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Facial Asymmetry of Italian Children: A Cross-Sectional Analysis of Three-Dimensional Stereophotogrammetric Reference Values

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Abstract: Reference data on the asymmetry of facial thirds of children is still scarce, although it can offer meaningful comparative information for clinical studies. This study aims to provide reference data on the facial asymmetry of Italian children using a 3D analysis of facial thirds divided according to the trigeminal nerve distribution (upper, middle, and lower). A 3D surface-based approach was conducted on the digital models of the faces of 135 children (74 M, 61 F), acquired by stereophotogrammetry. In addition to sex, two different age classes were analyzed (4–8 years and 9–12 years). For each facial third, the asymmetry was expressed as root-mean-square distance (RMS) by calculating the point-to-point distances between the original and the reflected 3D models. A 3-way ANOVA test verified significant differences between the two sexes, the two age classes, and the three facial thirds (p-value < 0.05), and also their interaction. Significant differences were found between the sexes (females were more symmetric, $p = 0.005$) and the two age groups (younger were more symmetric $p < 0.001$). According to Tukey's HSD post-hoc test, among the thirds, the middle one proved to be significantly more symmetrical ($p < 0.001$). No significant interaction impacting the asymmetry was found when the main factors were considered in any combination. Reference data on the "normal" facial asymmetry of Italian children was provided for further clinical purposes. Normal children have low average RMS values (0.30–0.51 mm) and younger, in particular females, proved more symmetrical than older children, while among the facial surfaces, the middle proved most symmetrical in both sexes, although with little clinical relevance. Since there is no consensus on the amount of symmetry deemed clinically acceptable, further studies on larger randomized samples are auspicial.

Keywords: facial asymmetry; three-dimensional imaging; analysis of variance; 3D facial analysis; reference values; anthropometry; pediatric population; stereophotogrammetry

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1. Introduction

The term symmetry, in anatomy, refers to the perfect bilateral correspondence of anatomical structures in size, shape, and position relative to an axis [1]. In particular, the symmetry of the human face can be considered theoretical [2] given that asymmetries are intrinsic to any face and body part of both healthy and non-healthy individuals [3,4]. Asymmetry in the craniofacial complex can range from barely noticeable to very evident differences between the right and the left facial halves and thirds, as well as between paired

facial structures. In these terms, asymmetry consists of differences in dimensions, angles, surfaces, volumes, and spatial positions, and it may involve hard tissues or be limited to overlying soft tissues. In both cases, the objective assessment of asymmetry is crucial because it can provide clues to several biomedical purposes, such as diagnostic, clinical, and surgical ones.

The definition of 'normal asymmetry' of the face and its reference amounts are important for several reasons [5,6]. The assessment of facial asymmetry is a significant part of the clinical examination. Beyond a threshold level of asymmetry, facial features become dysmorphic [4] and, if properly identified by clinicians, can be used in the correct diagnosis of a specific syndrome or pathological condition. Correct assessment of facial asymmetry is not only valuable for clinical examination but also for the planning and outcomes of surgery and orthodontic treatments [7]. It seems clear that our understanding of facial asymmetry involves many objectives, such as the definition of normal morphology, the appreciation of malformations and dysmorphologies, the evaluation of growth, and the assessment of treatments. Many are the factors leading to facial asymmetry, including genetic and congenital conditions, facial traumas, infections, and damage to facial/cranial nerves. Moreover, in children, facial asymmetry can be affected by different factors, such as chewing and sucking habits and different teeth eruption stages. The etiology of facial asymmetry still remains unclarified, although idiopathic asymmetries are common in the overall population and, for this reason, they are also termed as "asymmetry of development", even if not found at an early age but appear gradually throughout craniofacial development [8].

The proper diagnosis of facial asymmetry through clinical examination is often complicated. The correct evaluation of facial asymmetry, regardless of being general or limited to specific areas and structures, should involve all three spatial planes and rely on three-dimensional methods (3D) instead of two-dimensional images in order to avoid loss of information or the collection of incomplete or erroneous data. In fact, traditionally, radiological examinations, cephalometric analyses, and photography have always represented the golden standard for the evaluation of facial asymmetry, despite the fact that converting 3D structures into 2D ones inevitably causes distortions, errors, and loss of depth data [3,9]. Only recently have 3D imaging methods started to be applied in the analysis of facial asymmetry [2,10–12]. The new era of 3D surface-based techniques (e.g., stereophotogrammetry and laser scanning) opened the way for the evaluation of facial soft tissues from innovative perspectives, offering the opportunity to analyze facial asymmetry more comprehensively. However, regardless of the method used for assessing facial asymmetry, its comprehensive definition still lacks in the literature, and its amount has been sparsely investigated so far [13].

Unfortunately, different approaches have been used for assessing facial asymmetry and none are universally accepted by the scientific community. Additionally, no quantified data recognized as a valid threshold for defining boundaries of 'normal asymmetry' are available. The assessment of facial asymmetries through 3D imaging systems allows both facial analyses based on landmarks for linear and angular distances, as well as the investigation of the whole facial surface or facial thirds, with the latter describing more accurately the localization of asymmetry [3]. In particular, the novel 3D methods based on original mirror alignment algorithms proved to be promising. They can highlight differences in the morphological surface of two registered digital models of the face (for instance, right and left facial thirds), providing insights into the amount and localization of facial asymmetry, including its direction with positive and negative values and related distances, and thus giving a solid basis for diagnostic and therapeutic purposes [14]. This kind of approach has been already applied in clinical studies to provide data on the asymmetry of facial thirds of healthy subjects and patients by using the iterative closest point (ICP) algorithm for registering and overlapping the two surfaces (original mirrored) to superimpose [14–19]. In addition, there are several indicators that can be used for quantifying the degree of facial asymmetry when original and mirrored facial models are registered and superimposed: root-mean-square (RMS), mean absolute deviation (MAD),

and mean signed distance (MSD) [14,20,21]. Among these, RMS proved to be the most suitable, highly repeatable, and accurate [20].

All in all, it seems that no consensus exists on how to assess facial asymmetry, and the data in the literature are still non-homogenous, which makes it very difficult for any direct comparisons. Indeed, reference data on different growth and asymmetry patterns in facial thirds of healthy pediatric populations are generally still scarce and not yet provided through common 3D approaches, although they could offer meaningful comparative data for clinical studies on patients affected by oral maxillofacial and syndromic conditions.

In this study, we investigated the amount of facial asymmetry in a healthy pediatric population through a validated 3D method based on the superimposition of original and mirrored 3D facial images and the calculation of related RMS distance values. We calculated the RMS values for facial thirds (upper third (UT), middle third (MT) and lower third (LT)) to provide normal ranges of asymmetry as the reference data of healthy children for comparative studies.

2. Materials and Methods

2.1. Sample

The study involved 135 Caucasian children aged 4 to 12 years old of both sexes (74 males, 61 females). Children with a previous history of craniofacial traumas, congenital anomalies, or craniofacial surgery were excluded from the study. The sample, in addition to sex, was also subdivided into two age groups: 4–8 years old and 9–12 years old as age classes being possibly representative of different dentition stages [22]. The number of individuals for each subgroup (according to sex and age class) is summarized in Table 1:

Table 1. Number of individuals according to sex and age.

	Males	Females	Total
4–8 (years)	35	25	60
9–12 (years)	39	36	75
Total	74	61	135

The study is part of a greater project focusing on the evaluation of facial morphology which received the approval of the local ethical committee at the University of Milan (26 March 2014; n° 92/14). In addition, the study was conducted in accordance with the Declaration of Helsinki [23], and informed consent was obtained and signed by the parents/legal tutors of all participants. Verbal consent was obtained by each child, too.

2.2. Image Acquisition

The 3D facial stereophotogrammetric models of the involved children were acquired using the VECTRA M3 (Canfield Scientific Inc., Fairfield, NJ, USA), and VECTRA H1 (Canfield Scientific Inc., Fairfield, NJ, USA) stereophotogrammetric instruments, both of which allow the scanning of faces in a fast and non-invasive way with high comparable accuracy, reproducibility, and resolution [24]. The two instruments used routinely in our lab (LAFAS; Laboratory of Functional Anatomy of Stomatognathic system) proved to be comparable and equivalent, as suggested by previous studies [25,26].

Prior to the acquisition, soft tissue facial landmarks were marked on the person's face, as shown in Figure 1, according to an internal protocol developed by Ferrario et al. [27] that was already tested and validated [28].

The acquisition was performed with the child seated facing the instrument and with a neutral facial expression, closed mouth, and looking at the horizon. After acquiring the scan, the 3D analysis was performed with the software associated with the VECTRA device, namely the VECTRA Analysis Module (VAM); Canfield Scientific Inc., Fairfield, NJ, USA).

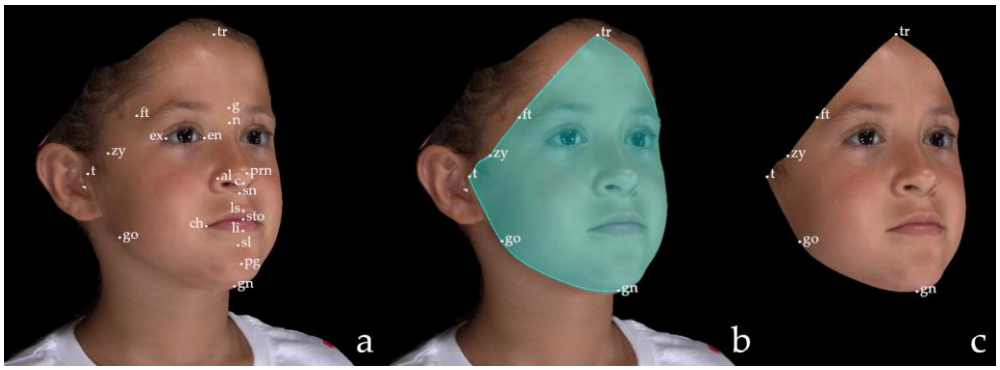

Figure 1. (**a**) Example of a 3D facial model where all the landmarks used for the entire protocol (selection of the facial area of interest (FAI) and facial thirds (ROIs)) are depicted. Only the landmarks of the mid-axis and right side are shown; (**b**) selection of the facial area of interest (FAI) using unilateral (trichion (tr); gnathion (gn)) and bilateral landmarks (frontotemporale (ft); zygion (zy); tragion (t); gonion (go)); (**c**) selected FAI from which the facial thirds will be selected.

2.3. Asymmetry Quantification

The whole protocol of landmark digitization and asymmetry quantification was performed using VAM software (version 5.3.1). For the entire procedure on the 3D facial models, we performed our internal protocol, which was already validated and used in previous studies [14,17,18]. This validated landmark-based protocol consists of several steps. First, we selected the entire face, namely the facial area of interest (FAI), by using the more external anthropometric landmarks specified in Table 2 (Figure 1). Next, we selected the upper, middle, and lower facial third (regions of interest, ROIs) from each side of the FAI based on the landmarks listed in Table 2 (Figure 2). Mirroring of the selected left ROI and its consecutive superimposition on the corresponding original ROI (the right ROI) was then performed (Figure 3).

Because our protocol is landmark-based, no planes were used neither for selecting the FAI nor for isolating the ROIs.

Among the steps required for performing the entire procedure, the digitization of the facial landmarks, whether for FAI or ROI selection, is the only operator-dependent step that, however, proved repeatable and reproducible in previous studies [28,29]. On the contrary, once the landmarks are positioned by the operator, the following selection of the FAI and the ROI is automatically executed by the software in a repeatable and operator-independent way, as proved by Codari et al. [14].

Table 2. Landmarks used for the selection of ROIs (regions of interest) to superimpose [14].

Surface	Landmarks
Facial area of interest (FAI)	trichion (tr); frontotemporale (ft); zygion (zy); tragion (t); gonion (go); gnathion (gn)
Upper third (UT)	trichion (tr); glabella (g); nasion (n); pronasale (prn); columella (c); alare (al); endocanthion (en); exocanthion (ex); frontotemporale (ft)
Middle third (MT)	columella (c); subnasale (sn); labiale superius (ls); stomion (sto); chelion (ch); zygion (zy); frontotemporale (ft); exocanthion (ex); endocanthion (en); alare (al)
Lower third (LT)	stomion (sto); labiale inferius (li); sublabiale (sl); pogonion (pg); gnathion (gn); gonion (go); tragion (t); zygion (zy); cheilion (ch)

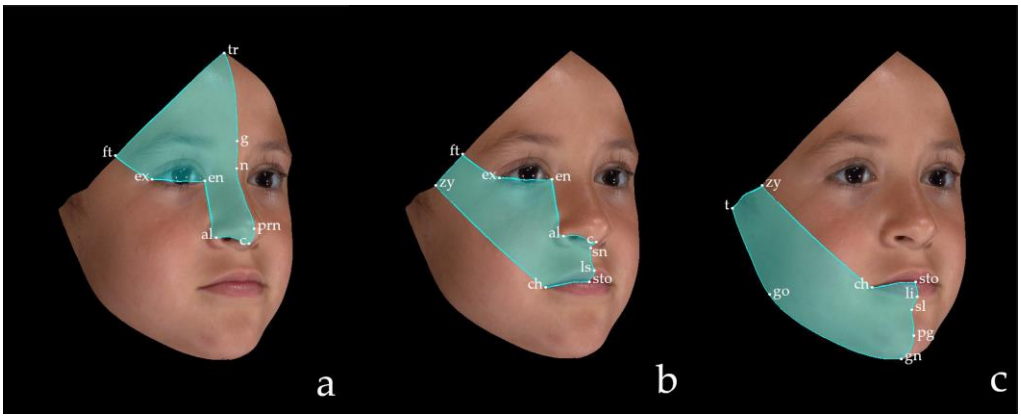

Figure 2. Selection of the three facial thirds (ROIs) on the right side of the FAI: (**a**) upper facial third (UT); (**b**) middle facial third (MT); (**c**) lower facial third (LT).

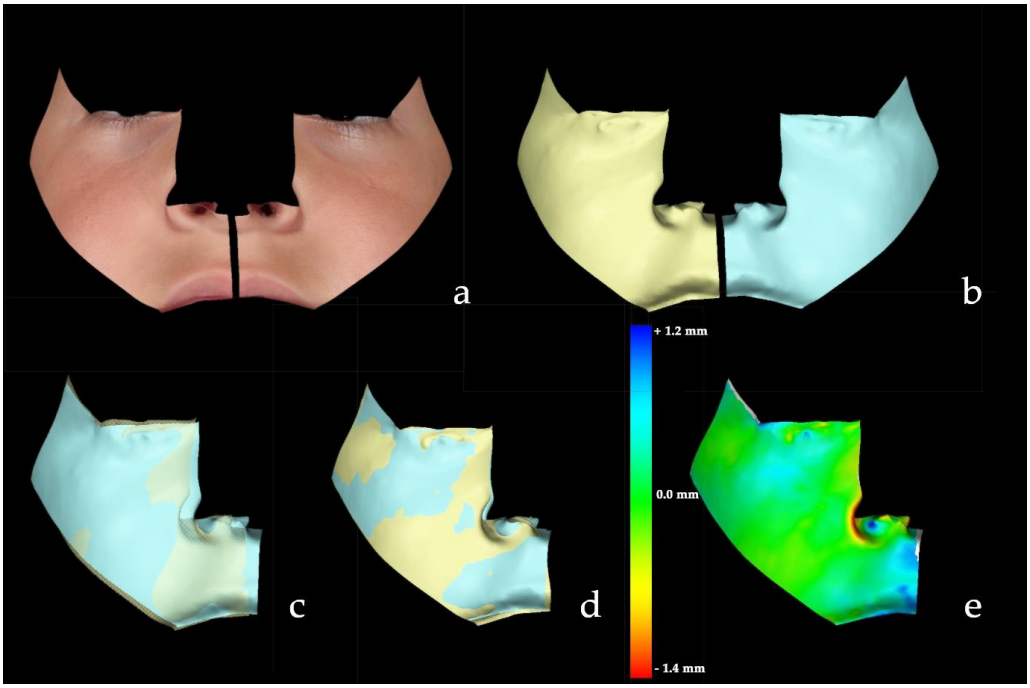

Figure 3. Protocol for the calculation of the asymmetry (RMS) showed for one facial third only (middle third; MT). (**a**,**b**) Right and left surfaces under evaluation, in b the right side is colored in light blue and the left side in light green; (**c**) mirroring of the left side; (**d**) automatic point-to-point closest distance superimposition of the left side over the right side; (**e**) color code map for the local distances between the original and mirrored side of the face.

The FAI corresponds to the surface encompassed by the 10 external facial anthropometric landmarks (trichion, frontotemporale, zygion, tragion, gonion, and gnathion) (Figure 1). This step is particularly important because allows discarding the regions that may affect the quantification of asymmetry, such as the hair and neck regions, and to obtain the model from which the three bilateral facial thirds are selected. Consequently, according to the territories of innervation of the trigeminal nerve branches, from both sides of the FAI, the facial third ROIs (upper UT, middle MT, and lower LT) are selected using the anatomical landmarks listed in Table 2 and depicted in Figure 2.

VAM software was also used for automatically quantifying the asymmetry among the two bilateral facial thirds. The original left ROI, once selected, was mirrored and superimposed on the corresponding selected right ROI (Figure 3). The superimposition was automatically performed by the software exploiting the point-to-point closest distance

between the two surfaces (registration of the left surface over the right mirrored surface), and the RMS distance value was calculated for each superimposition performed (Figure 3). RMS values that equal 0 attest to a perfect "correspondence" and thus a perfect symmetry; the higher the RMS value, the more asymmetrical the two superimposed bilateral surfaces are.

The intra-operator and inter-operator reliability were not assessed in the present study since the only operator-dependent step of the protocol (the digitalization of anthropometric landmarks) has been already tested in literature [27,28] and in samples including individuals of pediatric age [29]. In addition, the entire procedure (including both the operator-independent and operator-dependent steps) has already proved highly reliable in adults, with Bland–Altman repeatability coefficients ranging from 0.9% to 1.7% [14].

2.4. Statistical Analysis

Descriptive statistics of the RMS distance values calculated for each superimposition of upper thirds, middle thirds, and lower thirds were obtained, and the outliers detected through the interquartile method were excluded from the analysis [30].

The normality of data distribution was tested using the Shapiro–Wilk test. RMS values of all facial regions of interest in all subgroups were positively skewed; thus, a logarithmic ($\log_{10}$) transformation of the data was performed to obtain normal distributions. Three-way ANOVA (analysis of variance) was performed on the normalized data to compare RMS distance values between males and females, age classes, and facial parts, as well as the first-degree interactions among these independent variables. The Bonferroni correction was applied and post-hoc analyses were performed using Tukey's HSD test. The statistical analysis was performed using SPSS version 28 (IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY, USA, IBM Corp.), and the significance was set to a p-value of <0.05. For significant effects and interactions, the partial η^2 (eta squared) value was calculated to estimate the effect size; that is, the practical importance of the statistically significant differences. According to Ben-Shachar et al., partial η^2 values lower than 0.02 are considered very small, between 0.02 and 0.13, small, between 0.13 and 0.26, medium, and between 0.26 and 1.00, large [31].

3. Results

In this study, a total of 135 children (74 males, 61 females) included in two different age groups (4–8 years old, and 9–12 years) were analyzed. The younger group included 60 children (35 males and 25 females), while the older group consisted of 75 subjects (39 males and 36 females).

The descriptive statistics (mean, standard deviation, and range of minimum and maximum values) of RMS distance values of each subgroup (divided by age and sex) are reported in Table 3 for each facial third.

The three-way ANOVA analysis revealed significant differences for each main factor but with small partial eta squared values (Table 4). Males proved statistically significant higher RMS distance values (mean, 0.42 mm) than females (mean, 0.40 mm; $p = 0.005$; Table 4). Older children were more asymmetrical (smaller RMS distance, mean, 0.42 mm) than younger children (mean, 0.39 mm; $p < 0.001$).

Finally, statistically significant differences in asymmetry were found among the analyzed facial thirds ($p < 0.001$) (Table 4). The middle third showed the lowest mean RMS distance value (0.34 mm), while the lower and upper thirds showed the same mean RMS values (0.39 mm). In particular, as verified by Tukey's HSD post-hoc test, significant differences at $p < 0.001$ were found between the middle and the upper and lower third. Only the upper and lower thirds were not significantly different from each other ($p = 0.53$). The partial eta squared value computed for the facial thirds was small, even though it was the largest one of the ANOVA test. No statistically significant interactions were found between the main factors, as reported in Table 4. RMS distance values separately for each facial third, age class, and sex are presented as a boxplot in Figure 4.

Table 3. Descriptive statistics (mean, standard deviation, and minimum and maximum RMS range) of asymmetry of the diverse facial thirds expressed in RMS values for each age group divided by sex.

Facial Thirds	RMS (mm)	Male		Female	
		4–8 y (*N*)	9–12 y (*N*)	4–8 y (*N*)	9–12 y (*N*)
Upper third (UT)	Mean (mm)	0.39 (30 *)	0.41 (35)	0.34 (24)	0.41 (35)
	Standard deviation (mm)	0.05	0.09	0.07	0.10
	Range (Min–Max)	0.29–0.50	0.28–0.69	0.21–0.45	0.25–0.63
Middle third (MT)	Mean (mm)	0.33 (34)	0.37 (38)	0.30 (23)	0.36 (36)
	Standard deviation (mm)	0.07	0.10	0.05	0.08
	Range (Min–Max)	0.21–0.50	0.24–0.59	0.23–0.39	0.23–0.57
Lower third (LT)	Mean (mm)	0.38 (33)	0.42 (39)	0.36 (25)	0.38 (36)
	Standard deviation (mm)	0.10	0.11	0.12	0.09
	Range (Min–Max)	0.21–0.58	0.23–0.71	0.18–0.56	0.23–0.57

* Parentheses indicate the total number of 3D models analyzed, excluding outliers.

Table 4. Results from the three-way ANOVA test for all the main effects and first-degree interactions.

	F	*p*	Partial Eta Squared
Sex	8.04	0.005 *	0.021
Age	23.22	<0.001 *	0.058
Facial Thirds	12.17	<0.001 *	0.061
Sex × Age	1.54	0.22	
Sex × Facial Thirds	0.10	0.90	
Age × Facial Thirds	0.39	0.68	
Sex × Age × Facial Thirds	1.34	0.26	

* Statistically significant at $p < 0.05$.

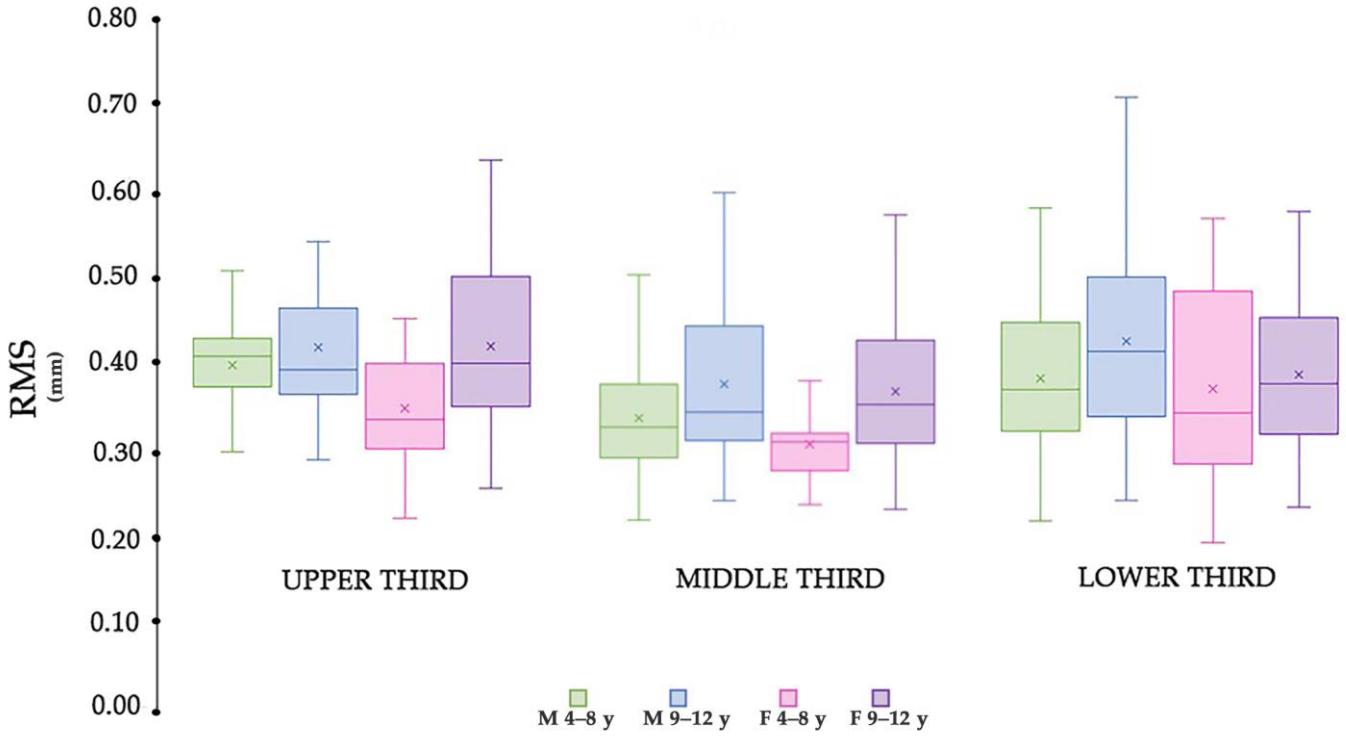

Figure 4. Boxplot illustrating the distribution of the RMS distance values for every facial region of interest (ROI) in the defined subgroups. Within each box, horizontal lines denote median values; cross marks indicate mean values; boxes extend from the 25th to the 75th percentile of each group's distribution; vertical lines represent the lower and upper quartile with the minimum and maximum values (represented by the small horizontal lines).

4. Discussion

Defining univocally normal facial asymmetry represents an important aim with some difficulties, often due to the choice of which method is used for its calculation, as well as the potential confounders related to ethnicity, sex, and age. Nonetheless, this objective needs to be addressed, as assessing facial asymmetry is crucial for many purposes that go from clinical examination to the planning and evaluation of surgical and orthodontic treatments involving the stomatognathic system.

Among the many methods proposed in the literature, those implementing 3D techniques overcome some of the important limitations deriving from the use of 2D methods [3]. The former includes methods based on the manual identification of landmarks [11,27] and automated measurements [32], calculation of asymmetries through the use of a plane of symmetry [33], and registration of a 3D surface with the related mirrored version [6,10,12,14]. Especially, the latter proved to be particularly encouraging since it does not require any plane of symmetry and provides dense shape information across the entire facial surface [34]. The surface registration-based methods have been recently validated for quantifying the amount of facial asymmetry, which is mainly expressed as the average magnitude or root-mean-square distance existing between two superimposed regions of interest [14,35–38]. Nonetheless, in the literature, there is still no consensus neither on which specific method to use for assessing asymmetry nor on the extent of normal asymmetry to refer to for clinical comparisons and research.

Our purpose was to originate reference values for facial asymmetry of normal/healthy children to be used in the future as potential comparative data for those clinical studies and examinations that follow the same protocol and approach. We gathered such data with the 3D method based on the ICP algorithm superimposition of original mirrored digital facial models. This method allows one to collect data expressed as RMS point-to-point distance whose suitability and accuracy were already proved in the literature and considered higher than those obtained by other indicators of the degree of facial asymmetry [20,39].

Overall, our study found that both sex and age have an independent effect on facial asymmetry during growth. Males proved to have more significant asymmetries than females, which is consistent with the results of previous studies [6,40–42]. Sajid et al. [40] suggested that asymmetry is slightly more significantly pronounced in males than in females of diverse ethnicities (European, African, Asian, and Hispanic) for 25 out of the 28 lateral facial linear distances verified. Using the original mirror superimposition procedure, Skomina et al. [41] found that the whole face of females was more symmetrical when compared with that of males, although it was significantly different only for individuals who were over 70 years old. Again, with a similar 3D approach, Djordjevic et al. [6] found in a 15-year-old adolescent population that the faces of males were significantly less symmetrical than those of females of the same age, without clinically relevant differences. Finally, Özener et al. [42] reported significant differences in paired lateral facial distances between the two sexes in two Turkish populations with diverse socioeconomic backgrounds, which might determine a different level of environmental instability. The extent of facial asymmetry was found higher for males of both populations regardless of the level of developmental stress.

Although any direct comparison with data reported in the literature on the extent of facial asymmetry is difficult given the diverse nature of each research (namely methods used, asymmetry indicators provided, and characteristics of the population), in general, the degree of asymmetry was always detected to be greater in males than in females, even in most of the studies that found no statistically significant differences [2,43,44]. In other words, the lack of a complete statistical agreement with other studies might lay in the use of a more sensitive 3D analysis used in the present study, which allowed us to detect even minimal differences with minor practical importance, as testified by the very small partial eta squared values. Nonetheless, although minimal, regardless age, ethnicity, and level of environmental instability, a greater extent of asymmetry in males was reported by all the studies investigating facial asymmetry. One hypothesis behind the greater extent of facial

asymmetry in males could be related to sex hormones [45], whose prenatal levels might play a crucial role in the development of body morphology including facial asymmetries [46,47]. Thornhill and Moller [48] suggested that facial asymmetries appear very early in human development as the result of development instabilities. Graham [45] suggested that because of the presence of prenatal testosterone, males may have a lower ability to respond to stresses, causing instability in the development and thus, asymmetry. In fact, growing evidence highlighted the immunosuppressive action of testosterone [49–51] and its inhibitory effect on stress-induced HPA activation [52,53]. Ergo, high levels of testosterone would be expected to increase the risk for the asymmetric developmental trajectory, as suggested by many studies focusing on putative markers of testosterone and fluctuating asymmetry of the face and body [46,54,55]. Indeed, Fink et al. [46] reported a significant indirect correlation between prenatal testosterone (deduced from D2:D4, i.e., the ratio of the length of the second and fourth fingers) and facial asymmetry. However, no direct link between the level of fetal testosterone and D2:D4 has been proved so far, and the lack of experimental evidence does not support a direct link between testosterone and facial asymmetry [56]. Certainly, whether the greater extent of facial asymmetry detected in males in the current study reflects prenatal levels of testosterone or calls on other factors is still to be verified in-depth and, above all, to be supported by solid scientific data.

In our study, we also found a significant influence of age on facial asymmetry. Once more, similarly to the influence of sex, given the very small partial eta squared value, we can state that older children present slightly more facial asymmetries but with minimal practical (clinical) relevance when compared with younger ones. However, recent findings revealed a relationship between age and facial asymmetry [44], with the latter as a function of age [57]. Particularly, Linden et al. [44] found a statistically significant positive correlation between increasing age and facial asymmetry in a population of 191 individuals with an age ranging from 0.3 to 88 years. Their population was analyzed with the 3D original mirror best-fit alignment method and the asymmetry values were calculated by the root-mean-square deviation difference between the original and the reflected image. The authors reported that the RMSD of facial asymmetry clustered between 0.4 and 1.3 mm in the whole population and suggested that asymmetry increased with age across all facial thirds but particularly in the lower two-thirds, with an increased root-mean-square deviation of 0.06 mm for each decade of life. We can consider the method used by the authors as very similar to ours, although not without differences concerning the subdivision of facial thirds. Nonetheless, the RMS values here are well-placed in the range of RMSD values provided by Linden et al. [44], and specifically, they collocate very near to the minimum values, partially confirming that asymmetry values in younger children are very low.

Back to the difference we found among the two age classes, although the partial eta squared value is reduced, it could be related to different dentition stages. Indeed, the comparison between our RMS values and those reported for adults (collected and calculated using the same method/protocol) might give some insight into this hypothesis. Children proved more symmetrical with very low mean RMS values ranging from 0.30 mm to 0.51 mm and had a low standard deviation (0.07–0.13 mm) regardless of the type of facial third, sex, and age. In particular, younger females (4–8 years old) showed to be more symmetrical and thus asymmetry could be slightly increased as the mixed dentition appears and permanent teeth start to erupt. Quite the reverse is instead the situation in adolescents and adults over 30 years, namely in subjects with a permanent dentition in completion or one that has already developed. Baserga et al. [17], in fact, reported higher mean RMS distance values for adolescent and adult subjects. RMS values ranged between 0.62 mm and 0.88 mm with a high standard deviation (between 0.12 and 0.35 mm), which brings attention to the possible influence that permanent dentition and/or its variation during aging might play on facial asymmetries of the mid-lower face. Further studies investigating the extent of facial asymmetry differences existing between individuals with deciduous, mixed, or permanent dentition might help to better understand the etiology

of facial asymmetry and also its causing factors since there is currently neither a full understanding nor any agreement.

Finally, no facial third proved perfectly symmetrical demonstrating that, regardless of age and sex, non-pathological facial asymmetries are relatively common in normal populations, as suggested by Shah and Joshi [58]. The three facial thirds were found to significantly differ in asymmetry, and the middle third proved to be the most symmetrical facial region. Contrasting results are reported in the literature about the localization of maximal asymmetry when referring to facial thirds. Farkas and Cheung [59] investigated the extent of asymmetry of six lateral paired projective measurements taken from the face of a large population of Canadian children. In their study, the most common and largest asymmetries were found more often for measurements whose landmarks are localized in the upper face [59], which is partially in accord with our results. In addition to the upper third, we also found the lower facial third as the most asymmetrical. The lower part of the face proved to be more asymmetrical in most of the studies found in the literature, regardless of whether they implemented 2D or 3D methods.

Indeed, many authors stated that measurements involving gonion, as well as 3D facial surfaces including gonion (both representing the lowest part of the face), have greater normal variability [43,60–62]. In particular, the findings presented by Primozic et al. [2,63] are very relevant to our study. The authors reported data on the asymmetry of facial parts in children (12 females and 15 males with a mean age of 5.3 years), which were analyzed using a 3D surface-based approach. However, the analyzed sample was limited to a few subjects, the 3D protocol performed for facial subdivision was different from ours, and the average asymmetry was differently calculated, thus preventing direct comparisons. Although many differences exist between our and their study design, by attempting a possible comparison, we can state that the asymmetrical values reported by the present study are partially overlapping with those reported by Primozic et al. [2,63], who found the lower face to be the most asymmetrical among the three analyzed facial parts.

One possible explanation for the greater extent of asymmetry in the lower face might be found in chewing activity. This assumption may be supported by the fact that most individuals have a preferred side where chewing predominantly occurs [64], thus possibly determining asymmetry of the facial part mainly involved by this habit. Indeed, Heikkinen et al. [65] found that twins with a preferred chewing side had more asymmetric faces than twins with symmetrical chewing. In fact, the chin becomes larger on the side opposite the side where chewing is preferred [65]. Effectively, unilateral chewing burdens the masticatory system unevenly [66], unilaterally strengthening bones and muscles of the preferred chewing side [65,67]. Furthermore, chewing unilaterally also resolves an asymmetrical function of the temporomandibular joint whose movements will be unequally distributed, causing a greater load on the non-preferred chewing side compared to the preferred one [66]. However, if this explanation represents a plausible hypothesis in supporting the results of the majority of studies reporting the lower facial third as the most asymmetrical [4,43,44,60–62], on the contrary, it explains neither the results found by Ercan et al. [68], who reported the middle third as the most asymmetrical in both sexes, nor those reported by Djordjevic et al. [6], who instead found no differences between any parts of the face.

In general, what emerges is a clear absence of consensus, which highlights the need to investigate more in-depth facial asymmetries in age- and gender-specific populations and in different facial parts, but particularly the need to make the data more uniform in the literature. All in all, the methodological approaches, calculation of asymmetry, facial parts subdivision, and characteristics of participants selected for the study are all factors that play a fundamental role in determining all the differences that arise when comparing the existing results of the literature on facial asymmetry. Djordjevic et al. [10] were among the first to suggest the theoretical possibility that diverse software might produce slightly different superimposition results, and if so, different asymmetry values. Analogously, a further point to consider is the subdivision of the face into the so-called facial parts or thirds

(upper, middle, and lower) that are not equivalent in prior studies. For instance, in our lab, we routinely adopt a protocol published in previous surgical studies [14,17,18] which relies on trigeminal innervation and which places most of the eyes and the nose in the upper third. Other researchers divide the face by using planes passing through nasion or glabella and subnasale [44,69], or planes passing through endocanthion and cheilion [2,10,20,70]. We can conjecture that different face subdivisions might determine slightly different results and auspicate for further research exploring this important methodological aspect since no data exists concerning this type of bias.

One last consideration is due to the correspondence between the extent of asymmetry of facial soft tissues and the underlying hard tissues, as the asymmetry of the latter is hypothetically more extended [12,71,72], even though data on their correlation are not provided in the literature yet. This means that asymmetries concerning the underlying hard tissues might not necessarily reflect superficially on facial soft tissues. Assessing asymmetry restoration outcomes indirectly with 3D optical methods could be optimal to avoid the exposure of the patients to X-rays, at least for what concerns its assessment in soft tissues and the satisfaction of patients about the outcomes. Of course, the two techniques are not correspondent since they investigate completely diverse aspects and structures of the stomatognathic system, and no one denies this. In order to provide a better overview of the meaning, interpretation, and etiology of asymmetries of the maxillofacial district, further research also investigating correlations existing between the asymmetry of the two anatomical levels.

Finally, our study is certainly not without limitations. The sample size is the main issue since by subdividing it according to sex and age classes, the resulting subgroups are characterized by a small number of individuals. Indeed, the lack of interaction between the main factors might be dependent on the small sample size, and further studies should help in clarifying this specific aspect. A larger sample size in terms of number, age, and dentition type could help to further confirm the data provided; an orthodontic verification on dentition stage and type could aid in finding a possible correlation between dental growth and asymmetry; and a controlled longitudinal study could possibly support the identification of specific factors that contribute to asymmetry. All these limits and lacks are aspects we wish to work on in the future.

5. Conclusions

We have provided reference values of the facial third asymmetry of healthy/normal children and auspicate that these data could be useful for comparative studies in biomedical and clinical sciences. All investigated children demonstrated a certain degree of asymmetry, but its value has a minimal impact.

No interactions between sex, age, and part of the facial surface exist, although significantly different RMS distance values were found when comparing female with male children, younger with older children, and the diverse facial surfaces between each other.

Future studies are needed for providing systematic data for other populations in order to avoid any speculation and inaccurate conclusions on facial asymmetry and its etiology.

Finally, because 3D systems and their analyses are routinely performed in some clinical, orthodontic, and surgical settings, further investigations are needed in order to verify possible bias deriving from the use of diverse protocols and methodologies, and particularly to be aware of which data one is comparing.

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Data Availability Statement: Due to privacy reasons, data supporting reported results are not publicly available. Requests can be addressed to the corresponding author.

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