis is shown (white rectangle). (B) Eight supernumerary teeth were extracted (12 years 1 month). (C) One supernumerary tooth germ developed again in the lower right premolar region (black arrow, 15 years 8 months). Mandibular symphysis was fused.

		Supernumera	ary Teeth	Comparison Among All Regions			
Region	Total No. in 11 Patients	Mean No. per Patient	Percentage in Total 62 Supernumerary Teeth	P Value	Post Hoc Tests		
Incisor							
Maxillary	3	0.27	4.84	<.001***	(Man-I, Max-M, Max-I, Man-M, Max-C, Man-C) $<$		
Mandibular	0	0	0.00		(Max-I, Man-M, Max-C, Max-P) < (Max-P, Man-P)		
Canine							
Maxillary	4	0.36	6.45				
Mandibular	4	0.36	6.45				
Premolar							
Maxillary	16	1.45	25.81				
Mandibular	31	2.82	50.00				
Molar							
Maxillary	1	0.09	1.61				
Mandibular	3	0.27	4.84				
Total							
Maxillary	24	2.18	38.71				
Mandibular	38	3.45	61.29				
Sum	62	5.63	100				

Table 2.	Prevalence	of the	Supernumerary	Teeth
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<sup>a</sup> The Kruskal-Wallis test and Bonferroni correction were performed. Max-I indicates maxillary incisor; Man-I, mandibular incisor; Max-C, maxillary canine; Man-C, mandibular canine; Max-P, maxillary premolar; Man-P, mandibular premolar; Max-M, maxillary molar; Man-M mandibular molar.

\*\*\**P* < .001.

with previous studies.<sup>5,13-15</sup> This finding can be explained by variable phenotypic penetrance of mutations in the RUNX2 gene.<sup>3,6</sup>

#### **Skeletal Phenotype of CCD Patients**

The finding that dysplasia (aplasia or hypoplasia) of the clavicles, delayed closure of the cranial sutures, open fontanelles, and wormian bone were observed in all 12 patients (Table 1) was in agreement with previous studies.<sup>4,14,20-22</sup> Golan et al.<sup>21</sup> reported that 97.2% of CCD patients had the

clavicular sign. Suda et al.<sup>14</sup> and Park et al.<sup>22</sup> reported that more than 94% of CCD patients had a patent suture or fontanelle.

In the present study, delayed fusion of the mandibular symphysis was observed in four patients (Table 1), which was similar to the results from the study by McNamara et al.<sup>23</sup> They reported that 22% of CCD patients had delayed fusion of the mandibular symphysis and observed that symphysis fusion occurred at 12 years in one patient who could be longitudinally observed.<sup>23</sup>

 Table 3.
 Emergence Time of the Supernumerary Tooth Germ of Five Patients Whose Longitudinal Series of Orthopantomograms Was Available

 Since Childhood<sup>a</sup>
 Since Childhood<sup>a</sup>

			Emerging Time		
Region	Right	Left	Mean		SD
Incisor					
Maxillary	5Y 6M (case 10)	Not found	5Y 6M		0
Mandibular	Not found	Not found		NA	
Canine					
Maxillary	8Y 9M (case 12)	8Y 9M (case 12)	8Y 9M		0
Mandibular	7Y 3M (case 12)	7Y 3M (case 12)	7Y 3M		0
Premolar					
Maxillary	8Y 5M (case 11), 11Y 3M (case 7),	8Y 5M (case 11), 10Y 3M (case 7),	10Y 7M		1Y 5N
	11Y 3M (case 7), 12Y 2M (case 9)	11Y 3M (case 7), 12Y 2M (case 9)			
Mandibular	8Y 5M (case 11), 8Y 5M (case 11),	8Y 5M (case 11), 8Y 5M (case 11),	10Y 2M		2Y 2N
	9Y 10M (case 7), 11Y 3M (case	8Y 5M (case 11), 9Y 10M (case			
	7), 12Y 2M (case 9), 15Y 8M	7), 9Y 10M (case 7), 12Y 2M			
	(case 7)	(case 9)			
Molar					
Maxillary	14Y 8M (case 9)	Not found	14 Y 8M		0
Mandibular	Not found	Not found		NA	

<sup>a</sup> Y indicates years; M, months; NA, not applicable.



Figure 5. Orthopantomogram of case 6 (14 years 9 months). There are eight supernumerary teeth germs in the maxillary and mandibular premolar regions (dotted circle), which developed at the occlusal position to the permanent premolars. One supernumerary tooth germ developed at the apical and distal position to the lower left first molar (black arrow). A total of 17 impaction or delayed eruption of permanent teeth were observed (gray arrow).

#### **Dental Phenotype of CCD Patients**

Supernumerary teeth. The finding that 11 of 12 patients (91.7%) had supernumerary teeth was consistent with previous studies, which reported that 75–100% of CCD patients had supernumerary teeth.<sup>14,17,21,22,24</sup>

The prevalence of supernumerary teeth by region has been contradictory in previous studies. Jensen and Kreiborg<sup>17</sup> reported that the prevalence of supernumerary teeth in the incisor region was higher than that in the premolar region (34.8% vs 26.6%). However, Richardson and Deussen<sup>24</sup> reported the opposite result (27.0% in the incisor region vs 65.1% in the premolar region). In the present study, supernumerary teeth were found significantly more often in the mandibular premolar region than in the other regions (P < .001; Table 2). Considering that the most common site of supernumerary teeth in nonsyndromic patients was the maxillary incisor region,<sup>8</sup> the prevalence region of the

Table 4. Frequency of Impaction or Delayed Eruption of Permanent Teetha

	Impaction or Delayed Eruption			Comparison Among All Regions		
Region	Total No. in 12 Patients	Mean No. per Patient	Percentage in Total Teeth in the Same Region	P Value	Post Hoc Tests	
Incisor						
Maxillary (48 teeth)	33	2.75	68.75	.009**	(Max-M, Man-M, Man-I, Man-C, Max-I) $<$	
Mandibular (48 teeth)	22	1.83	45.83		(Man-M, Man-I, Man-C, Max-I, Max-P) <	
Canine					(Man-I, Man-C, Max-I, Max-P, Max-C) <	
Maxillary (24 teeth)	20	1.67	83.33		(Max-I, Max-P, Max-C, Man-P)	
Mandibular (24 teeth)	15	1.25	62.50			
Premolar						
Maxillary (48 teeth)	36	3.00	75.00			
Mandibular (48 teeth)	45	3.75	93.75			
Molar						
Maxillary (48 teeth)	19	1.58	39.58			
Mandibular (48 teeth)	24	2.00	50.00			
Total						
Maxillary (168 teeth)	108	9.00	64.28			
Mandibular (168 teeth)	106	8.83	63.10			
Sum (336 teeth)	214	17.83	63.69			

<sup>a</sup> The Kruskal-Wallis test and Bonferroni correction were performed. Max-I indicates maxillary incisor; Man-I, mandibular incisor; Max-C, maxillary canine; Man-C, mandibular canine; Max-P, maxillary premolar; Man-P, mandibular premolar; Max-M, maxillary molar; Man-M mandibular molar.

\*\**P* < .01.

		Spontaneous	Comparison Among All Region		
Region	Total No. of Impacted Teeth	SE/IPT, %	Percentage in Total 89 Spontaneous Eruption Teeth	<i>P</i> Value	
Incisor					
Maxillary (12 patients)	18/33	54.55	20.22	.754	
Mandibular (12 patients)	12/22	54.55	13.48		
Canine					
Maxillary (12 patients)	8/20	40.00	9.00		
Mandibular (12 patients)	4/15	26.67	4.49		
Premolar					
Maxillary (12 patients)	14/36	38.89	15.73		
Mandibular (12 patients)	13/45	28.89	14.60		
Molar					
Maxillary (12 patients)	8/19	42.11	9.00		
Mandibular (12 patients)	12/24	50.00	13.48		
Total					
Maxillary (12 patients)	48/108	44.44	53.93		
Mandibular (12 patients)	41/106	38.68	46.07		
Sum (12 patients)	89/214	41.59	100		

Table 5. Ratio of Spontaneous Eruption (SE) of the Impacted Permanent Teeth (IPT) After Removal of Retained Deciduous Teeth and/or Supernumerary Teeth<sup>a</sup>

<sup>a</sup> The Kruskal-Wallis test was performed.

supernumerary teeth in CCD patients might be affected by CCD types.

Emergence timing and location of the supernumerary teeth in the present study were in agreement with Jensen and Kreiborg.<sup>17</sup> This observation supports the hypothesis that incomplete or markedly delayed resorption of the dental lamina is the main cause of supernumerary tooth development in CCD patients.<sup>17</sup>

Impaction or delayed eruption of permanent teeth. The finding that all 12 CCD patients had impaction or delayed eruption of permanent teeth (Table 4) was similar to previous studies, which reported that almost all CCD patients showed impaction or delayed eruption of permanent teeth.<sup>17,21,22</sup> The frequency of impaction or delayed eruption of permanent teeth is contradictory in previous studies. Richardson and Deussen<sup>24</sup> reported that these events occurred most frequently at the maxillary canines and molars (both 92%), followed by the mandibular premolars (84%) and then the maxillary incisors (75.0%). Park et al.22 reported that these events were highest at the mandibular canines (82%), followed by the maxillary incisors (71%) and then the mandibular premolars (56%). However, in the present study, impaction or delayed eruption occurred most frequently in the mandibular premolar region and least frequently in the maxillary molar region (93.8% vs 39.6%; P < .01; Table 4). These findings indicate that impaction or delayed eruption of permanent teeth in CCD might be related to the number or position of the supernumerary teeth. Another cause of impaction or delayed eruption of permanent teeth in CCD patients seems to be lack of resorption of alveolar bone. Lossdörfer et al.<sup>10</sup> reported that periodontal ligament cells of CCD patients had reduced capacity to induce differentiation of osteoclasts.

Spontaneous eruption of impacted permanent teeth. The ratio of spontaneous eruption of impacted permanent teeth in CCD patients has not been previously reported. The ratio of spontaneous eruption of impacted permanent teeth after removal of retained deciduous teeth and/or supernumerary teeth was approximately 41.6% in the present study (Table 5), which was lower than the results of nonsyndromic patients from the study by Smailiene et al.25 They reported that 54-76% of impacted maxillary incisors spontaneously erupted when supernumerary teeth were removed.25 In addition, Jensen and Kreiborg<sup>17</sup> reported that 4-26 permanent teeth per patient spontaneously erupted. Therefore, despite the relatively lower ratio compared with nonsyndromic patients, extraction of the deciduous teeth and removal of the overlying bone can induce spontaneous eruption of impacted permanent teeth in CCD patients. If there are no supernumerary teeth. eruption of impacted permanent teeth can be improved only by removing the deciduous teeth and surgically uncovering permanent teeth.<sup>26</sup>

In the present study, despite the removal of retained deciduous teeth and/or supernumerary teeth, 48.4% of the impacted permanent teeth did not spontaneously erupt (Table 5). This can be explained by abnormal or malformed roots with a lack of cellular cementum.<sup>9,17</sup>

## Clinical Implications for Orthodontic Treatment in CCD Patients

There are three primary considerations. First, because of the wide variation in the emergence time of supernumerary tooth germs in CCD patients (Figure 4), it is difficult to predict the exact number and location of supernumerary teeth. Therefore, it might not be recommended to remove every supernumerary tooth in a single procedure if the patient is still growing. Second, to increase the chance of spontaneous eruption of impacted permanent teeth, Jensen and Kreiborg<sup>26</sup> recommended removing the supernumerary teeth, retained deciduous teeth, and the overlying alveolar bone simultaneously when the roots of the impacted permanent teeth have reached about onethird of their final length. Third, as long as the clinical situation permits, it is recommended to induce spontaneous eruption of as many impacted permanent teeth as possible. This approach can reduce adverse effects, including loss of anchorage during simultaneous forced traction of multiple impacted teeth.

#### CONCLUSION

 The emergence time and development position of supernumerary teeth and the root development of impacted permanent teeth should be considered to determine the timing for the removal of supernumerary teeth and forced eruption of impacted permanent teeth.

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