# Root growth in the permanent teeth of 45,X/46,XX females

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SUMMARY Studies on individuals with sex chromosome anomalies have provided proof of a direct differential promoting effect of the X and Y chromosome genes on tooth crown growth. 45,X/46,XX females are one subgroup of Turner patients who have both normal XX and one X sex chromosome cell lines. Their permanent tooth crown size is reduced, which is mainly due to thin enamel. 45,X females likewise show reduced crown size and enamel thickness, and their root size is reduced. By contrast, the lengths of the roots in 47,XYY males or males with an extra Y chromosome and 46,XY females or females with a male sex chromosome constitution are increased. The aim of the present study was to investigate permanent tooth root lengths in 45,X/46,XX females to obtain additional information on their dental growth.

The study group consisted of 15 45,X/46,XX females, mean age 23.4 years; 10 female relatives, mean age 24.5 years; and 47 population control females, mean age 29.8 years, from the Kvantti research project. Root length measurements were made from panoramic radiographs on both sides of the jaw using a sliding digital calliper.

The results showed that permanent tooth root lengths in 45,X/46,XX females were, in most cases, significantly shorter than those of the population controls or relatives. It is apparent that a reduced tooth crown size in 45,X/46,XX females is followed by reduced root growth. This begins 3 years after birth and continues to at least 14 years of age. It is suggested that the reduction in crown and root growth in 45,X/4,XX females is due to a deficiency in the amount of dental growth-promoting genes on the sex chromosomes.

## Introduction

The incidence of Turner syndrome is approximately one in 2000 girls in Denmark (Nielsen and Wohlert, 1991). The chromosome constitution 45,X/46,XX is a chromosomal mosaic with both normal XX and one X sex chromosome cell lines. The condition is found in approximately 20 per cent of Turner patients (Nielsen et al., 1991). The degree of Turner characteristics in mosaic individuals has been found to reflect the degree of mosaicism (Sarkar and Marimuthu, 1983). 45,X/46,XX females have at least partial natural hormone production (Park et al., 1983; Nielsen et al., 1991). 45,X females have normal growth hormone and low oestrogen levels, and their skeletal maturity is significantly retarded, by an average of 2.4 years (Webber et al., 1982; Midtbø and Halse, 1992). The delay in skeletal maturity at the expected rate of puberty is commonly attributed to the lack of ovarian hormones, primarily oestrogen. By contrast, dental development is accelerated in 45,X females (Filipsson et al., 1965), the mean difference being one year (Midtbø and Halse, 1992).

Sex chromosome abnormalities that are associated with short stature exhibit complete or partial loss of sex chromosome material (Park *et al.*, 1983). The average height of Turner girls (including mosaics) at birth is a few centimetres less than normal (Park *et al.*, 1983; Nielsen *et al.*, 1991). The adult body height of 45,X/46,XX females reflects the effect of both cell lines, being above the average value for 45,X

females (Park *et al.*, 1983). Turner adults have size reductions on the longitudinal axis to a greater extent than in body width measurements (Park, 1977; Varrela *et al.*, 1984). Although 45,X females are smaller than normal in terms of most measured body dimensions, the differences in head dimensions are not significant (Varrela *et al.*, 1984). Turner patients do not have a spontaneous pubertal growth spurt of significance for final body height. Patients treated with growth hormone achieve an increase in height approximately 5–10 cm more than untreated patients (Nielsen *et al.*, 1991).

There are more changes in the growth of the facial region of 45, X/46, XX females than in other head dimensions; the maxilla and mandible are sagittally shorter with an enlarged ramus to corpus length ratio, and there is posterior rotation of the mandible and a tendency for bimaxillary retrusion (Grön et al., 1999). The occlusal morphology of 45,X and 45,X/46,XX females differs from that of normal females in that the prevalence of distal molar occlusion, lateral crossbite, and overbite and a tendency for open bite are increased (Laine et al., 1986; Harju et al., 1989). In comparison with 45,X women, the 45,X/46,XX patients show milder expressions of malocclusion (Harju et al., 1989). The mandibular dental arch is broader and the maxilla narrower than in normal females (Laine and Alvesalo, 1986). The anterior and posterior cranial bases are shorter (Grön et al., 1999). The changes in the cranial base may originate in the foetal period (Filipsson et al., 1965; Midtbø et al.,

1996), when the primary cartilages form the craniofacial skeleton.

The mesio-distal dimensions of the permanent tooth crowns of 45,X/46,XX females (Varrela et al., 1988) and 45,X (Filipsson et al., 1965; Alvesalo and Tammisalo, 1981; Townsend et al., 1984; Midtbø and Halse, 1994a) are significantly smaller than those of control females. The primary molars also tend to be smaller in 45,X females (Kari et al., 1980). The labio-lingual dimensions of 45,X/46,XX females, on the other hand, are close to normal (Varrela et al., 1988). The crown size reduction in the mesio-distal dimension in 45, X/46, XX and 45, X females is mainly due to a thin enamel layer, the dentine layer being close to normal (Alvesalo and Tammisalo, 1981; Alvesalo, 1985; Zilberman et al., 2000). The sexual dimorphism in permanent tooth crown sizes is due, to a decisive extent, to the thicker dentine laver in males (Alvesalo and Tammisalo, 1981; Harris and Hicks, 1998); males having larger crowns than females (e.g. Selmer-Olsen, 1949; Garn et al., 1967; Alvesalo, 1971). A simplified crown shape and also accessory cusps occur mostly in the maxillary teeth of Turner females (Kirveskari and Alvesalo, 1982; Midtbø and Halse, 1994a). There is an increase in the morphological asymmetry of the occlusal surfaces of the first permanent molars in 45,X/46,XX females (Pirttiniemi et al., 1998).

Premolars (Varrela, 1990; Midtbø and Halse, 1994b) and lower first molars (Midtbø and Halse, 1994b) of 45,X females show an increased number of root components in dissimilar variants and a significantly higher frequency of two-rooted mandibular premolars than normal females (Varrela, 1990), and 45,X/46,XX females have a tendency in the same direction (unpublished data). Taurodontism is an extension of the pulp chamber in which the furcation of the roots takes place later than in a normal molar. It appears in 45,X females (Varrela *et al.*, 1990) in the same way as in a normal population, a frequency of 0.5–5 per cent (Jaspers and Witkop, 1980). Exceptionally, the pulp chamber of the mandibular second premolar is often elongated in 45,X females (Midtbø and Halse, 1994b).

The aim of the present investigation was to determine permanent tooth root lengths in 45,X/46,XX females in order to obtain additional information on their dental growth.

## Subjects and methods

The Institutional Review Board of the Medical Faculty, University of Turku, Finland, reviewed and approved the protocol, of which the patients and their relatives were informed. The protection of the subjects was ensured and they were not at risk in any way.

#### Population

The patients, their relatives, and population controls were all participants in the Kvantti dental research project on individuals with sex chromosome abnormalities. They were from different parts of Finland, and all the 45,X/46,XX females' cytogenetic diagnoses had been made for medical reasons. The study group consisted of 15 45,X/46,XX females [mean age 23.4 years, standard deviation (SD) 8.42, minimum 7.13, and maximum 41.00]; two mothers and eight sisters of these (mean age 24.5 years, SD 7.55, minimum 15.10, and maximum 37.37), serving as relative controls; and 47 female population controls (mean age 29.8 years, SD 11.37, minimum 9.74, and maximum 59.06) who were relatives of patients other than the 45,X/46,XX females in the Kvantti research project. According to the obtained anamnestic information, 10 of the 15 patients with 45,X/46,XX had received hormone therapy (mainly oestrogen). Oestrogens are responsible for the development of the female secondary sex characteristics and act during the menstrual cycle on fertilization process.

## Measurements

Permanent tooth root lengths in the maxilla and mandible were measured from dental panoramic radiographs and crown heights were measured at the same time for further study. All the radiographs had been taken by the same person at the Institute of Dentistry, University of Turku, following a standardized procedure and with the same machine, an Orthopantomograph 3, Palomex Corporation, Helsinki, Finland. The magnification was in the range of 1.28–1.31 throughout the image layer of the panoramic radiograph.

A magnifying lens was used to determine the outlines of the tooth from the radiograph on a light table, after which the outlines were marked with a special pencil for plaster (Schwan All Stabilo 8008, Schwanhäußer GmbH & Co., KG Heroldsberg, Germany) and the measurements made in the same manner with a sliding digital calliper (Mitutoyo, digimatic 500-123U, CD-15B, Andover Hants, UK) to an accuracy of 0.01 mm. All the drawings and measurements were made by one author (RL).

The measurements of root length were made perpendicular to two parallel lines, one touching the outermost part of the root and the other joining the mesial and distal cervical margins of the enamel. Root length refers to the longest root on the radiograph in the case of premolars and the longest mesial root in the case of molars. The aim was to measure all the teeth with complete root formation on both sides of the jaw, except for the third molars. Teeth that were partly outside the plane-in-focus in the panoramic radiograph or showed obvious distortion because of being on the inner or outer surface of the image layer (Tammisalo, 1964), were excluded. Teeth with root resorption or incomplete root formation were also excluded, but those with large restorations or large caries lesions with pronounced loss of crown structure were measured whenever possible. Dilacerated or crooked roots were measured in terms of perpendicular length as explained previously. Some

impacted canine teeth with a closed apex were measured (Haavikko, 1970).

Acellular cementum is formed on the root surface until the tooth reaches the occlusion, at which time the proliferation of the epithelial root sheath is reduced and it may become entrapped within the forming matrix of cellular cementum (Thomas, 1995). Cellular cementum formation continues after the root form is complete. The apical cement layer was excluded from the present root length determinations.

The reliability of the measurements was examined by performing double determinations on a total of 45 dental radiographs from the Kvantti research material representing adult 45,X females and their female and male relatives, with 15 subjects in each group. The measurements were made by one author (RL) with an interval of 2 weeks. The line joining the mesial and distal cervical margins of the enamel marked on each tooth being erased out after the first measurement and determined again and redrawn for the second. The reproducibility of the double determinations of root length was expressed with the method error statistic (*S*;  $x_1$  = original measurement value,  $x_2$  = repeated measurement value, n = number of patients) S = $\sqrt{\sum (x_1 - x_2) / 2n}$  (Dahlberg, 1948).

The errors in root length measurement ranged from 0.35 to 0.75 mm, the corresponding percentages being 1.95 and 5.11. The values were considered acceptable for further evaluation.

Permanent tooth root length may be affected by several external factors, which could bias the results. Orthodontic treatment, especially with fixed appliances, may cause root resorption, as also for instance could traumatic occlusion, bruxism, nail biting, trauma, apical infection, or root treatment. According to anamnestic information, the 45,X/46,XX females or their female relatives had not had orthodontic treatment before the examination procedures. Also, anamnestic information on the population controls suggested that they had not undergone orthodontic therapy. This is supported by the fact that at the time in question there were only very few dental practices in Finland where fixed appliance orthodontics or orthodontics in general were carried out. Regarding the possible effects of other external factors, an assumption is made of an even distribution between the groups.

## Statistical analysis

The Statistical Package for the Social Sciences 10.0 (SPSS, Chicago, Illinois, USA) was used for statistical analysis. Mean values for root length were calculated and compared between the 45,X/46,XX females, female relatives, and population control females using the *t*-test for equality of means to indicate the significance of differences between the groups. The results were considered statistically significant when *P* was 0.05 or less.

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#### Results

The results showed that mean permanent tooth root lengths in 45,X/46,XX females were in most cases less than those of the population control females (Table 1), the differences being significant for 12 of the 14 comparisons in the maxilla and 11 of the 14 in the mandible, and the actual relative metric differences in the maxilla exceed those in the mandible in most instances. The 45,X/46,XX females had smaller tooth roots than their sisters or mothers, with only one exception (Table 2). The differences were significant in half of the comparisons, with the female relatives being closer to the population control values than the 45,X/46XX females.

## Discussion

After crown growth is complete, the dividing epithelial cells in the tooth root sheath determine the size, shape, and number

**Table 1**Mean maxillary and mandibular permanent tooth rootlengths in the 45,X/46,XX females and population control females.

Tooth	45,X/46,XX females				Population control females			
	Mean (mm)	SD	Ν	Р	Mean (mm)	SD	Ν	
Maxillary								
Right second molar	13.7	1.6	13		14.8	1.9	36	
First molar	13	1.3	14	**	14.7	1.9	35	
Second premolar	14.8	2.3	14	***	17.2	1.7	34	
First premolar	15.5	1.7	13	**	17.3	1.8	32	
Canine	19.5	2.5	14	***	22	2.1	40	
Lateral incisor	16	2.5	14	***	18.3	1.5	36	
Central incisor	15.9	3.2	15	***	18.9	1.4	39	
Maxillary								
Left central incisor	16.3	2.9	15	***	19.1	1.2	38	
Lateral incisor	16.4	2.4	15	***	18.4	1.7	35	
Canine	19.7	1.6	14	***	22.2	1.9	39	
First premolar	15	2.4	11	**	17	1.8	33	
Second premolar	14.7	2.2	12	***	17.2	1.7	35	
First molar	13.1	1.1	13	*	14.5	1.8	34	
Second molar	13.5	1.4	14	ns	14.3	1.9	34	
Mandibular								
Right second molar	16	2	13	*	17.2	1.4	33	
First molar	16.4	2.5	9		17.7	1.3	28	
Second premolar	16.5	2.9	11	*	18.2	1.9	36	
First premolar	16.2	1.3	14	**	17.6	1.8	41	
Canine	17.6	1.6	13	***	19.8	2	42	
Lateral incisor	14	1.1	14	***	15.7	1.7	45	
Central incisor	13.5	1.7	13		14.5	1.7	46	
Mandibular								
Left central incisor	13.8	1.7	14	ns	14.5	1.7	45	
Lateral incisor	14.2	1.4	14	**	15.7	1.8	44	
Canine	17.7	2.2	14	**	19.5	1.7	40	
First premolar	16.6	2	13	*	17.9	1.8	42	
Second premolar	17.2	2	13	**	18.8	1.7	39	
First molar	16.2	1.3	12	**	17.8	1.5	29	
Second molar	15.6	1.8	13	**	17.2	1.5	30	

SD, standard deviation. Statistical evaluation with the two-tailed *t*-test. ns, not significant; P < 0.1; \*P < 0.05; \*\*P < 0.01; \*\*P < 0.001.

Tooth	45,X/46	6,XX fe	males		Female relatives		
	Mean (mm)	SD	Ν	Р	Mean (mm)	SD	Ν
Maxillary							
Right second molar	14.1	1.2	8	ns	13.7	2.4	8
First molar	13	0.9	7		14.2	1.1	7
Second premolar	14.8	2.3	8		16.5	1.9	8
First premolar	15.4	1.8	8	*	17.7	1.9	8
Canine	19	2.4	9		20.9	2.2	9
Lateral incisor	15.6	2.4	9	*	17.7	1.8	9
Central incisor	15.4	2.7	10	*	18.1	1.8	10
Maxillary							
Left central incisor	15.6	2.5	10	**	18.5	1.4	10
Lateral incisor	16.2	2.7	10	*	17.8	1.5	10
Canine	19.3	1.5	9	ns	20.6	2.2	9
First premolar	15.4	0.9	7	**	17.8	1	7
Second premolar	15.2	1.3	7	ns	16.2	1.1	7
First molar	13	1	8	ns	13.6	1.6	8
Second molar	13.2	1	6	*	15	1	6
Mandibular							
Right second molar	16.6	1.7	7	ns	17.5	2.2	7
First molar	16.9	1.7	6	*	18.9	0.7	6
Second premolar	17.5	2.4	8	ns	18.5	2.4	8
First premolar	16.2	1.4	9	*	17.9	2	9
Canine	17.4	1.4	9		19.6	3	9
Lateral incisor	14	1	10	***	16.7	1.9	10
Central incisor	13.8	1.4	9	**	15.5	2	9
Mandibular							
Left central incisor	13.8	1.6	8	*	15.6	2.2	8
Lateral incisor	14.1	1	10	***	16.8	1.7	10
Canine	17	1.6	9	**	19.8	2.3	9
First premolar	16.4	2	8	ns	17.7	2.2	8
Second premolar	17.6	0.9	9	ns	18.7	2.3	9
First molar	16.4	0.8	6	*	18.4	1.4	6
Second molar	16.2	1.8	8	ns	17.1	2.9	8

**Table 2**Mean maxillary and mandibular permanent tooth rootlengths in the 45, X/46, XX females and female relatives.

SD, standard deviation. Statistical evaluation with the two-tailed *t*-test. ns, not significant; P < 0.1; \*P < 0.05; \*P < 0.01; \*\*P < 0.001.

of the roots (Ten Cate, 1994). Root dentine is formed later than crown dentine and requires a proliferation of epithelial cells from the cervical loop of the dental organ around the growing dental papilla to initiate the differentiation of root odontoblasts. The formation of primary physiological dentine continues until the external root form is complete (Ten Cate, 1994).

The discrepancy in tooth root size between the 45,X/46,XX females and the population controls and female relatives is of the same order of magnitude as that observed in permanent tooth crown sizes between these females (Alvesalo, 1985). The fact that the mean root lengths of antimeric teeth differ to some extent may be due to the sample sizes, varying numbers of measurements available, and technical reasons. Accordingly, the measurements of natural tooth roots also showed differences between the means for antimeric teeth (Selmer-Olsen, 1949).

The reported difference between normal 46,XY males and 46.XX females in permanent tooth root lengths is approximately 6 per cent, males showing larger roots than females (Selmer-Olsen, 1949; Garn et al., 1978; Lähdesmäki and Alvesalo, 2004). There also seems to be a clear gender difference in extreme root lengths, with extremely short roots found most often in females and extremely long roots in males (Jakobsson and Lind, 1973). Permanent tooth roots in 45,X females (Turner syndrome), or those with one X chromosome, are reduced in length compared with normal females (Midtbø and Halse, 1994b). Recent results on tooth root sizes in 47.XYY males, or males with an extra Y chromosome (Lähdesmäki and Alvesalo, 2004), have shown increased root length relative to normal males, and 46,XY females, or females with a male sex chromosome constitution, have root lengths close to those of normal males (Lähdesmäki and Alvesalo, 2005). These results indicate that the promoting effect of Y chromosome genes on tooth crown growth is also expressed in root growth.

In terms of population development standards, these results together indicate that irreversible changes in tooth growth become evident 3 years after birth and continue up to 14 years of age. Recent results have shown an increase in the lengths of permanent tooth roots in 47,XYY males (Lähdesmäki and Alvesalo, 2004) and 46,XY females (Lähdesmäki and Alvesalo, 2005). Considering these findings and the results regarding root length in 45,X females, it may be suggested that the reduction in root growth in 45,X/46,XX females is due to a deficiency in the amount of growth-promoting genes located on the sex chromosomes. It is possible that these are the same genes that promote crown growth.

It has been suggested that the expression of the difference between the genders in various dental features results from the direct differential effects of the X and Y chromosome genes on crown growth. The Y chromosome promotes growth of both enamel and dentine, whereas the effect of the X chromosome on crown growth seems to be restricted to enamel formation. The effect of the Y chromosome on dental development, particularly in increasing mitotic activity, explains the expression of sexual dimorphism in terms of tooth crown size and shape, timing of tooth development, and the number of teeth, e.g. supernumerary permanent teeth are approximately twice as common in normal males as in normal females, and permanent teeth (except third molars) are more frequently missing in females than in males (Alvesalo, 1985, 1997). Also, assuming genetic pleiotropy, sexual dimorphism in root size can be explained by this effect (Lähdesmäki and Alvesalo, 2004) and the difference between the genders in the expression of the torus mandibularis, the timing of skeletal maturation, statural growth, and the gender ratio at birth (ratio of the number of males to females) and in the earlier stages of development (Alvesalo, 1985, 1997). It is of great interest that molecular studies have shown that the loci for human

amelogenin, the main protein component of the enamel organic matrix, are to be found on both the X and Y chromosomes. The amino acid sequences of X and Y chromosome genes seem to differ to some extent, however. These genes are located on the distal short arm of the X chromosome and possibly on the proximal long arm of the Y chromosome, although the short arm of the Y chromosome has also been suggested (Lau *et al.*, 1989; Nakahori *et al.*, 1991; Salido *et al.*, 1992).

#### Conclusions

The present results regarding permanent tooth root growth in 45,X/46,XX females, or Turner mosaics, and earlier findings on their tooth crown sizes indicate that evident irreversible growth reduction occurs in these females relative to normal females beginning 3 years after birth and continuing up to 14 years of age, expressing an effect which is apparently continuous in nature. Earlier results for 47,XYY males and 46,XY females have shown an increase in tooth crown and root growth, and growth reduction of these tooth components in 45,X females. It is suggested that the reduction in root growth in 45,X/4,XX females is due to a deficiency in the amount of dental growthpromoting genes located on the sex chromosomes. It is possible that these genes are the same that promote crown growth.

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