ER5 and ER3 – Bone age assessment by simplifications of the Eklof and Ringertz method

Maturidade óssea: estimação por simplificações do método de Eklof e Ringertz

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Abstract

Purpose: The aim of this work was to evaluate bone age assessment using two simplifications of the Eklof and Ringertz method, which provide automated auxiliary data for the medical diagnosis.

Methods: Hand radiographic images of 685 children and adolescents (male and female subjects; age: 6-16 years old) were used to estimate skeletal age using simplifications of the Eklof and Ringertz method – ER5 and ER3 (five and three hand bone ossification centers, respectively). Data were analyzed using Pearson's correlation test and Student's t-test (0.05 level of significance).

Results: The values of bone age estimation using the two simplifications of the Eklof and Ringertz method were compatible with the average medical reports obtained by using three standard methods – Greulich & Pyle, Tanner & Whitehouse and Eklof & Ringertz methods. In most cases no statistically significant difference in bone age was found ($P > 0.05$).

Conclusion: It is possible to conclude that both proposed simplifications (ER3 and ER5) can be used for bone age estimation, using fast and simplified configuration, with results similar to the average of the traditional methods. Also, these simplifications are appropriate to estimate bone age in large databases because they are fast and objective.

Key words: Bone age estimation; Eklof and Ringertz method

Resumo

Objetivo: Apresentar metodologia para estimação da idade óssea utilizando simplificações do método de Eklof & Ringertz, que operam de forma automática, proporcionando laudos que auxiliam o diagnóstico médico.

Metodologia: Foram utilizadas imagens carpais de 685 crianças e adolescentes na faixa etária de 6 a 16 anos para a estimação da idade óssea com as simplificações E&R5 – simplificado para 5 centros de ossificação; E&R3 – simplificado para 3 centros de ossificação. A automatização dos métodos simplificados explora procedimentos específicos para o processamento de imagens radiográficas da mão.

Resultados: Os resultados obtidos na estimação com as duas simplificações propostas foram compatíveis com a média dos laudos médicos obtidos com os três métodos clássicos – Greulich & Pyle, Tanner & Whitehouse e Eklof & Ringertz. A verificação foi realizada utilizando o teste T de Student pareado com faixa de significância de 5% e, na maioria dos casos, não ocorreram diferenças estatisticamente significantes ($P > 0,05$).

Conclusão: Analisando os resultados, conclui-se que é possível estimar a idade óssea utilizando a simplificação do método de E&R, no qual o processo de estimação é feito de forma rápida e automatizada, obtendo resultados compatíveis com o laudo médico.

Palavras-chave: Estimação da idade óssea; método de Eklof & Ringertz

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Introduction

Bone age (or skeletal age, or skeletal maturity) assessment using a radiograph of the left hand is a common procedure in pediatric radiology. Based on that radiological evidence of skeletal development, bone age is assessed and then compared with the corresponding chronological age. A large discrepancy between these two ages indicates abnormalities in skeletal development. Growth hormone–related growth diseases, which can include childhood obesity, are issues of increasing concern. Early detection is very important to the treatment of such conditions, and thus bone age assessment has come to the center of public attention.

The wrist-hand region is the most indicative of skeletal maturation, especially because it includes many ossification centers in a small area. Many methods have been developed to estimate skeletal age, such as those of Tanner and Whitehouse (TW) (1), Greulich and Pyle (GP) (2), and Eklof and Ringertz (ER) (3). The GP method, used by over 76% of pediatricians (3), is based on a general comparison with the images in the atlas that correspond closest with the chronological age of the patient. The TW method uses a detailed analysis of each individual bone; owing to its complexity, it is employed by less than 20% of radiologists, even though it yields the more reliable results (4,5). Both methods are not only time-consuming, but they suffer from inconsistencies due to the subjective nature of the analysis as performed by various observers with different levels of training. The ER method measures the distances that correspond to the width and length of the hand and wrist bones (10 ossification centers) for bone age estimate. The ossification centers are composed of length of radius distal epiphysis; length and width of capitate; length and width of hamate; length of metacarpals II, III, and IV; and length of proximal phalanx II and III (1-3).

In 1991, Pietka et al. (5) carried out a computer-assisted bone age assessment method using phalanx lengths, atlas lengths, and atlas matching under some restrictions of the quality of hand radiographs. Two years later, they also found that only area and bone contour length of carpals were significant features of bone age development by two-step local threshold algorithm (6). In 1997, Mahmoodi et al. (7) constructed the automatic ossification centers locating algorithm by computer vision technique. The survey is based on multi-scale method, roughly finding the contour of the hand then identifying the contour of the fingers by analyzing the geometry of finger. The constraints of the method are few so it can make the bone age estimation system more practical.

In 2001, Pietka et al. (8) addressed a method for preprocessing and epiphyseal/metaphyseal ossification centers feature extraction and its potential use in computer-assisted bone age assessment. The method was based on ratios of epiphyseal and metaphyseal diameters (9). In the same year, Marques Da Silva et al. (10) introduced a method for determining a signature of the medius to estimate skeletal maturity; however, a threshold has to be selected manually in the process to obtain the proximal phalanx length and the gap between the metacarpal and phalanx from the signature (8). After 2001, Pietka et al. integrated some algorithms such as semi-auto *Computer-Aided Design* system; however, their bone age estimation computer-assisted system may refer the medical doctor's opinion and judgment to get a reasonable result.

This paper is focused on the ER method, which allows the direct use of uncomplicated computational methods and produces important results that assist in monitoring human growth. Another important criterion for this choice is the fact that it is not based on inspectional and comparative analyses. We present an automatic methodology formed by two simplifications of the ER method, called ER5 and ER3.

Methodology

The proposed methodology was tested on two databases composed of 909 radiographs from the Radiology Clinic of the University of Campinas (FOP-UNICAMP) and Bauru (FOB-USP) in Brazil. Database I is formed by radiographic images of 308 males and 367 females, and Database II by 130 males and 104 females. Based on the diagnosis of radiologists, the assessed bone ages varied from 6 to 16 years, as shown in Table 1. These radiographs were obtained by conventional X-ray device (Pendullun 300MA – 150 kV, high frequency) using standard values, i.e., voltage 45 kV, current 0.3 mA and focus-film distance 1m, and directing the X-ray beam perpendicularly to the center of the film. Hand-wrist radiographs were classified using the ER, GP, and TW methods (1-3,9-11).

Database II was included in the study only for comparison, because some results showed discrepancy with the average of the medical reports (ER, GP and TW) of Database I.

The software tool developed to support the image processing in this work, named hereafter as Anacarp, was built with Borland – Builder C^{++}, and the results were analyzed statistically by BioEstat 5.0 (12) software (Mamirauá Civil Society/MCT, CNPq, Belém, Brazil).

Table 1. Organization of the Databases.

Bone age (years)	Database I		Database II	
	Number of images		Number of images	
	Male	Female	Male	Female
6	10	27	5	4
7	37	22	15	12
8	27	47	9	11
9	34	51	7	6
10	36	30	17	9
11	36	47	11	13
12	34	32	26	15
13	33	37	13	8
14	37	29	15	17
15	10	20	4	5
16	14	25	8	4
Total	308	367	130	104

ER method – Proposed Simplifications

One of the problems encountered in the bone age estimation process by the ER method is related with bone overlap in some carpal regions (13-15). This hinders the measurement of ossification centers and may, therefore, produce unreliable results (16,17). To avoid this problem, the bone age was estimated based on five ossification centers, formed by phalanxes and metacarpals, and by disregarding the carpal bones, which provided a simplified method of ER, called ER5.

The ER5 simplification

In this simplification, the bone age estimation is performed based on analysis of only two proximal phalanxes and three metacarpals bones, as shown in Figure 1.

Subsequently, an in-depth statistical study was made aiming at a new simplification of the ER5 method, which led to the ER3 method.

The ER3 simplification

The aim in this study was to determine the minimum number of ossification centers able to provide statistically significant results, i.e., close to the average value of medical reports. To do so, all possible combinations were tried among the five ossification centers (taken from two to two, three to three, and average of five bones) selected in the study (see Fig. 2). The names for the bones used in combinations were D1, D2, and D3 for the length of metacarpals II, III and IV; and D4 and D5 for the length of proximal phalanxes II and III.

The line plotted in Figure 2 with black dots (at 9.00 in the y axis) refers to the average of medical reports for the image used for the illustration. The points selected from this image were the combinations: (D1 and D3) and (D1, D3 and D5), represented by the circles in this sequence.

After analyzing all the images in the database, it was possible to notice that the combination (D1, D3 and D5) shows an excellent approximation regarding the average of medical reports, pointing to a possible new simplification, named ER3. Figure 3 presents the ossification centers used by ER3.

Methodology for bone age estimation

In the block diagram of Figure 4 can be observed the procedure for the bone age estimation.

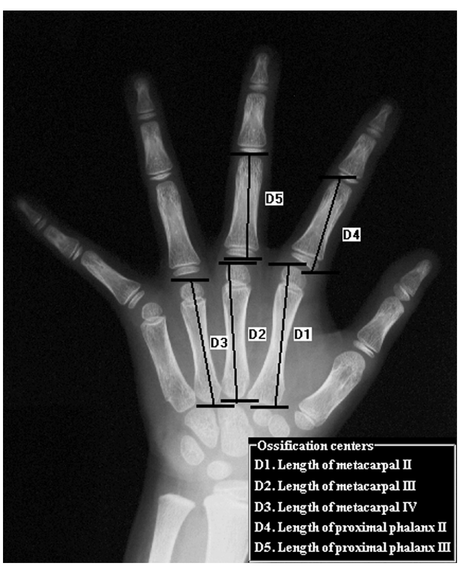

Fig. 1. Ossification centers used by ER5 method.

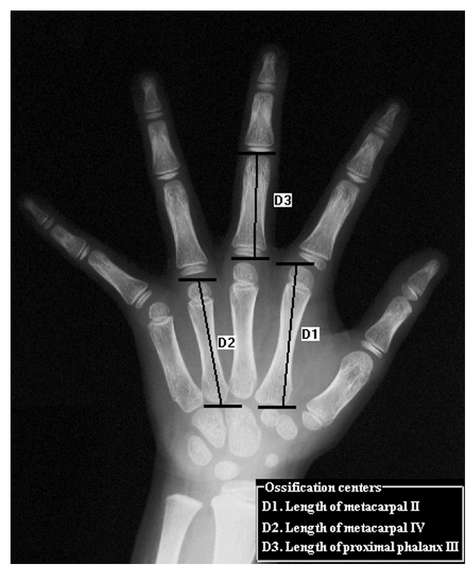

Fig. 3. Ossification centers used by ER3 method.

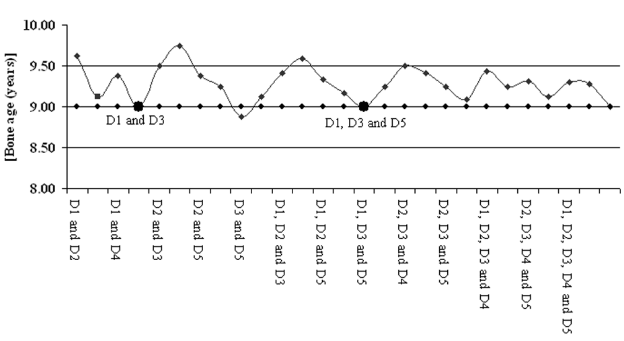

Fig. 2. Combinations in relation to the medical reports average.

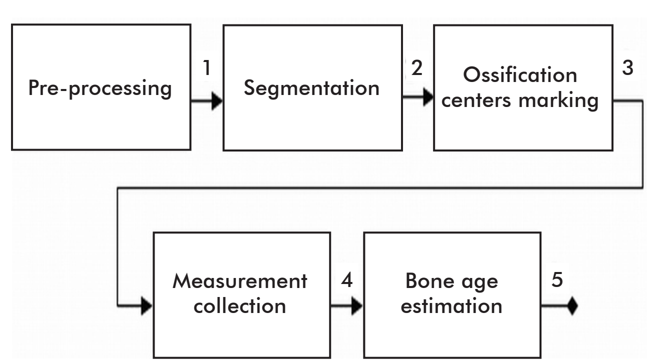

Fig. 4. Procedure used in the methodology.

1. Pre-processing: to eliminate the non-uniformity variations found in the background of the images, an algorithm developed by Marques and Nascimento (18) was applied. It corrected the Heel effect, a phenomenon compromising the regular distribution of X-ray intensity, generating non-uniform illumination in the background of images. Then, a low-pass filter was applied to minimize the noise present in the images (19,20).
2. Segmentation: an efficient threshold method should be capable of automatically providing a value for which all points with intensity lower than this value are eliminated (19-21). This phase is used to eliminate the pixels that do not belong to the bone structures. The implemented methods were: Otsu, Pun, Niblack and Rosenfeld (20-22).
3. Ossification centers marking: a procedure to automatically mark the ossification centers was created, delimiting the beginning and end of every bone – metacarpals II and IV; proximal phalanxes III and III – which are utilized for bone age estimation.
4. Measurement collection: after selecting all regions of interest, the length of every bone was calculated using the Euclidian distance.
5. Bone age estimation: with the length of the all bones, the ER table (relation between dimensions and ages) was searched to find the corresponding ages. The final age was calculated through the average of all bone ages.

Data analysis

The data were tabulated and analyzed statistically. We used the BioEstat 5.0 software (14) to perform statistical tests and then calculated the correlation factors, by the Pearson's correlation, between simplifications methods (ER5 and ER3) and the average of the medical reports (obtained by GP, TW and ER methods). A statistical comparison was performed using Student's t-test for paired samples and by calculating the 95% confidence interval ($P<0.05$).

Results

To improve the presentation and analysis of results, images are classified according to the average of the medical reports, considering groups aged 6 to 16 years, where each group is formed by a number of individuals. For example, the 6-year-old group includes patients between 6 years and 6 years 11 months. Table 2 shows the mean age and the standard deviation from the average of the reports (GP, TW and ER), assessed skeletal ages by ER5 and ER3 of male sexes, the correlation results (obtained by Pearson's correlation), and Student's t-test.
When Table 2 is analyzed, it is possible to verify that the bone age estimation performed by ER5 – male – reached a positive correlation with the average of the reports (Pearson's correlation between 0.58 and 0.96). Only the results for individuals within the age range of 11 years were not statistically significant, with p (Student's t-test) equal to 0.4512.
To investigate whether the ER5 method could not be used for bone age estimation for the range of 11 years of age (male), 32 individuals were selected from Database II and submitted to the ER5 method. The results were statistically significant (Student's t-test equal to 0.0076 and Pearson's correlation equal to 72%), contradicting the results obtained in Database I.
The results from the image set of males, when using the ER3 method, showed strong correlations (Pearson's correlation equal to 97%) and within the significance range ($P<0.05$). Only the results for individuals in the 9 to 14 age range were not statistically significant. An evaluation of the results of the 9-year-old group – a total of 28 images – showed that 2 images (7.14%) had estimated ages that differed by 7 and 8 months respectively from the expected value (the average of the reports). In the age range of 14 years, approximately 10% of the age estimations were generated above the standard deviation of 6 months in relation to the average of the reports.

Table 2. Mean age and standard deviation from the average of the reports, ER5 and ER3. Pearson's correlation and Student t-test, assessed skeletal ages by ER5 and ER3 – male grouped by age ranges.

		Groups – bone age (years)										
		6	7	8	9	10	11	12	13	14	15	16
AR	Mean age	6.30	7.51	8.38	9.45	10.54	11.37	12.42	13.50	14.32	15.20	16.24
	Standard deviation	0.42	0.30	0.31	0.34	0.31	0.25	0.31	0.31	0.31	0.29	0.38
ER5	Mean age	6.06	7.75	8.49	9.52	10.64	11.38	12.56	13.51	14.52	15.15	16.11
	Standard deviation	0.35	0.41	0.46	0.43	0.40	0.45	0.52	0.44	0.44	0.34	0.30
	Pearson Correlation	0.637	0.616	0.784	0.821	0.769	0.589	0.827	0.770	0.764	0.961	0.564
	Student t-test (*P*)	0.035	0.000	0.059	0.008	0.005	0.451	0.008	0.004	0.003	0.021	0.050
ER3	Mean age	6.63	7.78	8.55	9.42	10.34	11.23	12.12	13.56	14.33	15.02	16.11
	Standard deviation	0.47	0.55	0.40	0.35	0.43	0.35	0.52	0.35	0.37	0.49	0.60
	Pearson Correlation	0.684	0.647	0.715	0.352	0.970	0.766	0.681	0.638	0.382	0.756	0.673
	Student t-test (*P*)	0.011	0.000	0.000	0.264	0.001	0.002	0.000	0.012	0.486	0.050	0.018

AR: average of the reports.

Figure 5 shows the correlations between the average of the reports (obtained by GP, TW and ER) and the estimated ages by ER5 and ER3, to the images of the male sex, illustrating data in Table 2. Note that ER5 and ER3 obtained strong correlation (values above of 0.5) in almost all the age groups.

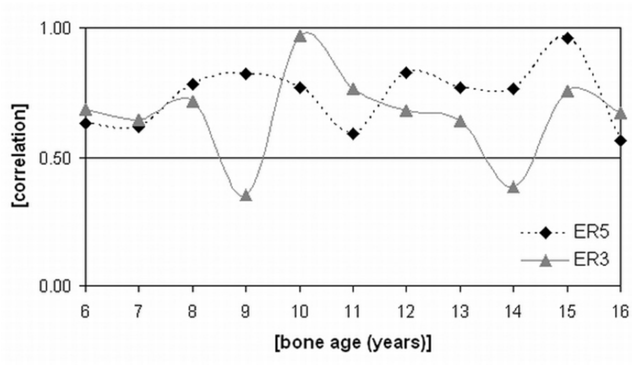

Fig. 5. Correlation between the average of the reports (obtained by TW, GP and ER) and estimated ages by ER5 and ER3 for images of the male sex.

A similar analysis was performed for female sex and the results are presented in Table 3. When Table 3 is analyzed, it is possible to verify that the results were positive and showed high correlations with the average of the reports (Pearson's correlation equal to 91%). The worst result was a correlation of 53.71% and Student's t-test equal to 0.283 (group 14 years of age). The 31 images in this group were separately evaluated, and in 5 cases bone age estimated differed from the average value of the medical reports, assuming a standard deviation of 6 months.

Results also were not significant for the 9- and 10-year-old groups ($P > 0.05$). The analysis of individual reports for these age groups indicated that, for the range of 9 years, 7.50% of reports differed in the average of the reports. For the 10-year-old group, this error was 3.70%. Performing the estimation to the other individuals of the other age groups in Database II, Pearson's correlation was above 79% and p-values (Student's t-test) within the significance range was smaller than 0.003.

Discussion

The methods that traditionally have been used as reliable references in bone age estimation are based on carpal radiography analysis: GP, TW and ER. The GP and TW require a comparative analysis, adding a significant amount of subjectivity in the process. The ER method is the most used in specialized clinics that use computerized tools to aid diagnosis. This method presents some operations difficulties, i.e., all of the points composing the ossification centers are marked manually, which results in a long period of time to establish the 20 points needed to estimate bone ages.

We chose to explore the ER method because besides its being one of the most commonly used, it allows the application of computational procedures in a more simple way than the other methods. Based on the original parameters of the ER method, a software tool was developed, named *Anacarp*, which operates automatically and in a simple way, where marks are inserted to isolate the ossification centers for bone age estimation. Results obtained by *Anacarp* show a high relationship with the average of the medical reports.

Data analysis was performed using Pearson's correlation and Student's t-test for paired samples. When the ER5 method was applied among males in the 9 and 14 age range and among females in the 9 and 10 age range, the initial estimated results were not statistically significant according to the average of the reports. These results motivated the use of Database II images, which showed that the bone age estimated by GP and TW for Database I contain slightly different values from those expected for the ages of 9 and 14. This showed that the subjectivity present in the GP and TW methods can sometimes produce results with low accuracy.

Table 3. Mean age and standard deviation from the average of the reports, ER5 and ER3. Pearson's correlation and Student's t-test assessed skeletal ages by ER5 and ER3 considering the average of the reports – females grouped by age ranges.

		Groups – bone age (years)										
		6	7	8	9	10	11	12	13	14	15	16
AR	Mean age	6.23	7.35	8.38	9.45	10.41	11.39	12.44	13.46	14.66	15.36	16.00
	Standard deviation	0.68	0.32	0.33	0.38	0.33	0.26	0.33	0.29	0.24	0.31	0.01
ER5	Mean age	6.45	7.28	8.22	9.37	10.56	11.53	12.54	13.65	14.61	15.53	16.38
	Standard deviation	0.70	0.47	0.45	0.44	0.49	0.50	0.52	0.45	0.55	0.55	0.48
	Pearson Correlation	0.905	0.908	0.737	0.880	0.870	0.489	0.869	0.614	0.532	0.801	0.830
	Student t-test (P)	0.014	0.041	0.001	0.010	0.034	0.048	0.029	0.002	0.283	0.004	0.010
ER3	Mean age	6.48	7.26	8.22	9.48	10.38	11.52	12.32	13.18	14.51	15.12	15.75
	Standard deviation	0.59	0.47	0.74	0.44	0.42	0.43	0.30	0.48	0.50	0.43	0.45
	Pearson Correlation	0.773	0.845	0.737	0.478	0.342	0.570	0.467	0.702	0.763	0.897	0.956
	Student t-test (P)	0.038	0.031	0.041	0.281	0.274	0.038	0.022	0.000	0.040	0.000	0.038

AR: average of the reports.

With the ER3 method, the estimated ages were not statistically significant, according to the average of the reports, when applied in images from the male 11-year-old group and the female 14-year-old group. An analysis of these age groups using Database II and estimating ages for both sexes showed the results to be consistent with respect to the average of the reports, considering a statistical significance of 5%.

Table 3 also shows no significant results for the 9- and 10-year-old groups. An analysis of the individual reports for these age groups (for all images in the range) revealed that 7.5% of reports differ from the average value for the 9-year-old range. In the 10-year-old group, this error was 3.7%. With the aim of verifying these statistical differences in these age groups, the estimation for individuals in the second set of images (Database II) – same age ranges – was repeated and the results evaluated from Pearson's correlation were above 79% and p values (Student's t-test) were within the range of significance. Again, this proved that the subjectivity present in the GP and TW methods sometimes produce results with low accuracy.

Conclusions

For both sexes, a high relationship between the average of the reports (obtained by GP, TW and ER methods) and the estimated ages with ER5 and ER3, was found. There was no significant statistical difference between the average of the reports and skeletal ages estimated by ER5 and ER3, as shown in Tables 2 and 3. These results showed that the simplifications of the ER method are also suitable for the analysis of the bone age estimation in large databases, which requires processing large amounts of data.

The proposed simplifications have the advantage of being relatively simple processes to implement, can operate on a simplified and automated manner, can produce results free of subjectivity, are consistent with the average of the reports, and can be used as an aid to medical diagnosis.

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