

Hard- and soft-tissue symmetry comparison in patients with Class III malocclusion

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Objective: Our aim was to describe hard- and soft-tissue asymmetry in people who have a skeletal Class III malocclusion, and to compare with those without asymmetry. We also performed a regional analysis of a possible correlation between facial soft- and hard-tissue asymmetries. **Methods:** This retrospective study was performed with the use of the computed tomographic scans of 60 subjects. The skeletal Class III subjects were categorized into 2 subgroups: soft-tissue menton deviation ≤ 4 mm ($n = 20$) versus >4 mm ($n = 20$). The Class III groups were compared with a Class I symmetry group ($n = 20$). Hard and soft tissues were segmented into different morphologic areas and deviation calculated. Pearson correlation coefficients were obtained, and 1-way analysis of variance was conducted for statistical analysis. **Results:** The highest deviation in the hard tissues of the Class III asymmetry group was in the corpus region (5.55 ± 3.05 mm), with the second highest in the angulus region (4.70 ± 2.43 mm). The highest average deviation in the soft tissues was seen in the lower cheek (7.04 ± 3.46 mm). In the different study groups, the amounts of asymmetry measured in anatomic structures on the mandible were found to be highly correlated between neighboring structures. **Conclusions:** Clinically and statistically significant differences were found in the anatomic regions located in the middle and lower thirds of the face. There was a medium or high correlation between condyle, coronoid process, ramus, and angulus regions. A low level of correlation was observed between middle face and mandibular asymmetries in hard-tissue upper cheek and lower cheek regions were correlated with different mandibular regions. (Am J Orthod Dentofacial Orthop 2019;155:509-22)

Facial symmetry is defined as anatomic structures being the same distance from an arbitrary reference plane or morphologically similar to each other. Disruption of the symmetry is called asymmetry, and minimal asymmetries are accepted as natural.¹ However, severe asymmetries can affect facial attractiveness and may result in the need for orthodontic-orthognathic treatment.² It is thought that a multifactorial etiology, which includes congenital, developmental, and environmental factors plays an important role in the development of facial asymmetry.² Although asymmetry can occur in almost all anatomic

facial structures at different severity, it is observed more often in the mandibular region and lower third of the face. According to Severt and Proffit,³ 5%, 36%, and 74% of asymmetries were seen on the upper, middle, and lower face, respectively. Also, it was reported that skeletal Class III malocclusions and facial asymmetries were closely related, and skeletal asymmetry is frequently observed with skeletal Class III malocclusion.⁴ The characteristics of the skeletal Class III malocclusion with mandibular prognathism at the sagittal plane have been investigated, but there are not enough studies about the properties of this anomaly on the frontal plane. Maeda et al⁵ reported that only 23% of asymmetries were observed in the maxillary region and that facial asymmetry usually localized in the mandibular corpus and ramus region in Class III patients. Haraguchi et al⁴ mentioned a possible reason for this finding as having a more flexible connection between the mandible and the cranial base compared with the maxilla, and they also stated that the mandible would grow for a longer period time.

Facial asymmetries are usually observed with skeletal Class III malocclusions, and traditional orthognathic

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surgery alternatives (Le Fort I osteotomy, bilateral sagittal split osteotomy, etc.) are frequently preferred in the treatment.^{6,7} Although orthognathic surgery can successfully change the position of bony structures, some local morphologic differences between right and left parts of the face might also affect the perception of the facial esthetics because of continuing minor asymmetries. Patients with facial asymmetries may be dissatisfied after orthognathic surgery because of these local deviations.^{8,9} Therefore, minor asymmetries can be corrected with some less invasive techniques, such as bone contouring and microfat grafting, which are either alternate to or supportive of the current traditional surgical methods. These techniques can be effective and significantly improve the patient's quality of life.^{10,11} But the process requires detailed diagnosis and treatment planning. In Class III anomalies, remaining local asymmetries between the right and left regions of the face, including maxilla or mandible, after orthognathic surgery is important for the prediction of the need of local surgical interventions.

Soft-tissue properties have become important owing to increasing esthetic concerns, which led researchers to investigate the relationship between soft- and hard-tissue symmetry.¹² Hwang et al⁹ reported that asymmetric soft tissues could be observed in individuals with symmetric hard tissues. A recent 3-dimensional (3D) study reported that the external soft tissues were highly correlated with internal skeletal structure morphology.¹³ Localizing the asymmetry and determining the relationship between hard- and soft-tissue asymmetries are important factors for detailed diagnosis and treatment planning. The conventional 2-dimensional (2D) imaging methods are not sufficient in achieving those goals. The whole complex facial structure can be evaluated with the use of 3D imaging methods and more effective patient-oriented treatment planning can be made.^{14,15} In the present study, we aimed, with the use of advanced biomedical engineering software, to describe hard- and soft-tissue asymmetry in individuals with asymmetric and symmetric skeletal class III malocclusion and to compare them with skeletal class I subjects without asymmetry. We also investigated the relationship between facial anatomic regions.

METHODS

Ethical approval for this study was obtained from the Ege University Ethics Committee. In this cross-sectional study, computed tomographic (CT) images of white patients selected from the Gülhane Faculty of Dentistry department of orthodontics archive from 2012 to 2015 were analyzed. CT images were obtained for diagnostic

reasons such as implant placement or orthognathic surgical treatment planning. All images were taken in supine position with the use of a CT scanner according to the manufacturer's instructions (Acquillon, Toshiba Medical Systems, Japan). The following settings were used: 0.5 mm slice thickness, 0.3 mm increments, 120 kV, and 75 mA. Sixty adult patients (23 female, 37 male) without a congenital or craniofacial anomaly or condylar pathology, who did not have a history of trauma, surgery, or orthodontic treatment, and who had a normal vertical growth pattern ($\text{Sn/GoGn} = 32 \pm 6^\circ$) were included. The patients that met inclusion criteria were then analyzed to determine the sagittal skeletal properties considering the ANB and SNB angles. The mean age of patients was 26.32 ± 3.17 years (range 19–41). Individuals with skeletal Class III were divided into 2 subgroups of symmetry and asymmetry according to the distance from the hard-tissue menton point to the midsagittal reference (MSP) plane. Three anatomic points (sella, nasion, and basion) were defined on the cranial base, and the plane that passes through these designated points was defined as the MSP plane.¹⁶ A distance between the MSP and skeletal menton >4 mm was accepted as asymmetric. Finally, 3 groups were constituted: skeletal class III with asymmetry ($n = 20$) and without asymmetry ($n = 20$; $\text{ANB} \leq 1^\circ$, $\text{SNB} > 82^\circ$) and skeletal Class I without asymmetry ($n = 20$; $1^\circ \leq \text{ANB} \leq 3^\circ$). The aforementioned angles which were determined to evaluate the vertical growth pattern and sagittal skeletal malocclusion were analyzed with the use of lateral cephalometric images derived from 3D images.

The DICOM images were opened with Mimics software (Materialise, Leuven, Belgium) and the segmentation process was started. During this process, which is known as semiautomatic segmentation, the threshold values was determined as ranging from 226 to 3071 Hounsfield units (HU) for the hard tissues (Fig 1, A) and from -700 to 225 HU for the soft tissues (Fig 1, B). The segmentation of the nasal septum was performed manually owing to its irregular structure.¹⁷ Hard and soft tissue images were converted to the standardized stereolithography (STL) file format and transferred to 3-Matic (Materialise, Leuven, Belgium) software for both separation of anatomic areas and calculation of the amount of asymmetry. The teeth and alveolar process were removed. Reference planes were generated on midface (Fig 2, A), mandible (Fig 2, B), and soft tissues (Fig 3) to create hard- and soft-tissue regions. The landmarks which were used to determine the reference planes on the face are presented in Table 1. Nasal bone, right and left zygomatic bones, maxilla, and the nasal septum were obtained in the midface (Fig 2, A). The reference lines and sutures that were

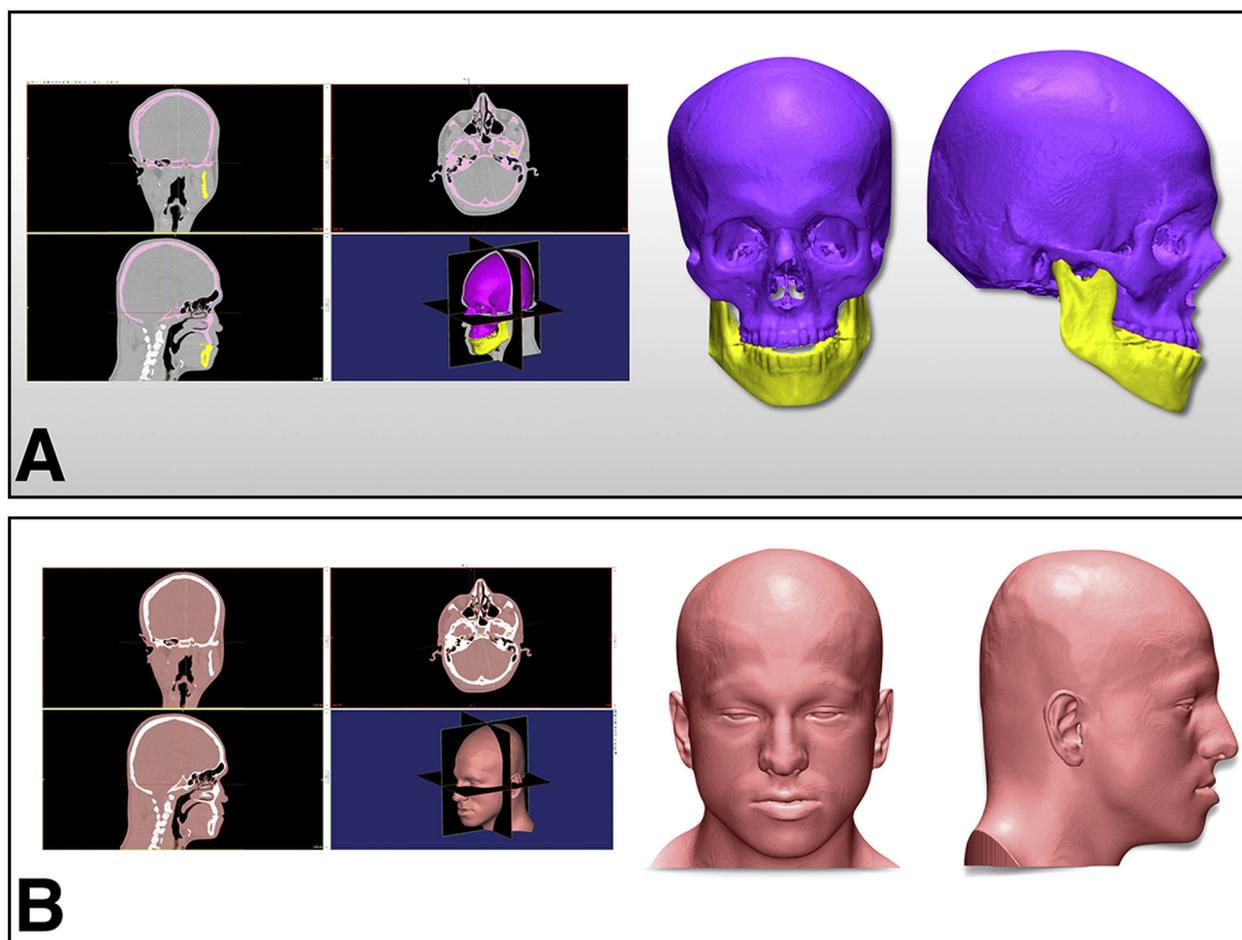


Fig 1. Segmentation process. **A**, Hard tissues; **B**, soft tissues.

used to segment these anatomic regions were: Fz-N plane: a plane between nasion (N) and left and right frontozygomatic suture (Fz) points; Zy-PNS plane: a plane perpendicular to the horizontal plane which was determined between the posterior nasal spine (PNS) and left and right zygion (Zy) points; Po-N plane: a plane between N and left and right porion (Po) points; zygomaxillary suture: the suture between the zygomatic bone and maxillary bone; nasomaxillary suture: the suture between N and the maxillary bone.

The mandible was segmented into the corpus, angulus, ramus, condyle, and coronoid process regions (Fig 2, B). The planes that were used to obtain aforementioned regions in the mandible were as follows: Sn-Ap plane: the plane between Sn and Ap points; Sn-Pp plane: the plane between Sn and Pp points; Pp-An plane: the plane between Pp and An points; Ap-An: the plane between the Ap and An points.

The method used by Kujipers et al¹⁸ was modified for the segmentation of the soft tissues. Anatomic

structures, such as nose, upper lip, lower lip, upper cheek, and lower cheek, were obtained (Fig 3). The planes that were used to obtain aforementioned regions in the soft tissues were as follows: tragus plane: the plane passing through left and right tragus (Tra) and orbita (Or) point; cervical plane: the plane passing through left and right Tra and cervicale (Cr) points; nasion plane: the plane parallel to the tragus plane and passing through soft-tissue nasion (N'); subnasal plane: the plane parallel to the tragus plane and passing through the subnasale (Sn) point; mouth plane: the plane parallel to the tragus plane and passes through the left and right commissure (Com) points; lower lip plane: the plane parallel to the tragus plane and passing through the sublingual (SI) point; left and right vertical plane: the plane passing through endocanthion (En) and Com points.

The segmented hard and soft tissues were cut at the same time considering the reference MSP and separated into 2 parts. Thus, an equal number of anatomic regions

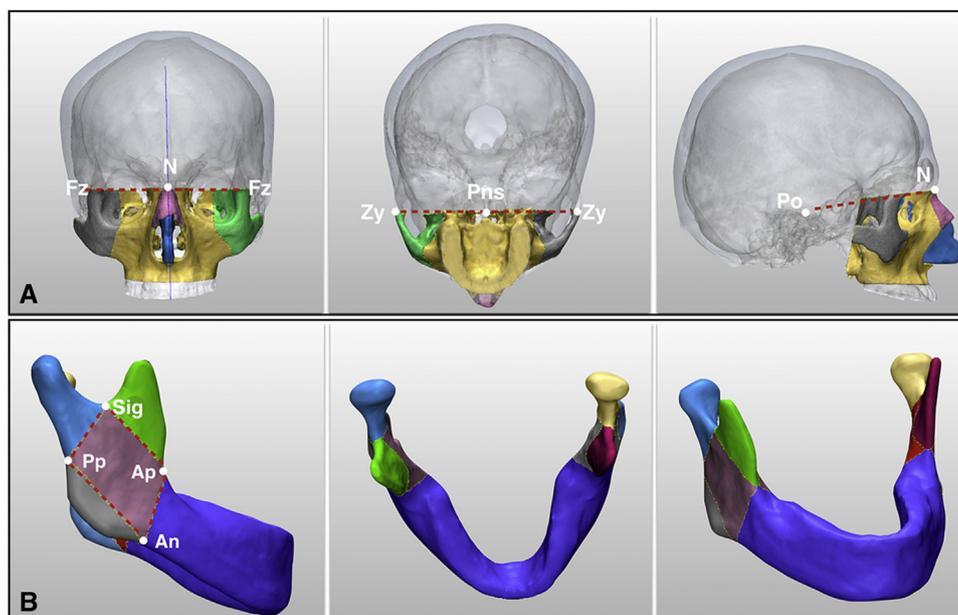


Fig 2. Determination of skeletal anatomical regions. **A**, Midface (*Fz*, frontozygomatic suture; *N*, nasion; *Pns*, posterior nasal spine; *Po*, porion). **B**, Mandible (*Sig*, sigmoid notch; *Ap*, anterior point; *Pp*, posterior point; *An*, antegonial notch).

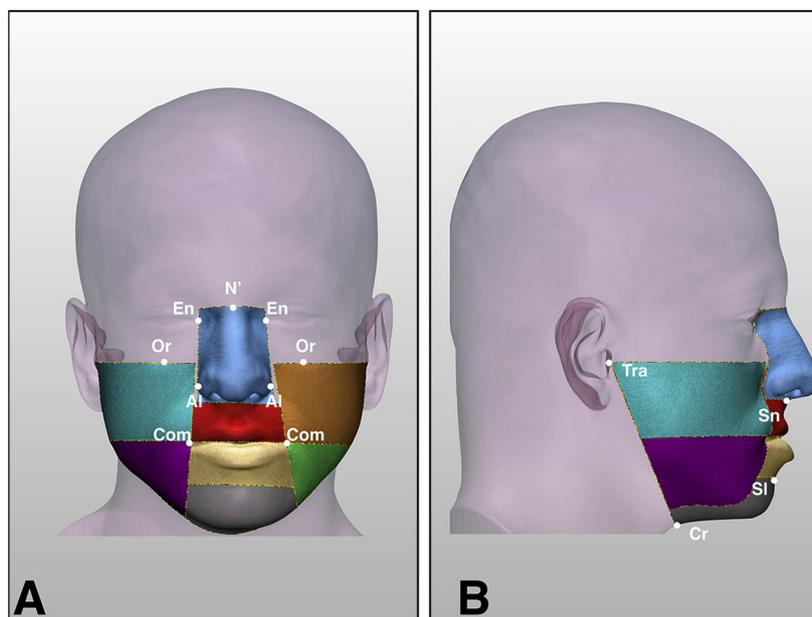


Fig 3. Determination of soft tissue anatomical regions. **A**, Frontal view (*N'*, soft tissue nasion; *En*, endocanthion; *Or*, soft tissue orbita; *Al*, alare; *Com*, commissure). **B**, Lateral view (*Tra*, tragus; *Sn*, subnasale; *SI*, sublinguale; *Cr*, cervicale).

were obtained for the left and right sides of the face (Figs 4 and 5, A). The anatomic structures on the right side of the face were mirrored on the left side, taking the midsagittal plane as a reference (Figs 4 and 5, B).

This means that the left and right anatomic structures overlapped each other (Figs 4 and 5, C). Finally, the amount of surface deviation between overlapped same anatomic regions were measured by means of unsigned

Table I. Description of facial landmarks

Landmark	Abbreviation	Definition
Nasion	N	Middle point of the nasofrontal suture
Frontozygomatic suture	Fz	Middle point of the frontozygomatic suture
Zygion	Zy	Middle point of the zygomaticotemporal suture
Porion	Po	Most upper point of meatus acusticus externus
Posterior nasal spine	Pns	Most posterior point of palatal bone
Anterior point	Ap	Deepest point of ramus anterior border
Posterior point	Pp	Deepest point of ramus posterior border
Sigmoid notch	Sig	Deepest point between condyle and coronoid process of the mandible
Antegonial notch	An	Deepest point of the concavity between ramus and corpus of the mandible
Tragus	Tra	Prominence in front of the opening of the outer ear canal
Cervical point	Cr	Intersection point of neck and chin region
Endocanthion	En	Point at the inner commissure of the eye fissure
Soft tissue orbitale	Or'	Most inferior point of infraorbital rim
Alare	Al	Most lateral point on alar contour
Soft tissue nasion	N'	Most retruded point in the tissue overlying area of the frontonasal suture
Subnasal point	Sn	Most retruded point in the concavity between nose and upper lip
Comissure	Com	Point at labial commissure
Sublabiale	Sl	Deepest midpoint on the labiomental soft tissue contour

point-based part comparison analysis with the use of the same software (Fig 6).

Statistical analysis

Statistical analysis of the data was conducted with the use of SPSS v20 (Chicago, Ill) software. The descriptive statistics of asymmetry values were calculated as minimum, maximum, mean, and SD. The normality of the data was evaluated by means of the Shapiro-Wilk test. The mean deviation differences between study groups for all morphologic regions were analyzed by means of 1-way analysis of variance with Bonferroni

correction. The level of significance was defined as $P < 0.017$ ($0.05/3$) to reduce the degrees of freedom. Pearson correlation coefficients were calculated to determine possible correlations between all anatomic regions for the Class III symmetry, Class III asymmetry, and control groups. One month later, 20 randomly selected images were resegmented by the same operator (G.S.D.) and deviation analyses were repeated. Afterward, the method error for each parameter was calculated, based on the principles defined by Dahlberg,¹⁹ using the following formula (Table II):

$$S_e = \sqrt{\sum d^2 / 2n}$$

where S_e = method error; d = difference between first and second measure; and n = number of images used. After the method error for each parameter had been determined, the 95% confidence interval of the real method error were calculated with the use of the following formula:²⁰

$$S_e^2 / \chi^2 \cdot 0.975/n < d_e^2 / \chi^2 = S_e^2 / (\chi^2 \cdot 0.975/n) < \delta_e^2 < S_e^2 / (\chi^2 - 0.025/n)$$

where χ^2 = n degree of freedom of chi-square ($n = 20$). As shown in Table II, the greatest method error was made in the lower cheek parameter, which was 0.54 mm. The lowest method error was in the lower lip parameter, which was 0.18 mm.

RESULTS

Power analysis was made with the use of 2-sample Satterthwaite t test. The sample size of 10 in each group produced a power $>90\%$ at a significance level of $P < 0.05$; SD1 was 2.91 and SD2 was 0.84. The true difference of means was 4.21 mm between Class I symmetry and Class III asymmetry groups. The descriptive statistics of the deviation values in groups (minimum, maximum, mean, and SD) were presented in Table III.

In the Class I symmetry group, the deviation values in all hard and soft tissues were found to be <2 mm. In the Class III symmetry group, the highest average deviations were in the angulus region of the mandibular hard tissues (mean 2.17 ± 0.90) and lower cheek region of the soft tissues (mean 2.45 ± 1.24). In the Class III asymmetry group, the highest average deviations was in the corpus region of the hard tissues (mean 5.55 ± 3.05 mm) and the lower cheek region of the soft tissues (mean 7.04 ± 3.46 mm).

In all anatomic regions, the differences between the average values of the Class I symmetry control group and the Class III symmetry group were <0.5 mm and

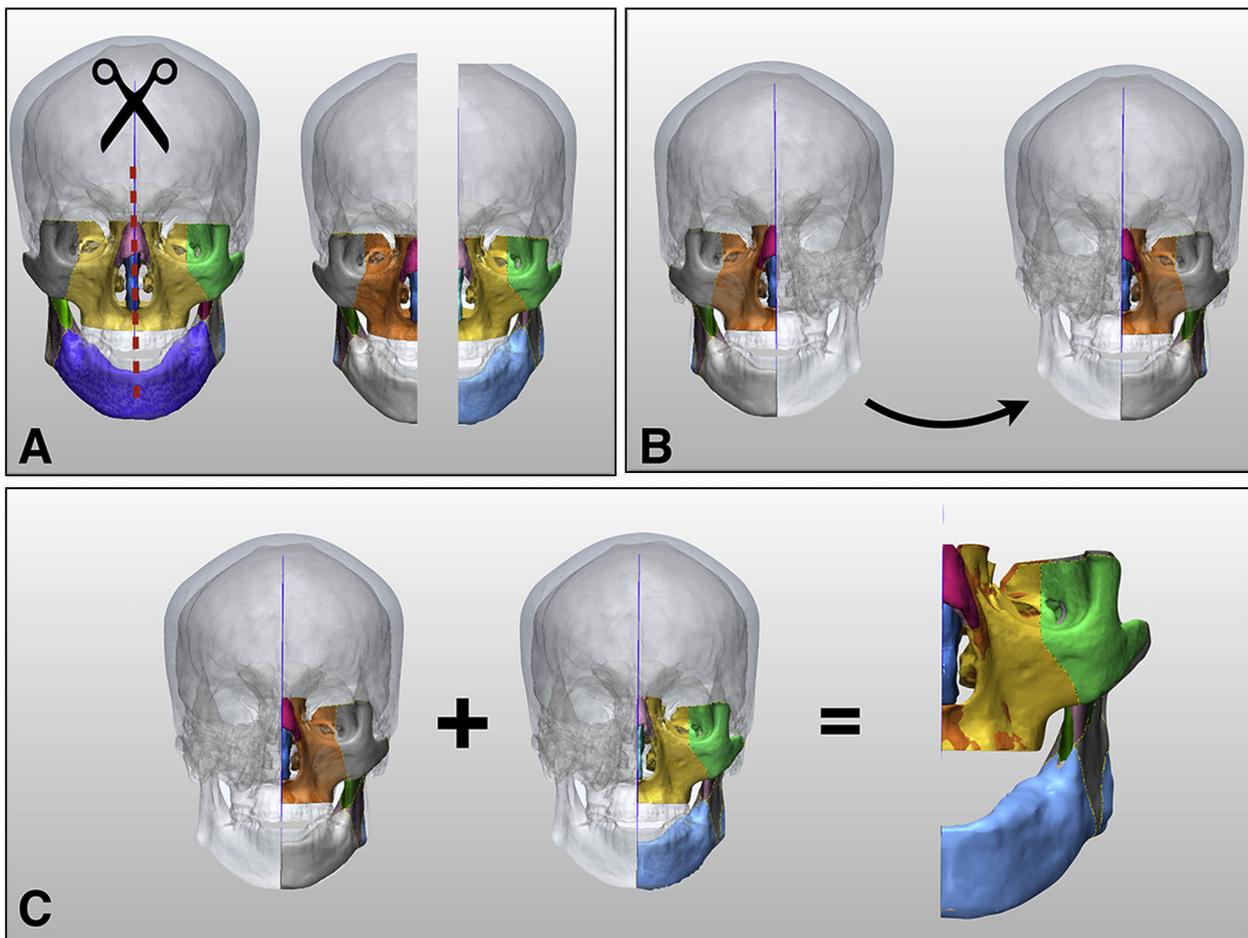


Fig 4. Cutting and overlapping of skeletal anatomical regions: **A**, cutting process according to MSP; **B**, mirroring process; **C**, overlapping process.

were statistically insignificant. The highest difference between the average values of the Class III asymmetry group and control group was observed in the corpus region of the hard tissues (mean -3.93 ; 95% CI -5.64 to -2.22). Also, the highest differences were found in the chin and lower cheek regions in soft tissues (means -4.59 , 95% CI -6.35 to -2.83 ; and -4.58 , 95% CI -6.63 to -2.52 , respectively). The differences between average values in the Class III asymmetry and control groups were statistically significant in all areas except the condyle and zygomatic process regions. Differences between average values in the Class III symmetry and asymmetry groups were significant in nasal bone and cheek upper regions in addition to these regions. The difference between average values in the Class III asymmetry and control groups were not significant in all regions (Table IV).

As the correlations between the anatomic regions were evaluated, a high positive correlation was observed

between neighboring regions in the mandibular structures. A significant correlation was observed between the angulus region and corpus, upper cheek, and lower cheek ($r > 0.5$). Similarly, a high positive correlation was found between the upper cheek–coronoid and ramus–angulus regions ($r > 0.5$; Table V). There was not a strong correlation in the group of anatomic regions that are close to midface and soft-tissue anatomic regions (Table VI). In soft-tissue regions, statistically significant positive correlations were found between upper cheek and coronoid process and between ramus and gonion regions. Similarly, significant positive correlation was found between lower cheek and corpus regions in all groups ($r > 0.5$; Table VII).

DISCUSSION

In this cross-sectional study, facial hard- and soft-tissue asymmetry was evaluated in individuals with

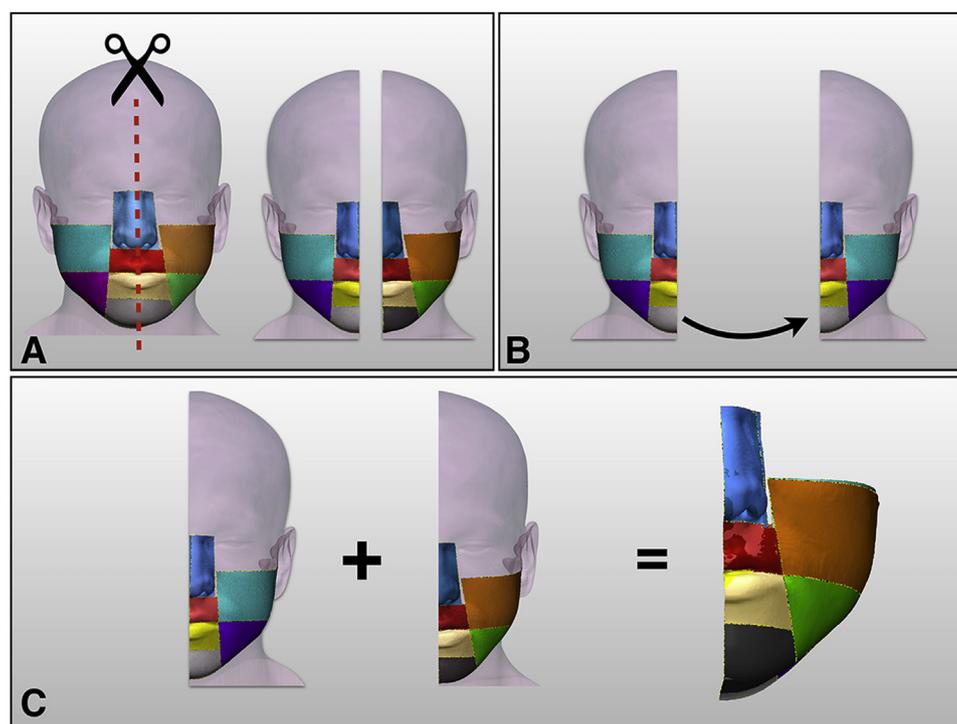


Fig 5. Cutting and overlapping of soft tissue anatomical regions: **A**, cutting process according to MSP; **B**, mirroring process; **C**, overlapping process.

skeletal Class III malocclusion and compared with non-asymmetric Class I and III individuals. Also, the correlations in amount of asymmetry between different anatomic regions on the middle and lower thirds of the face were evaluated. Determination of the possible location and quantity of asymmetry in the hard and soft tissues of the face in Class III cases, which are clinically categorized as symmetric and asymmetric with respect to a certain reference plane, is important for predicting esthetic concerns that may be encountered after treatment. It was thought that mild asymmetries may be present between the right and left sides of the face and that this was considered to be natural.²¹ However, facial asymmetries could be detected in the lower third of the face in the Class III individuals, and laterality is observed to the left side of the face.⁴ Ovsenik et al²² stated that the asymmetry in Class III individuals was not significant in the prepuberty stage, but the severity of the asymmetry could increase because of continuation of growth. Harguchi et al^{4,22} also stated that asymmetry might occur because of hyperactivity and unilateral stimulation of the condylar region during long-term growth of the mandible. However, there are not enough studies evaluating the multifactorial etiology of facial asymmetry or the interaction of the functional and intrinsic asymmetric growth potential of the mandible.

Asymmetry is a complex situation which includes 2 components: morphologic and spatial. Although it can occur because of morphologic differences, it can also occur because of different spatial localization of the left and right structures, despite the presence of similar morphology. Accordingly, mandibular asymmetry was categorized into 2 groups by Obwegeser and Makek: hemimandibular hypoplasia and hemimandibular elongation.²³ It is difficult to distinguish these conditions, which together can be the reason of asymmetry. Therefore, there are other classifications of asymmetry in the literature. For example, Baek et al²⁴ classified asymmetry into 4 groups considering anatomic features, but they claimed that there should be more than 4 categories for asymmetry classification. Because of the difficulty to clearly categorize the spatial and morphologic asymmetries, any distinction was not considered in this study. The distance between the menton (Me) and the midsagittal plane plays an important role in making a determination for asymmetry. So far, different amounts of distance (2–4 mm) were considered as a reference to constitute the asymmetry groups.^{3,4,25,26} It is stated that asymmetry in the chin region is more difficult to perceive than in other parts of the face and that low quantities are imperceptible.²⁷ Van Kaulen et al²⁸ reported that chin deviations >4 mm could be noticed

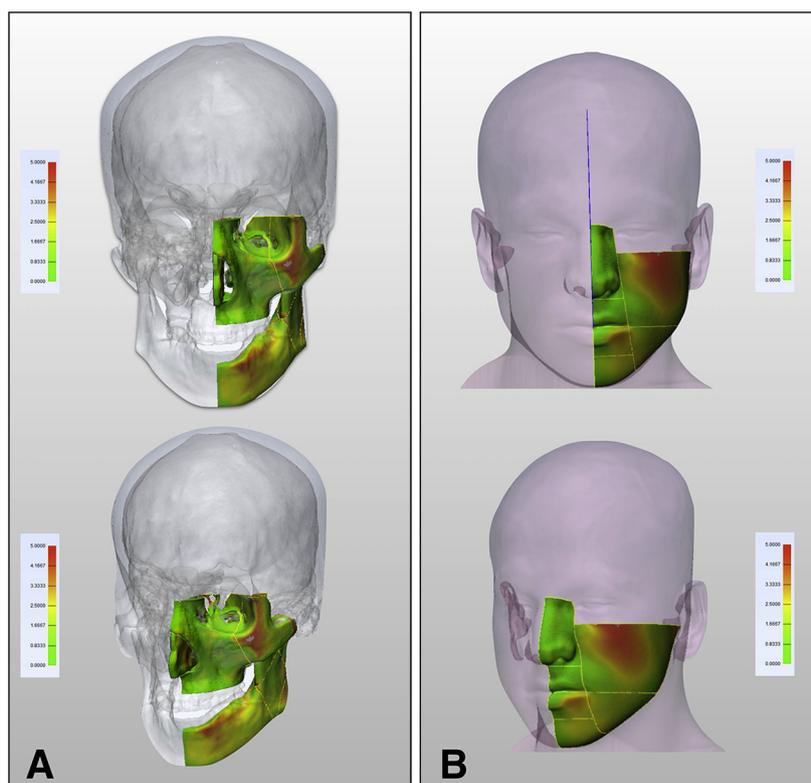


Fig 6. Heat map images of asymmetric regions. **A**, Hard tissues; **B**, soft tissues.

Table II. Method error and lower and upper 95% confidence limits for each parameter

Anatomic region	S_e	Lower limit	Upper limit
Condyle	0.44	0.33	0.63
Coronoid process	0.28	0.21	0.40
Ramus	0.39	0.30	0.57
Angulus	0.30	0.23	0.44
Corpus	0.34	0.26	0.50
Maxilla	0.33	0.25	0.49
Nasal septum	0.22	0.17	0.32
Zygomatic process	0.19	0.15	0.28
Nasal bone	0.23	0.17	0.33
Cheek upper	0.40	0.29	0.58
Nose	0.39	0.30	0.57
Upper lip	0.20	0.15	0.30
Lower lip	0.18	0.14	0.27
Cheek lower	0.54	0.41	0.78
Chin	0.25	0.19	0.36

by observers. For that reason, MSP-Me distances >4 mm were considered to designate the study group for evaluating asymmetry.

Facial asymmetries were traditionally evaluated on 2D panoramic,²⁹ cephalometric, and posteroanterior radiograms⁴ and photographs¹⁴ with the use of

linear-angular measurements. However, it is possible to encounter several problems, such as image distortions, superimpositions and magnification errors, with 2D techniques.³⁰ Although facial asymmetries are mostly perceived on horizontal or transversal planes by patients and observers, it can occur in all 3 planes of space.³¹ The advancement in imaging and software technology made it possible to visualize hard and soft tissues at the same time, as well as their 3D reconstructions. In addition to linear-angular measurements by means of biomedical engineering software, asymmetry can also be evaluated by means of volumetric measurements and deviation analyses with the use of 3D reconstruction.³² It has been reported that 3D measurement techniques are more effective than 2D imaging methods for asymmetry evaluation.³³ In addition to the quantitative measurement ability of morphometric techniques, heat maps (available through advanced software), are crucial for obtaining large amounts of information, including the localization and the amount of the facial symmetry. This information can be used as a guide for clinicians in treatment planning.³⁴

The mirroring method was used in our study instead of making linear or angular measurements between designated points on the face. In this technique, one

Table III. Descriptive statistics of the study groups

Anatomic region	Class I symmetry (n = 20)				Class III symmetry (n = 20)				Class III asymmetry (n = 20)			
	Min	Max	Mean	SD	Min	Max	Mean	SD	Min	Max	Mean	SD
Hard tissues												
Mandible												
Condyle	0.72	2.80	1.58	0.69	0.79	3.67	1.86	0.95	0.93	7.73	2.15	1.68
Coronoid process	0.99	4.26	1.84	1.03	0.70	3.13	1.63	0.79	1.00	10.05	3.84	2.60
Ramus	0.64	4.20	1.70	0.97	0.76	3.59	1.96	1.00	1.12	8.12	3.58	1.92
Angulus	1.02	5.07	1.95	0.95	1.09	3.95	2.17	0.90	1.31	9.21	4.69	2.43
Corpus	0.87	3.60	1.43	0.71	0.51	3.16	1.61	0.71	2.15	10.95	5.55	3.05
Middle face												
Maxilla	0.61	1.21	0.91	0.15	0.78	1.52	1.08	0.25	0.82	2.31	1.41	0.50
Nasal septum	0.61	1.83	0.99	0.37	0.30	1.69	0.90	0.33	0.83	4.12	2.00	1.20
Zygomatic process	1.08	1.82	1.50	0.24	0.83	2.46	1.53	0.50	0.87	2.73	1.52	0.49
Nasal bone	0.06	1.24	0.52	0.29	0.25	1.14	0.69	0.27	0.38	1.66	0.88	0.36
Soft tissues												
Middle third												
Cheek upper	0.82	3.64	1.74	0.81	0.70	4.78	2.14	1.20	0.88	5.20	3.05	1.30
Nose	0.35	1.74	0.97	0.43	0.34	1.24	0.76	0.27	0.47	3.59	2.12	1.12
Upper lip	0.35	1.35	0.75	0.32	0.21	1.25	0.61	0.29	0.75	4.98	1.86	1.24
Lower third												
Lower lip	0.30	1.88	1.16	0.46	0.43	1.58	0.93	0.33	0.51	9.48	3.96	2.62
Cheek lower	0.51	4.64	1.97	1.18	0.40	4.79	2.45	1.24	1.69	12.25	7.04	3.46
Chin	0.29	2.07	1.10	0.58	0.46	2.79	1.39	0.63	3.16	13.77	5.98	3.18

Table IV. Results of 1-way analysis of variance with Bonferroni correction

Anatomic region	Class I symmetry vs Class III symmetry		Class III symmetry vs Class III asymmetry		Class I symmetry vs Class III asymmetry	
	Mean difference (95% CI)	P	Mean difference (95% CI)	P	Mean difference (95% CI)	P
Condyle	0.27 (-0.81 to 1.36)	0.815	-0.56 (-1.65 to 0.53)	0.797	-0.28 (-1.38 to 0.80)	0.429
Coronoid process	-0.20 (-1.75 to 1.34)	0.944	-2.00 (-3.55 to -0.45)	0.004*	-2.21 (-3.76 to -0.66)	0.008*
Ramus	0.25 (-1.01 to 1.51)	0.878	-1.88 (-3.14 to -0.61)	0.009*	-1.62 (-2.89 to -0.36)	0.002*
Angulus	0.22 (-1.24 to 1.69)	0.928	-2.74 (-4.21 to -1.27)	<0.001*	-2.52 (-3.99 to -1.05)	<0.001*
Corpus	0.17 (-1.53 to 1.88)	0.967	-4.10 (-5.81 to -2.39)	<0.001*	-3.93 (-5.64 to -2.22)	<0.001*
Maxilla	0.16 (-0.14 to 0.47)	0.412	-0.49 (-0.80 to -0.18)	0.037*	-0.32 (-0.64 to 0.01)	0.001*
Nasal septum	-0.09 (-0.78 to 0.60)	0.946	-1.00 (-1.70 to -0.30)	0.001*	-1.09 (-1.79 to -0.39)	0.003*
Zygomatic process	0.02 (-0.37 to 0.42)	0.984	-0.02 (-0.41 to 0.37)	0.999	0.00 (-0.39 to 0.40)	0.991
Nasal bone	0.16 (-0.12 to 0.45)	0.338	-0.35 (-0.64 to -0.07)	0.258	-0.19 (-0.47 to 0.09)	0.012*
Cheek upper	0.39 (-0.64 to 1.43)	0.624	-1.30 (-2.34 to -0.26)	0.095	-0.90 (-1.94 to 0.12)	0.011*
Nose	-0.21 (-0.86 to 0.44)	0.714	-1.14 (-1.79 to -0.48)	<0.001*	-1.35 (-2.01 to -0.70)	<0.001*
Upper lip	-0.13 (-0.84 to 0.56)	0.879	-1.11 (-1.81 to -0.41)	<0.001*	-1.25 (-1.95 to -0.54)	0.001*
Lower lip	-0.22 (-1.65 to 1.19)	0.920	-2.80 (-4.22 to -1.37)	<0.001*	-3.02 (-4.45 to -1.60)	<0.001*
Cheek lower	0.47 (-1.57 to 2.53)	0.839	-5.06 (-7.11 to -3.00)	<0.001*	-4.58 (-6.63 to -2.52)	<0.001*
Chin	0.28 (-1.47 to 2.04)	0.918	-4.87 (-6.63 to -3.12)	<0.001*	-4.59 (-6.35 to -2.83)	<0.001*

*Statistically significant, which was defines as $P < 0.017$ (0.05/3) to reduce the degrees of freedom.

side of the face is mirrored on the other side of the face to evaluate facial asymmetries.³⁵ The parts comparison analysis in our study was similar to the shape correspondence analysis used in the study by Cevidanes et al.¹⁶ Because spatial differences were considered in our study along with morphologic differences, we did not perform surface-based superimposition. After anatomic regions

had been mirrored, corresponding areas were accepted as symmetric, the absolute value of the deviation between both parts was calculated, and the deviation values were defined as the amount of asymmetry. The MSP is an arbitrary line, and it was considered as a reference for the mirroring and segmentation processes. However, there are various methods to define the MSP.³⁶

Table V. Pearson correlations between mandibular hard tissues and segmented anatomic regions

Anatomic region	Mandibular hard tissues														
	Condyle			Coronoid process			Ramus			Angulus			Corpus		
	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C
Hard tissues															
Condyle	1	1	1												
Coronoid process	0.652*	0.678†	0.726†	1	1	1									
Ramus	0.696†	0.629†	0.840†	0.894†	0.786†	0.806†	1	1	1						
Angulus	0.474	0.345	0.770†	0.731†	0.760†	0.625*	0.750†	0.938†	0.552*	1	1	1			
Corpus	0.464	0.043	-0.127	0.276	0.265	0.310	0.230	0.418	0.586*	0.813†	0.694*	0.761†	1	1	1
Maxilla	0.188	0.249	0.547*	0.008	0.523	0.552*	0.120	0.392	0.391	0.117	0.376	0.228	-0.192	0.033	0.401
Nasal septum	0.495	-0.133	-0.110	0.349	-0.515	0.366	0.464	-0.282	0.015	0.005	-0.282	0.089	-0.239	-0.464	0.466
Zygomatic process	0.145	0.279	0.643*	0.372	0.533	0.701†	0.339	0.426	0.414	0.385	0.444	-0.003	0.100	-0.082	0.053
Nasal bone	0.240	-0.334	0.191	-0.261	-0.342	0.407	0.024	-0.309	0.459	-0.341	-0.086	0.129	-0.317	0.255	0.027
Cheek upper	0.638*	0.826†	0.676*	0.576*	0.748†	0.630*	0.552*	0.797†	0.651*	0.779†	0.814†	0.626*	0.304	0.291	0.487
Soft tissues															
Nose	0.083	-0.045	0.306	-0.231	-0.017	0.510	-0.860	0.020	0.335	-0.383	0.135	-0.153	-0.256	0.118	-0.072
Upper lip	0.287	0.139	0.125	0.184	0.383	0.453	-0.006	0.367	0.124	0.034	0.384	0.133	0.326	0.471	0.529
Lower lip	0.116	-0.397	-0.283	0.320	-0.128	0.178	0.045	-0.128	0.077	0.034	-0.052	0.463	0.216	0.519	0.731†
Cheek lower	0.174	0.345	-0.436	0.421	0.342	0.066	0.365	0.727†	0.207	0.714†	0.759†	0.735†	0.717†	0.533*	0.686†
Chin	0.253	-0.164	-0.158	0.183	-0.132	0.110	0.154	-0.097	0.101	0.243	-0.019	0.563*	0.566*	0.495	0.811†

A, Class I symmetry group; B, Class III symmetry group; C, Class III asymmetry group.
 *Correlation significant at the 0.05 level (2-tailed); †Correlation significant at the 0.01 level (2-tailed).

Table VI. Pearson correlations between midface hard tissues and segmented anatomic regions

Anatomic region	Midface hard tissues											
	Maxilla			Nasal septum			Zygomatic process			Nasal bone		
	A	B	C	A	B	C	A	B	C	A	B	C
Hard tissues												
Condyle	0.188	0.249	0.547*	0.495	-0.133	-0.110	0.145	0.279	0.643*	0.024	-0.334	0.191
Coronoid process	0.008	0.523	0.552*	0.349	-0.515	0.366	0.372	0.533	0.701†	-0.261	-0.342	0.407
Ramus	0.120	0.392	0.391	0.464	-0.282	0.015	0.339	0.426	0.414	0.024	-0.309	0.459
Angulus	0.117	0.376	0.228	0.005	-0.282	0.089	0.385	0.444	-0.003	-0.341	-0.086	0.129
Corpus	-0.192	0.033	0.401	-0.239	-0.464	0.466	0.100	-0.082	0.053	-0.317	0.255	0.027
Maxilla	1	1	1									
Nasal septum	0.107	-0.268	0.315	1	1	1						
Zygomatic process	0.458	0.264	0.752†	-0.012	-0.125	0.155	1	1	1			
Nasal bone	0.021	-0.342	0.353	0.528	0.302	0.403	-0.237	-0.019	0.321	1	1	1
Soft tissues												
Cheek upper	0.071	0.526	0.438	0.139	-0.240	0.225	0.389	0.414	0.400	-0.256	-0.061	0.416
Nose	-0.170	0.181	0.224	0.522	0.151	0.532	-0.149	-0.036	0.127	0.690†	0.658*	0.716†
Upper lip	-0.144	0.208	0.291	-0.130	-0.386	0.577*	-0.164	0.063	0.132	-0.044	-0.263	0.147
Lower lip	-0.176	0.018	0.062	-0.218	-0.280*	0.494	-0.090	-0.383	0.048	-0.008	0.132	-0.043
Cheek lower	0.077	0.409	0.100	-0.218	-0.497	0.190	0.078	0.446	0.081	-0.274	0.027	-0.005
Chin	-0.207	-0.205	0.131	-0.021	-0.481	0.311	-0.258	-0.206	-0.009	-0.159	-0.025	-0.154

A, Class I symmetry group; B, Class III symmetry group; C, Class III asymmetry group.
 *Correlation significant at the 0.05 level (2-tailed); †Correlation significant at the 0.01 level (2-tailed).

The traditional method is to define the MSP that passes through landmarks on the various parts of the craniofacial complex. In addition to this method, there have been attempts to define the MSP with the use of various morphometric methods, such as the interactive closest point and procrustes analyses. Although the MSP is defined successfully with these methods, the use of these methods in severe asymmetries is still unclear.³⁷ In non-syndromic individuals, the cranial base is considered to be symmetric. Landmarks on the cranial base were used to determine of the MSP owing to their convenience in landmark determination and the distance of the cranial base from the facial structures to be measured.¹⁶ With change of the body position, gravity could affect soft tissues dynamically along the different axes.³⁸ All images in the present study were taken in standard supine position. However, the readers should also consider this effect of gravity while scrutinizing the data.

In our study, we observed that hard- and soft-tissue asymmetries were especially localized on the lower third of the face. These results could be considered natural and expected because patients having chin point deviation >4 mm from the midsagittal reference plane were assigned to the asymmetry group. In individuals with mandibular prognathism, 21% of asymmetries in the structures which belong to both mandibular and

midface occur together.⁵ According to our results, we found a low correlation between mandibular structures and the midface region. This result can be due to different growth periods between maxilla and mandible, and the maxilla having a more rigid connection between the cranial base rather than the mandible.⁴ Besides, it can be natural and self-explanatory to see a high level of correlation between 2 variables when they are located close to each other. We found that amount of asymmetry in the condyle region and the adjacent structures were positively correlated in each of the 3 groups; however, this correlation decreased in the corpus region. In addition to condylar pathologies, an adaptive remodeling was observed in response to the disruption of occlusal balance in mandibular symmetries and in condylar morphology changes in some deviated and nondeviated regions.³⁹ We think that function, occlusion, and muscles can affect the condyle and corpus in different ways which also affect the final shape of the structures.

The nasal septum also has an important role in the growth and development of the midface. On a symmetric face, it is expected that the nasal septum should be on the MSP.^{17,40} Hun et al⁴⁰ stated that there is a strong relationship between nasal septum deviation and the hemiface width of the face. Hartman et al¹⁷ found that there is a relationship between the nose and premaxilla asymmetries with nasal septum deviations, but they

Table VII. Correlation coefficient values of facial soft tissues

Anatomic region	Soft tissues																	
	Cheek upper			Nose			Upper lip			Lower lip			Cheek lower			Chin		
	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C
Hard tissues																		
Condyle	0.638*	0.826 [†]	0.676*	0.083	-0.045	0.306	0.287	0.139	0.125	0.116	-0.397	-0.283	0.174	0.345	-0.436	0.253	-0.164	-0.158
Coronoid process	0.576*	0.748 [†]	0.630*	-0.231	-0.017	0.510	0.184	0.383	0.453	0.320	-0.128	0.178	0.421	0.342	0.066	0.183	-0.132	0.110
Ramus	0.552*	0.797 [†]	0.651*	-0.086	0.020	0.335	-0.006	0.367	0.124	0.045	-0.128	0.077	0.365	0.727 [†]	0.207	0.154	-0.097	0.101
Angulus	0.779 [†]	0.814 [†]	0.626*	-0.383	0.020	-0.153	0.034	0.384	0.133	0.034	-0.052	0.463	0.714 [†]	0.759 [†]	0.735 [†]	0.243	-0.019	0.563*
Corpus	0.304	0.291	0.487	-0.256	0.118	-0.072	0.326	0.471	0.529	0.216	0.519	0.731 [†]	0.717 [†]	0.533*	0.686 [†]	0.566*	0.495	0.811 [†]
Maxilla	0.071	0.526	0.438	-0.170	0.181	0.224	-0.144	0.208	0.291	-0.176	0.018	0.062	0.077	0.409	0.100	-0.207	-0.205	0.131
Nasal septum	0.139	-0.240	0.225	0.522	0.151	0.532	-0.130	-0.386	0.577*	-0.218	-0.280*	0.494	-0.218	-0.497	0.190	-0.021	-0.481	0.311
Zygomatic process	0.389	0.414	0.400	-0.149	-0.036	0.127	-0.164	0.063	0.132	-0.090	-0.383	0.048	0.078	0.446	0.081	-0.258	-0.206	-0.009
Nassal bone	-0.256	-0.061	0.416	0.690 [†]	0.658*	0.716 [†]	-0.044	-0.263	0.147	-0.008	0.132	-0.043	-0.274	0.027	-0.005	-0.159	-0.025	-0.154
Soft tissues																		
Cheek upper	1	1	1	-0.264	0.228	0.246	0.114	0.197	0.410	-0.006	-0.007	0.417	0.449	0.878 [†]	0.643*	0.136	0.031	0.306
Nose				1	1	1	0.249	0.234	0.479	-0.264	0.193	0.044	-0.200	0.100	-0.250	0.143	0.116	-0.093
Upper lip							1	1	1	0.485	0.327	0.743 [†]	0.499	0.321	0.291	0.448	0.543*	0.680 [†]
Lower lip										1	1	1	0.161	0.286	0.804 [†]	0.527	0.734 [†]	0.905 [†]
Cheek lower													1	1	1	0.452	0.334	0.735 [†]
Chin																1	1	1

A, Class I symmetry group; B, Class III symmetry group; C, Class III asymmetry group.
 *Correlation significant at the 0.05 level (2-tailed); [†]Correlation significant at the 0.01 level (2-tailed).

did not find any correlation with the soft-tissue cheek area. According to our study, there was no strong level of correlation between nasal septum deviations and amount of asymmetry in other anatomic regions.

Besides hard tissue, the symmetric or asymmetric appearance of a face can be affected by the thickness of the soft tissues. It was found that in Class III malocclusions, 80% of skeletal asymmetries on the frontal direction decreased to 56% in soft tissues. That means asymmetry of the hard tissues could be masked by soft tissues.⁹ On the other hand, Young et al¹³ studied the correlation between the morphologic structure of external soft tissue and the internal skeletal structure, and they found a high covariance between the soft and underlying hard tissues. According to our results, soft tissues of the upper cheek, lower cheek, and chin correlated with their underlying hard tissues. Regarding this result, it was reported that lip asymmetry accompanies soft-tissue chin deviations.⁴¹ We also found a high correlation between chin and lip asymmetries in subjects with skeletal Class III asymmetry.

Facial asymmetries are usually treated with traditional orthognathic surgical methods. However, orthognathic surgery may not be sufficient to eliminate soft-tissue- or local bone morphology-dependent asymmetries. Therefore, some of the patients with facial asymmetry might be dissatisfied with the orthognathic surgery.⁸ Soft-tissue contours can be corrected by means of less invasive treatment modalities, such as local bone contouring, lipid grafts, and tissue implants.² Because facial asymmetries are considered to be one of the indications for the use of 3D imaging techniques such as CT and cone-beam CT, advanced software that allows for the simultaneous visualization of both soft and hard tissues should be preferred. Using this software and related analysis in measuring and visualizing differences in the whole structure provides more detailed data. These data can be used to increase patient cooperation and to enable more stable and more efficient treatment planning. Substantial diagnostic information can be obtained by using our method for quantitative 3D evaluation of the interventions on facial structures in asymmetry patients. Consequently, the method described above is important for treatment planning to determine where and how these local surgical options will be performed. Currently, various noninvasive surface scanning systems, such as 3D stereophotogrammetry and dynamic motion capture, can be used before advanced analyses for soft tissues.⁴² It has become possible to investigate asymmetries in various malocclusion groups without radiation through advances in 3D technologies.

Because subjects in the study had to meet both sagittal and transversal measurement criteria, the difficulty of finding images that were captured in a standard manner and the distortions or missing anatomic regions in the images prevented us from creating study groups randomly generated from large group of patients with various malocclusions. In addition, blinding of subjects could not be done, because the investigator could notice the sagittal and transversal properties of the subject and be aware of the group of the image. These could be considered for potential bias in this study. Also, further studies that evaluate asymmetry including different ethnic groups and malocclusion types could maximize the external validity.

CONCLUSIONS

1. Asymmetry was observed in all anatomic structures at varying amounts in all groups. Mean difference in asymmetry values between the Class III asymmetry group and the Class III symmetry and Class I control groups were significant. The difference was more remarkable in anatomic regions that were located in the lower facial third regions.
2. A low level of correlation was observed between amount of asymmetry in midface and mandibular hard tissues. There was a medium or high correlation between condyle, coronoid process, ramus, and angulus regions.
3. In soft-tissue asymmetry values, the upper cheek and lower cheek regions correlated with different mandibular regions. The lower cheek area correlated with the corpus and angulus regions. It was also observed that the chin asymmetries were highly correlated with the lips region in the class III asymmetry group.

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