

Estimation of pediatric skeletal age using geometric morphometrics and three-dimensional cranial size changes

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Abstract This paper presents a method for estimating the skeletal age of children based on the centroid size of their face and their basicranium, derived from the three-dimensional coordinates of anatomical landmarks. The sample consists of computed tomography scans of 127 children (54 boys, 73 girls) of mixed origin living in the area of Toulouse (France), ranging in age from a few days to 18 years. The purpose of the present investigation was, first, to increase the variety of age-related structures theoretically available for pediatric skeletal age estimation and, second, to devise a method that can be applicable from early postnatal age to the end of adolescence with a satisfactory accuracy independent of age and even a better accuracy with greater age. We examined the relationship between the chronological age and the centroid size, calculated by using geometric morphometric methods and a linear model. With the aid of cross-validations, the statistical analysis indicates that the centroid size of the facial skeleton can be used as an age-related variable without any loss of accuracy with increased age, contrary to most of the methods of pediatric age estimation. The standard error was always lower or equal to 2.1 years (at the 95% confidence level) and decreased in our sub-sample of older children represented by a larger number of individuals.

Keywords Age estimation · Geometric morphometrics · Skeletal growth

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Introduction

To estimate the skeletal age of a child, it is necessary to identify the closest relationship between the chronologic age and the times of appearance and fusion of ossification centers, or the size and morphology of bones. The study of fetal osteology by Fazekas and Kósa [5] represents a famous example of this kind of research. In forensic practice, the most common methods of evaluation of skeletal age in the postnatal period use the lengths of long bone diaphyses or the changing morphological appearance of primary centers and epiphyses as, for example, the standards of Greulich and Pyle [8], Tanner et al. [17], or Thiemann and Nitz [18]. There is a considerable number of studies that have been dedicated to forensic age determination during recent years. For reasons of space, we cannot refer to all these studies. We can provide the following recent examples with respect to methods devised to skeletal [9, 14–16] or to dental [2, 10, 11] forensic age determination. However, there appears to be much less information available on the skull than on the rest of the skeleton and than on teeth, because most of the cranial components fuse prenatally or during early childhood [13].

A significant innovation in the analysis of skeletal maturation concerns the way in which size and shape are characterized. New concepts and methodologies collectively known as geometric morphometrics [1, 3] are increasingly being used in evolutionary contexts because they permit a rigorous and greater resolution of ontogenetic changes and, importantly, because they offer the possibility to discriminate into a component of size change through time (growth) and one of shape change through time (development). Geometric morphometrics allow the quantitative analysis of variation in organisms from the three-dimensional coordinates of anatomical landmarks collected

with specialized devices by digitizing the surface of body parts (e.g., hand-held laser scanner) or from computed tomography (CT), independent of any choice of coordinate system. Geometric morphometric methods use a mathematical definition of shape. Shape encompasses all features of landmark configuration except for overall size, position, and orientation. These extraneous factors are removed by the Procrustes method, which scales all configurations to unit size, superimposes them by their centers of gravity (centroids), and rotates them to an orientation of optimal fit to a consensus configuration [3].

This paper represents an application of geometric morphometrics in the assessment of pediatric skeletal age from the analysis of skeletal growth (changes in size) in three dimensions (3D) of two major cranial components (see [4])—the face and the base—each represented by skeletal landmarks. We examined the relationship between the chronologic age and the centroid size (defined as the square root of the sum of the squared deviations of landmarks from their centroid; Gower [7]) of each cranial component by using a linear model. Using cross-validations, we propose a new method to assess pediatric cranial skeletal age that fulfills the specific demands of forensic practice, as defined by Ritz-Timme et al. [12].

Materials and methods

Material

This study used a cross-sectional sample of CT scans registered from 73 non-adult female subjects ranging in age from 3 days to 17.67 years (212 months) and 54 non-adult male subjects ranging in age from 3 to 16.5 years (198 months; Table 1). The chronological age was calculated by subtracting the date of birth from the date of the CT. This sample is based on a review of CTs performed over the period 2002–2004 in the Neuroradiology Unit of the Clinique Pasteur, Toulouse (France). All patients underwent CTs because of trauma, impacted and residual teeth, inflammation in the maxillary sinuses, or neonatal distress. Patients were selected if they were reviewed as anatomically normal independently by two radiologists and were considered to exhibit normal skeletal age. This data cleansing consisted to eliminate approximately 10% of the total sample available, a proportion which corresponded to cases with severe asymmetric facial and/or basicranial deformities. The CT data were anonymous and numbered (with each number entered in an Excel file with exclusively the date of birth, the date of the CT, and the sex). Our study was ethically approved by a French institutional board (Commission Consultative de Protection des Personnes pour la Recherche Biomédicale).

Table 1 Age and sex distribution of the sample studied (age category “0–1” is from birth to the first anniversary)

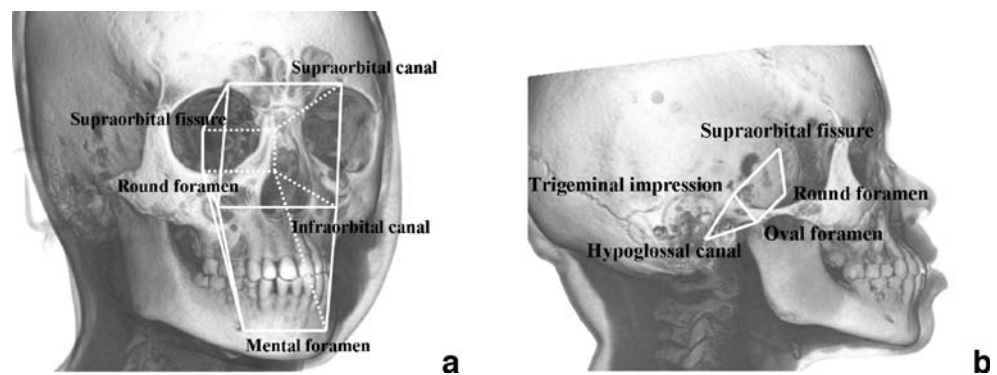
One-year age categories (in years)	Number of females	Number of males	Total
0–1	8	6	14
1–2	0	1	1
2–3	0	2	2
3–4	1	3	4
4–5	2	1	3
5–6	0	0	0
6–7	0	0	0
7–8	3	0	3
8–9	2	6	8
9–10	2	4	6
10–11	9	5	14
11–12	6	7	13
12–13	8	7	15
13–14	10	5	15
14–15	10	2	12
15–16	7	2	9
16–17	1	3	4
17–18	4	0	4

Landmarks and wire frames

The anatomical locations of bilateral skeletal height landmarks were selected on CTs with their Cartesian 3D coordinates (using “Gamme Cépha” © <http://cepha.free.fr/gammecepha.php>): (1) the anterior opening of the supra-orbital canal demarcates anteriorly the anterior fossa, (2) the supraorbital fissure, at the level of the optic foramen, is very close to the posterior margin of the anterior fossa and to the superior/medial part of the middle fossa, the round (3) and oval (4) foramina located, respectively, on the anterior/medial, and inferior parts of the middle fossa, (5) the trigeminal impression, at the anterior part of the posterior fossa, (6) the middle of hypoglossal canal, above and lateral to the foramen magnum, (7) the anterior opening of the infraorbital canal, (8) the mental foramen. All these landmarks are located on the main pathways of the trigeminal and hypoglossal nerves and are easily seen in axial CTs. We distinguished two 3D landmark configurations, or wire frames, each representing a major cranial component: (1) The facial wire frame (Fig. 1a) connects all landmarks, except the hypoglossal canal, the trigeminal impression, and the oval foramen, (2) the basicranial wire frame (Fig. 1b) connects all landmarks, except those located on the anterior face (supraorbital, infraorbital and mental). The two wire frames are separated by the plane joining the two infra orbital fissures and the two round foramina.

To quantify the intra-observer and inter-observer agreement during the selection of landmarks, two examiners selected all the landmarks twice on 30 CTs. Differences

Fig. 1 Anatomical landmarks used for the assessment of the three dimensional centroid size of the face (a) and the basicranial skeleton (b)



between pairs of 3D landmark coordinate sets always represented less than 5% of coordinate mean values.

Geometric morphometrics

For each individual and each wire frame, the centroid size was calculated by using Morphologika © (<http://www.york.ac.uk/res/fme/resources/software.htm>). The centroid size is a measure of size uncorrelated with all pure shape changes [1].

Linear model and age assessment

The skeletal age was calculated using a conventional least square linear regression, which predicts the dependence of the chronological age on the centroid size. The residual was measured as the difference between the known chronological age and skeletal age. The standard error of the estimates calculated using 95% confidence limits was used as an overall indication of the accuracy.

We computed the linear function between chronologic age and centroid size by using the leave one out technique. As it is well established that girls mature, in terms of skeletal age, at a different rate than boys do, the function is trained separately not only on each wire frame but also on each sex subset of the database.

To detect a possible systematic age dependent error in the age estimations, we distinguished results between children younger or older than 10 years of age. For each of our four trials (girls and boys, before and after 10 years) and any individual tested, each skeletal age assessment was compared to the chronological age and subsequently assigned to a 1-year interval of accuracy, ranging from -6 to +6 years (-72 to +72 months; e.g., an accuracy falling between -72 and -60 months, between -60 and -48 months...etc). This approach allowed the study of the distribution of the reliability across 12 categories of accuracies. The maximum deviation of ± 1 year from the chronological age (represented by the following two categories: between -1 and 0 years, or between 0 and 1 year) corresponds to the highest accuracy, i.e., better agreement between age assessment and the chronological age. The percentages of individuals classified

into these categories represent a measure of the reliability associated with the highest accuracy.

Results

The smaller standard errors (at the 95% confidence level) were obtained for the facial wire frame of children older than 10 years of age: girls (± 1.27 years), boys (± 1.37 years). A comparison of the mean accuracy (the mean difference between the known chronological age and the skeletal age) between the various trials (e.g., facial wire frame of girls before 120 months of age...) revealed that the estimations were significantly and systematically (i.e., for both wire frames, in girls and in boys) more accurate when applied to individuals older than 10 years of age (Supplementary material). The method based on the facial wire frame showed a substantial and systematic (i.e., in girls and in boys, before and after 10 years of age) improvement in mean accuracy over the basicranial method. The percentage of the highest accuracy (i.e., a maximum deviation of ± 1 year from the chronological age) did not differ significantly for girls, before (Fig. 2a) and after (Fig. 2b) 10 years, neither for the facial wire (44% and 40% respectively), nor for the basicranial frames (34 and 36%, respectively). For boys, this reliability (or percentage of the highest accuracy) did not differ significantly either before (Fig. 2c) or after (Fig. 2d) 10 years, for the basicranial wire frame (30 and 32%, respectively) only. For the facial wire frame of boys, the percentage of the highest accuracy was significantly higher after (52%) than before (18%) 10 years of age.

Most trials overestimate age by at least 1 year, except in older male samples in which the age is underestimated by only 0.17 (± 1.37) year and 0.37 (± 1.52) year, respectively, for the facial and basicranial wire frames (Supplementary material). To detect possible systematic age-dependent errors, we also examined the distribution of the reliabilities across the 12 categories of accuracies, each representing a 1-year interval. For boys (Fig. 2c and d), estimated ages were generally too old (Fig. 2c: 74 and 83%, respectively, for the facial and basicranial wire frames) for “young”

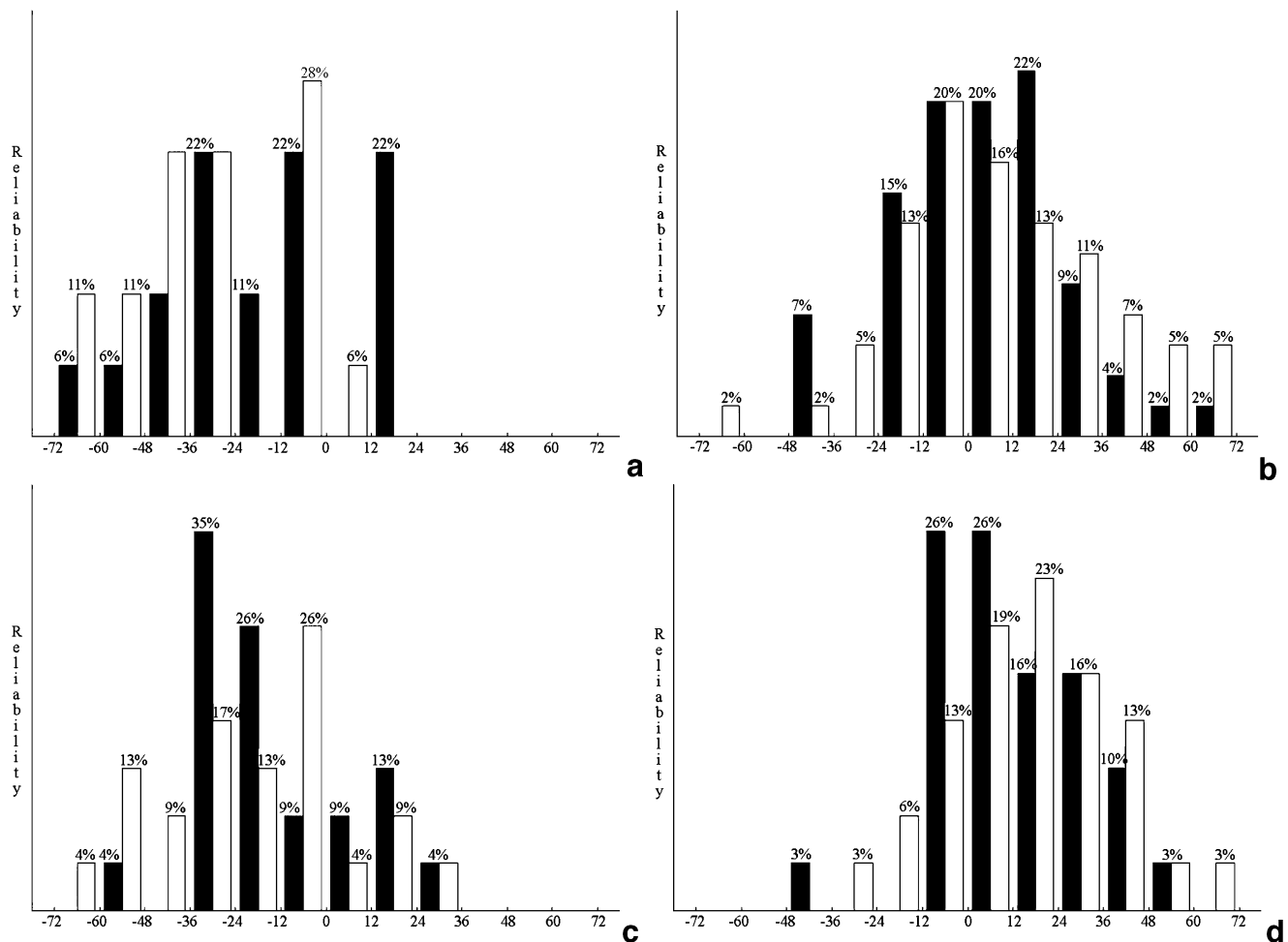


Fig. 2 Distributions of the reliabilities across the 12 categories of accuracies, each representing a 1-year interval: **a** is for the girls before 10 years of age; **b** is for the girls after 10 years of age; **c** is for the boys

individuals (i.e., younger than 10 years of age) and too young (Fig. 2d: 71 and 78%, respectively, for the facial and basicranial wire frames) for older individuals (i.e., older than 10 years of age). This effect is well known and is called “regression toward the mean.” For girls, estimated ages were generally too old (Fig. 2a: 78 and 94%, respectively, for the facial and basicranial wire frames) for “young” individuals. However, for older girls (Fig. 2b) and for both wire frames, there was more balance between overestimation (42%) and underestimation (58%).

Discussion

Ritz-Timme et al. [12] reviewed the quality standards of the methods of pediatric age estimation based on the radiological examination of dental and skeletal development. They noted that these methods, when applied between 0 and 18 years, showed a standard error ranging from 0.5 to 2.5 years (based on dental development) and from 0.5 to 2 years (based on skeletal development). A standard error

before 10 years of age; **d** is for the boys after 10 years of age. Results for the facial and basicranial wire frames are indicated, respectively, in black and in white

of 2 years means that 95% confidence intervals of about ± 4 years or even more [6] have to be considered in age estimation. In our study, all the standard errors are given at the 95% confidence level and were systematically lower or equal to 2.1 years for the facial wire frame (ranging from 1.27 to 2.09; [Supplementary material](#)). For the basicranial wire frame, these values ranged from 1.52 to 2.64 years. Therefore, we regard our method of age estimation to be more accurate when it is based on 3D facial size changes only. Moreover, we note that for the facial wire frame as for the basicranial one, when sample size increases, the accuracy increases significantly ([Supplementary material](#)). For example, we believe that the improvement of accuracy noticed, in both girls and boys, after 10 years and for the facial wire frame is, at least in part, due to the increase in sample size ([Supplementary material](#)). Indeed, as presented in our results, the percentage of the highest accuracy did not differ significantly for the wire frame of girls, before (Fig. 2a) and after (Fig. 2b) 10 years of age (44 and 40%, respectively). These results are interesting, as they demonstrate that our method is not necessarily less accurate with

increasing age, contrary to most of the methods of pediatric age estimation developed so far [12]. This result of a better accuracy with greater age, when we use the centroid size of the facial skeleton, might also be due to the fact that, in contrast to the cranial vault and the basicranium which growth slows considerably after about the third or fourth year of childhood (in association with brain growth), the facial skeleton continues to enlarge markedly for many more years until adolescence [4]. However, to confirm a real independence of age on the accuracy when applying our method, we need to develop more trials with increased sample sizes and other age categories. An additional number of cases is also needed to increase the evidential proof of our method.

Besides accuracy and the age range applicability of our method, other questions must be addressed. The genetic origin represents a potential factor of influence on skeletal maturation. However, even with genetic markers, the genetic identity is difficult to define. Our sample was composed of individuals of various geographic origins (France and North Africa) living in the south of France (mainly in the area of Toulouse). As this sampling represents only one of the four major genetic groups (Caucasoids), we cannot assess the influence of the genetic origin on the quality of our method. Our method can be recommended for cadavers or human remains representing historic and archaeological cases. In living individuals, when no other skeletal method provides a sufficient accuracy and/or reliability of age estimation, as the different tissues and organs have varying sensitivity to radiation exposure, the actual dose to the face from an X-ray (CT) procedure should be reduced to a minimum.

Conclusions

The combination of geometric morphometric methods, growth studies, and age predictions is new, and to our knowledge, there are no case studies so far. Moreover, with respect to methods devised for adolescents (mainly based on the changing radiological appearance of epiphyses), few attempts have been made to develop tools for skeletal age assessment based on the examination of the skull. In this paper, we demonstrate that geometric morphometrics represent a promising addition to the approaches currently used in forensics for the assessment of skeletal age in non-adults. The main advantages of our method (over dental ones) are that it is applicable from early postnatal age to the end of adolescence and, second, that it is applicable to cranial remains and, consequently, increases the variety of age-

related structures theoretically available to overcome the problem of biological variation of single skeletal features.

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