Original Article

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The prediction formula of mesiodistal width of unerupted permanent canine and premolars from a group of Vietnamese, a preliminary study.

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The purpose of this study was to create new equations and to test their validity for estimating the sum of mesiodistal tooth sizes of unerupted canine and premolars of Vietnamese children. Two hundred and forty permanent teeth, including central incisors, through first molars were measured on twenty dental casts of Vietnamese. Correlation coefficient of all possible combinations of predictor were evaluated. Cross validation was also conducted both for selection of the prediction-model and validation of the prediction-result. Correlation coefficient and leave-one-out cross validation mean absolute error and root mean square error (LOOCV MAE and RMSE) were finished and indicated that the best prediction model was to use the width of mandibular central incisor and maxillary first molar (Md1Mx6) to predict the width of canine and premolars. Since there was no significant difference for sexual dimorphism (p>0.01), combined gender equations were developed from the regression analysis. The maxillary prediction formula was that Y= 0.77X+9.8 and the mandibular equation was that Y= 1.02X+5.1 where Y represented the predicted widths of canine and premolars and X represented the widths of mandibular central incisor and maxillary first molar (Md1Mx6). Validation as finished by LOOCV MAE and RMSE indicating that the error of these newly developed prediction equations was acceptable. LOOCV MAEs were 0.55 and 0.71 mm for maxillary and mandibular teeth, respectively. Further, these equations may be used with further investigation on larger sample or different specific geographic populations in Vietnam.

Keywords: prediction formula, mesiodistal tooth width, canine and premolars, mandibular central incisor and maxillary first molar, tooth width prediction, Vietnamese

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Introduction

Mixed dentition space analysis (MDSA) estimates the mesiodistal widths of unerupted premolars and canine when the first molars and incisors are already erupted [1]. Many publications have indicated attempts to predict the width of unerupted permanent canine and premolars since 1940's [2]. These methods, namely prediction tables of Moyers (1963) and Tanaka and Johnston equations (1974) are the most largely used because of their simplicity [1, 3]. Besides, numerous unerupted tooth width estimation methods have been published. They could be classified into three main categories based on the predictor (independent variable);

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1) the estimation based on the erupted teeth [1, 2].

2) the radiographic images of un-erupted teeth are measured [4, 5].

3) the combination of the first and second methods is used as a predictor [3, 6].

Validation is also a crucial step to evaluate how well a prediction method performs for new subjects [7, 8]. Generally, validation consists of internal and external validations. Internal validation assesses the setting from where the development data originated (learning data set). This internal validation often instigated the internal overfitting called optimism. External validation is performed on recently treated patients or patients from other places (validation data set). However, among different internal validation techniques in orthodontic research, leave-one-out cross-validation (LOOCV) is still an acceptable technique, especially when sample size is small [9]. It also should be noted here that during the process of LOOCV calculation, all subjects of learning data set will be repeatedly reselected and re-evaluated. Therefore, LOOCV also reflects the predictive ability even from the learning data set. As a result, it also provides parameters for prediction model selection [10, 11].

Recent studies have reported that the different combination of the sizes of teeth (i.e. permanent first molars and incisors) are better predictors for the permanent canine and premolars than that of the four lower permanent incisors [12, 13]. Therefore, researchers were compelled to find effective and more accurate prediction equations of crown widths of the unerupted permanent canine and premolars for Vietnamese child population. The objectives of this study were:

- To develop new formulas based on erupted teeth to predict the sum of mesiodistal widths of unerupted permanent canine and premolars for Vietnamese child population
- To evaluate the validity of the newly created prediction equations for Vietnamese child population using modern statistical method.

Materials and methods

The sample consisted of dental casts that were collected from Vietnamese students in Thailand. All dental study casts that met the inclusion criteria were included as study subjects. The samples consisted of 240 tooth measurements from 4 males and 6 females age between 24-34 years old.

Inclusion criteria:

- All subject were Vietnamese for at least two generations.
- The dental casts with fully erupted permanent teeth (except second and third molars) present
- The dental cast with no malformed tooth, restorations, proximal fractures or proximal caries
- Cases with first molar occlusion Class I and only mild crowding were included (crowding ≤ 4 mm) [13]

The final study protocol was approved by the Human Research Ethic Committee of the Faculty of Dentistry, Mahidol University (Certificate of approval COA.No.MU-DT/PY-IRB 2015/ 023.0806). The permanent teeth, including central incisors through first molars were measured and recorded. A pair of Mitutoyo 573-721 Digimatic Absolute Point Calipers with narrow tip jaws (0.0005"/ 0.01 mm resolution) were used to record all mesiodistal dimensions following Hunter and Priest's guidelines [15].

To ascertain that measurement error would be in an acceptable limit, the main investigator (VTH) measured all dental casts twice, one day apart. An experienced orthodontist (ST), remeasured all these dental casts three days after. Shapiro-Wilk test was used to test the normality of the sum width of central incisor to first molar using "dplyr" and "ggpubr" packages of R statistical analysis program volume 3.4.3 [16-18]. The intra- and inter-observer agreements were also computed using

Bland-Altman Limits of Agreement (LoA) analysis with "BlandAltmanLeh" package of R statistical analysis program volume 3.4.3[19-21]. Descriptive statistics to describe the tooth sizes of the individual teeth were mean and standard deviation (SD). Sexual dimorphism was also conducted to decide whether to construct the separate or combined gender prediction equation.

To find the best predictor from erupted teeth measurements, all possible combinations of predictor grouping of erupted teeth measurements (first molars, lateral and central incisors) were arranged. However, maxillary lateral incisor was excluded due to tooth size variability. The results were optimal predictor combination selected from 9 combination possibilities. The correlation coefficients were calculated to detect the optimal predictors. As mentioned before, LOOCV is able to reflect the best prediction model. Mean absolute error (MAE) and root mean square error (RMSE) calculated via LOOCV method were also finished and compared. The independent variables that provided the largest correlation coefficients (r) and the smallest LOOCV MAE and RMSE for male and female samples were used to construct the prediction equation [22]. Simple linear regression was used to establish regression equations for predicting the sum of mesiodistal widths of maxillary and mandibular canine and premolars. Finally, LOOCV MAE and RMSE were used to explain the predictive ability of newly developed prediction equations [23]. Basically, LOOCV MAE and RMSE facilitate the comparison of the error of estimation. The short detail of these parameters was given as following:

- True error (E) is estimated as average error rate:

$$\mathrm{E} = \frac{1}{K}\sum_{i=1}^{K} E_i$$

MAE is the average of the absolute values of the differences between predicted and the corresponding values. RMSE is the difference between forecast and true values are each squared, and then averaged over the sample. Finally, the square root of the average is taken. MAE is intuitive measurement and retains the measuring unit intact, while RMSE is useful when large errors are particularly undesirable. MAE and RMSE should be used together to provide a complete picture of the error distribution [22].

$$\mathrm{MAE} = \frac{1}{N}\sum_{i=1}^{N}|E_i|, \quad \mathrm{RMSE} = \sqrt{\frac{1}{N}\sum_{i=1}^{N} E_i^2}$$

It should also be noted here that in this study MAE and RMSE were calculated by LOOCV which each subject of the learning data set was repeatedly evaluated to show both the predictive ability of the prediction model and internal validation result of newly developed equations. To ease the understanding, it should be mentioned here that when MAE and RMSE were calculated repeatedly via LOOCV, they could also be called goodness-of-fit parameter.

Results

All subjects were Vietnamese for at least two generations as their parents had to show Vietnamese last names. The distribution of birthplace also covered all main regions of Vietnam (Table 1). Moreover, the normality test of the sum of mesiodistal width from central incisor to first molar using Shapiro-Wilk test, showed the normal distribution ($p > 0.05$). Therefore, these normally distributed variables were statistically analyzed using parametric methods.

Table 1 Birthplaces of all subjects in this study. They were distributed to the most populated 6 regions out of the total 8 regions of Vietnam.

Birthplace	Region of Vietnam	Population (million)	Number of participant
Thai Nguyen	Northeast Vietnam	8.6	1
Nam Dinh	Red River Delta (North Vietnam)	19.7	1
Quang Binh	North Central Coastal Vietnam	10.5	1
Hue	North Central Coastal Vietnam	10.5	1
Nha Trang	South Central Coastal Vietnam	9.2	1
Binh Dinh	South Central Coastal Vietnam	9.2	2
Ho Chi Minh City	Southeast Vietnam	16.1	1
Binh Phuoc	Southeast Vietnam	16.1	1
Can Tho	Southwest Vietnam/ Mekong Delta River	17.6	1
	Northwest	4.4	0
	Central Highland	5.6	0

Intra- and Inter-observer errors

To investigate the reliability of tooth width measurement, intra- and inter-observer error tests were finished on the summation of the central incisor to first molar width. The difference plot showed level of agreement (LoA) estimated at 95% confidence intervals and the average difference. Consecutively, for intra- and inter-observer agreement errors LoA ranged from -0.32 to 0.53 and -0.27 to 0.74 mm were showed (Figure 1, 2). The difference between the two means was 0.11 and 0.23 mm on average, consecutively for intra- and inter-observer agreement errors. The means and SD of the mesiodistal widths of individual measured teeth were also presented for the male and female groups (Table 2).

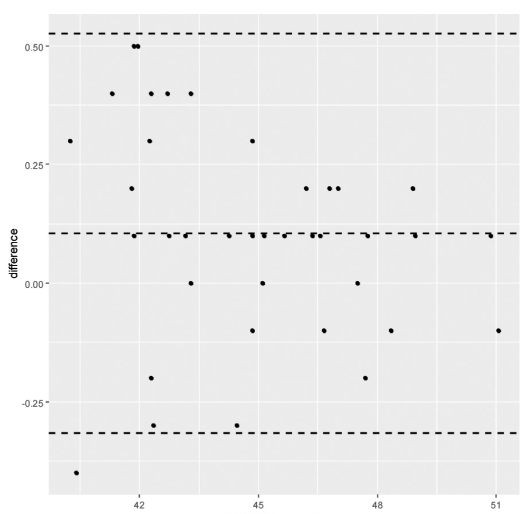


Figure 1 Intra-observer error was showed using Bland and Altman plots of difference between twice measurements of the main investigator. The difference plot showed level of agreement (LoA) estimated at 95% confidence intervals and the average difference. Ninety-five percent LoA was from -0.32 to 0.53 mm. The difference between the two means was 0.11 mm on average.

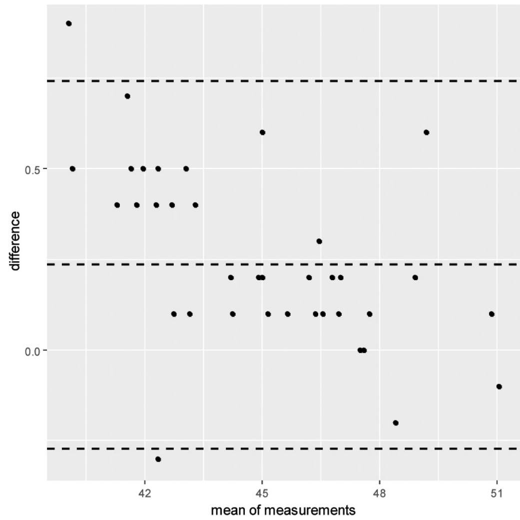


Figure 2 Bland and Altman plots of difference between orthodontist and investigator's measurements. The difference plot showed level of agreement (LoA) estimated at 95% confidence intervals and the average difference. Ninety-five percent LoA was from -0.27 to 0.74 mm. The difference between the two means was 0.23 mm on average.

Table 2 Descriptive statistics for maxillary and mandibular mesiodistal widths of individual teeth for the combined genders, male and female groups in millimeters.

Maxillary tooth	Male		Female		Combined genders	
	Mean	SD	Mean	SD	Mean	SD
Central incisor	8.19	0.31	8.75	0.39	8.52	0.45
Lateral incisor	6.68	0.29	6.93	0.60	6.83	0.51
Canine	7.73	0.52	7.86	0.32	7.81	0.40
First premolar	7.08	0.36	7.20	0.37	7.15	0.36
Second premolar	6.50	0.20	6.61	0.49	6.57	0.40
First molar	9.77	0.56	10.14	0.53	9.99	0.56
Central incisor	5.20	0.19	5.39	0.43	5.31	0.36
Lateral incisor	5.66	0.17	6.07	0.28	5.90	0.31
Canine	6.68	0.31	6.85	0.23	6.79	0.27
First premolar	6.85	0.30	7.13	0.54	7.02	0.47
Second premolar	6.61	0.44	7.15	0.66	6.93	0.63
First molar	10.80	0.40	11.24	0.50	11.06	0.50

Sexual dimorphism

The amount and distribution of sexual dimorphism may vary comparing different populations. There were evidences for [24, 25] and against [26, 27] this sexual dimorphism of mesiodistal tooth width. In this study, t-test showed that there were no significant differences of summations of tooth widths between male and his counterpart p>0.01, Table 3). These included statistical analysis of three groups of tooth width summations. The first group was the summation of tooth width of central incisor to first molar. The second group was the dependent variable, the summation of canine, first and second premolar widths. Finally, the third group was the predictor (independent variable), sum of mandibular central incisor and maxillary first molar widths (Md1Mx6). Furthermore, when there is no statistically significant difference, the prediction equations should be constructed by combining tooth width together between gender. Therefore, the prediction of this study was constructed accordingly.

Correlation, goodness-of-fit parameters and regression analysis

Correlation coefficients and goodness-of-fit parameters including MAEs and RMSEs using LOOCV were performed between the sums of mesiodistal tooth width of best predictive groups with those of canine and premolars. The best combination selected for prediction equations development was the combination of mandibular central incisor and the maxillary first molar (Md1Mx6). In detail, the correlation coefficients were 0.70 and 0.75 for the prediction of maxillary and mandibular canine and premolars, respectively (Table 4). While correlation coefficients have been traditionally used to indicate the best prediction model for MDSA, it does not demonstrate clinical validity in measurement unit of millimeter. Upon completion of these parameters consideration, Md1Mx6 were ascertained as the predictors to formulate the prediction equations.

Table 3 Descriptive statistics showing arithmetic mean and standard deviation of sum of tooth width of one quadrant (central incisor to first molar) of male and female. The descriptive statistics of variables for prediction equation including sum of canine and premolars of one side and sum of mandibular central incisor and maxillary first molar of male and female were also showed. T-test showed that all groups show no significant difference (p>0.01) between the summation of tooth width between male and female. (NS: not statistically significant at the p-level of 0.01)

Summation of tooth width		Mean and S.D.(mm)		p
Central incisor to first molar	Maxillary arch	Male	45.90 ± 1.57	NS
		Female	47.49 ± 2.11	
	Mandibular arch	Male	41.79 ± 1.06	NS
		Female	43.83 ± 2.06	
Canine and premolars	Maxillary arch	Male	21.31 ± 0.82	NS
		Female	21.67 ± 1.03	
	Mandibular arch	Male	20.75 ± 1.03	NS
		Female	21.13 ± 1.24	
Mandibular central incisor and maxillary first molar		Male	17.27 ± 2.59	NS
		Female	17.91 ± 2.66	

Table 4 The comparison of correlation coefficient of all possible combined teeth groups in male and female subjects. Underlined numbers showed all highest values. The sum width of mandibular central incisor and maxillary first molar(Md1Mx6) showed the highest correlation coefficients for both dental arches. The second highest for the maxillary teeth was the combined width of mandibular lateral incisor and maxillary first molar (Md2Mx6). The second highest for the mandibular teeth was the combined width of mandibular lateral incisor and maxillary first molar (Md2Mx6) and maxillary and mandibular central incisors (Mx1Md1).

Tooth combination	Correlation coefficient	
	Maxillary teeth	Mandibular teeth
Md1Md6	0.57	0.69
Md2Md6	0.49	0.62
Md1Mx6	<u>0.70</u>	<u>0.75</u>
Md2Mx6	<u>0.65</u>	<u>0.72</u>
Mx1Md6	0.42	0.60
Mx1Md1	0.52	<u>0.72</u>
Mx1Md2	0.37	0.61
Mx1Mx6	0.47	0.69
Md6Mx6	0.40	0.63

Mx: Maxillary Md:Mandibular

Number indicated the tooth numbering system following the FDI system without quadrant number.

Determination of new equations

To attain the prediction equations, the simple linear regression equations were computed. Following published documents [3, 24], these gender-combined equations were produced for both male and female. The simple regression lines with 95% individual prediction bands (PB), which described the probability of the response value of a single new observation from the same population, were seen on Figures 3.

The prediction formulas derived from the regression analysis are as follows:

Maxillary: $Y = 0.77X+9.8$

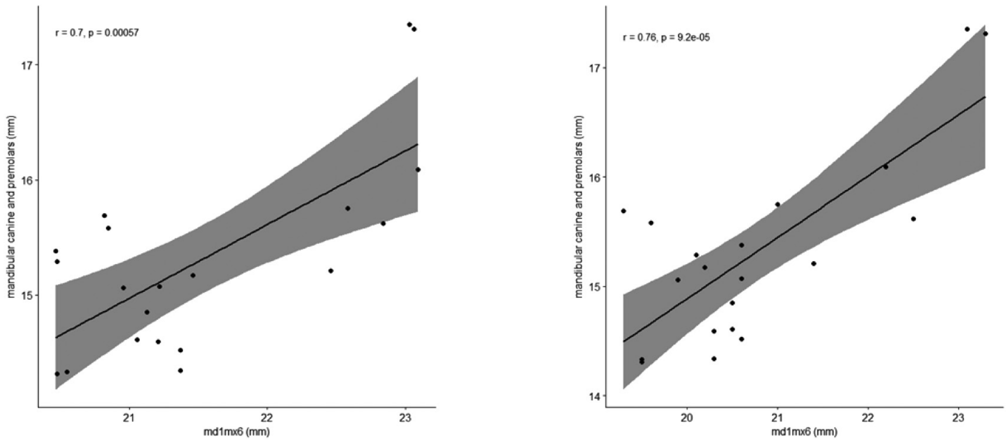
Mandibular: $Y = 1.02X+5.1$

Y represents the predicted widths of canine and premolars.

X represents the widths of Md1Mx6.

Validation of these prediction methods

To analytically demonstrate the prediction model performance of these new equations, comprehensive comparison was required. LOOCV, as mentioned, demonstrated both model selection and validation ability. When assessing the performance of the new equations, the LOOCV MAE of the maxillary equation was 0.55 mm (RMSE = 0.70). The LOOCV MAE of mandibular equation was 0.72 mm (RMSE = 0.86, Table 5).



Figures 3 The simple regression line and scatter plots of the sum widths of maxillary (left) and mandibular (right) canine and two premolars (Mx345, Md345) on the sum widths of mandibular central incisor and maxillary first molar (Md1Mx6). The correlation coefficient was 0.70 and 0.75 ($p< 0.01$) for maxillary and mandibular arches, respectively. The simple regression lines with 95% individual prediction bands (PB), which described the probability of the response value of a single new observation from the same population, were also showed.

Table 5 shows independent variables versus the correlation coefficients and goodness-of-fit parameters i.e. MAEs and RMSEs using LOOCV. For both maxillary and mandibular arches, the correlation coefficients rom the combination of mandibular central incisor and maxillary first molar (Md1Mx6) were 0.70 and 0.75, respectively. LOOCV MAEs and RMSEs was 0.55, 0.70 and 0.72, 0.86 mm respectively also for maxillary and mandibular arches. Md1Mx6 showed the highest correlation coefficients and the lowest goodness-of-fit parameters (underlined numbers).

Dental arches	r			LOOCV MAE(mm)			LOOCV RMSE		
	Md1Mx6	Md2Mx6	Mx1Md1	Md1Mx6	Md2Mx6	Mx1Md1	Md1Mx6	Md2Mx6	Mx1Md1
Mx arch	<u>0.70</u>	0.65		<u>0.55</u>	0.62		<u>0.70</u>	0.76	
Md arch	<u>0.75</u>	0.72	0.72	<u>0.72</u>	0.71	0.72	<u>0.86</u>	0.87	0.87

Mx: Maxillary Md:Mandibular

Number indicated the tooth numbering system following the FDI system without quadrant number.

Discussion

By and large, there are 8 regions in Vietnam. The domicile by birth of the sample of this study was investigated and covered 6 out of 8 regions of Vietnam. In addition, these 6 regions were the most populated regions in Vietnam (Table 1) [28]. Therefore, the samples of this study distributed throughout the most populated area of Vietnam. The MDSA equations developed may reflect as the equation for Vietnamese.

To achieve the reliability in tooth width measurement, a test was done to evaluate the intra- and inter-observer errors. From this study, the average differences between the two means were 0.11 and 0.23 mm, consecutively. LoAs of Bland and Altman test were narrow and lay over zero with most of the data points fell inside this total error criteria (Figure 1, 2). Therefore, tooth measurements finished by main investigator (VTH) and an experienced orthodontist (ST) revealed the intra- and inter-observer agreement. Hence, when consider the size of these differences, it could be speculated that these may be the result of measurement error and may be clinically unimportant.

A degree and distribution of sexual dimorphism may vary between populations. It has been known for some time that within a population, the dimension of the crown of permanent dentition tends to be larger in males [24, 25]. While, some studies found non-significant differences in the mesiodistal tooth crown widths in their populations [26, 27]. There were evidences supporting both sides. In addition, there were evidences support the use of combined sex prediction equations [3, 24]. In this study, since there wes no statistically significant difference of tooth width between gender and to reduce the number of prediction equations, the linear regression was finished as combined sex equations.

Sum of mesiodistal widths of four mandibular incisors has been widely used as a predictor for estimation of unerupted canine and premolars width in mixed dentition analysis [1]. This correlation was detected, but there was a wide range of correlation coefficients from 0.58 to 0.64 [1-3]. Although these correlations could be applied to develop prediction models, the higher correlations were seen in the other tooth combinations. These results were in agreement with previous researches which indicated that using the sum of four lower incisors may provide simple clinical practice, however, in some studies, they might not show the best correlation coefficient [9-10].

Donatelli and Lee validated the 811 samples from study by Seo and co-workers [9-29]. As mentioned, they reported the MAE by LOOCV for the sample size of 100 and 200 to be 0.683 and 0.677 mm, respectively. LOOCV method in this study reported that MAE was of 0.55 mm for maxillary predictions. The MAEs for mandibular prediction was 0.71 mm. Comparing to Donatelli and Lee's study, the prediction errors of this study were comparable to the error of their study. These small errors of approximately 0.6 mm for the sum widths of three teeth (canine and two premolars) should be clinically acceptable.

From this study, all goodness-of-fit parameters showed that new equations were acceptable. However, it is still interesting to thoroughly examine the prediction model selection method and describe the amount of optimism. Moreover, the regional difference of ethnicity in Vietnam might affect the accuracy of these predictions. Further research might involve larger sample size specifically into regional population. To further investigate the accuracy, signal to noise ratio and bootstrap statistical analysis may be implemented [30].

Conclusion

In this studied population, the sum of the mandibular central incisor and first maxillary molar (Md1Mx6) showed high correlations, low LOOCV MAEs and RMSEs for both maxillary and mandibular teeth. Therefore, the sum of these teeth was used as best predictors to develop new prediction equations. It would be rational to mention that these newly derived prediction methods might be clinically useful in Vietnamese for tooth size predictions. In addition, more researches for external validation and modern statistical method are essential to assess the applicability of these prediction equations on larger population and on different geographic populations in Vietnam.

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