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## The effect of orthognathic surgery on soft-tissue facial asymmetry: a longitudinal three-dimensional analysis.

--Manuscript Draft--

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| Abstract: | In modern orthognathic surgery, the functional results cannot disregard a good aesthetic outcome. In this study, a stereophotogrammetric longitudinal analysis of the symmetry of facial thirds was performed in 18 patients affected by Class III skeletal malocclusion, with clinical asymmetry, treated with a bimaxillary osteotomy. Their 3D facial images were acquired in the preoperative phase and 6, 12 and 24 months after surgery, and compared to those obtained in a control group of 23 subjects with Class I skeletal occlusion, without clinical asymmetry and no history of traumas or alterations at the maxillo-facial area. Images of the hemi-faces of the subjects were divided into thirds (upper, middle, lower), mirrored and superimposed to their contralateral ones; soft-tissue facial symmetry was obtained as the Root Mean Square Distance (RMSD) between the hemi-faces in the three thirds. In patients, no significant differences in facial symmetry (RMSD) were found among the study time points (ANOVA, $p > 0.05$); the lower facial third was more asymmetric than the upper one (Tukey's HSD $p < 0.05$). Patients were significantly more asymmetric than the control subjects (Student's t, $p < 0.05$). In conclusion, patients with Class III malocclusion exhibited a higher level of facial asymmetry than control subjects; their asymmetry did not change significantly in the different phases of the surgical and orthodontic treatment and throughout a 24-month follow-up. In skeletal Class III patients, bimaxillary osteotomy did not modify the level of asymmetry in any facial third. |

Dr. Mutaz B. Habal
Journal of Craniofacial Surgery

Milano, 17 October 2019

Dear dr. Habal,

Please find enclosed the manuscript “The effect of orthognathic surgery on soft-tissue facial asymmetry: a longitudinal three-dimensional analysis” by Filippo Da Pozzo, Daniele Gibelli, Giada A. Beltramini, Claudia Dolci, Aldo Bruno Giannì, and Chiarella Sforza, which I would like to submit as original article for the publication in the Journal of Craniofacial Surgery.

In the paper, we longitudinally investigated the modifications in facial symmetry after orthognathic surgery using stereophotogrammetry with a 2 years follow up. The topic has been addressed in the Journal by previous papers (eg, Soft tissue changes after orthodontic surgical correction of jaws asymmetry evaluated by three-dimensional surface laser scanner. J Craniofac Surg. 2012;23(5):1448-52), but with a relatively short follow up time. Additionally, 3D facial photographs were obtained by stereophotogrammetry, the current reference technique in this field, following a protocol recently published by the Journal (Stereophotogrammetric evaluation of labial symmetry after surgical treatment of a lymphatic malformation. J Craniofac Surg. 2017;28(4):e355-8).

All authors made substantial contributions to the conception and design of the study, or acquisition of data, or analysis and interpretation of data; they either prepared a draft version of the article or revised it critically for important intellectual content. The final manuscript has been seen and approved by all the authors; they have taken due care to ensure the integrity of the work.

Thank you for your kind attention.

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Mutaz B. Habal, M.D.
Editor-in-Chief
Journal of Craniofacial Surgery

Milano, 24 December 2019

Dear dr. Habal,

Please find enclosed the revised version of manuscript RE: SCS-19-01568, entitled "The effect of orthognathic surgery on soft-tissue facial asymmetry: a longitudinal three-dimensional analysis."

In revising the paper, we attentively considered the precious suggestions of the reviewers, and modified the MS accordingly. A detailed list of changes is included below, and the relevant parts of the text are highlighted.

We thank you and the reviewers for all the time and expertise you are devoting to our submission, and we are also grateful to the editorial staff for all the backstage work.

We trust that the present version of MS will be suitable for publication in the Journal of Craniofacial Surgery.

Thank you for your kind attention.
My personal best wishes for this holiday season.

Prof. Chiarella Sforza
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Reviewers comment:
The study is conducted with scientific rigor and is complete in the treatment of a surgical subject that is always very important in maxillary mandibular deformity surgery. The results are scrupulously analyzed and the surgical procedure was performed with a safe and well-tested control. in an important topic such as that of facial asymmetries the pre and post surgical evaluation of the sub-chin-VERTEX projection - was not taken in any way. Is it possible to avoid reaching a safe degree of correctness of evaluation in the following phase recorded? The work can be published after this explanation.

Answer:
We are grateful to the reviewer for these kind words and appreciation of our work.

During the diagnostic work flow, all patients were analyzed also with sub-chin-vertex projections, that were repeated after the surgical treatment. Both X-rays and stereophotogrammetric images were obtained and evaluated. An example of the stereophotogrammetric right-left superimposition for the quantitative assessment of pre-post facial asymmetry is included in the revised MS (Figure 3). Modifications to the text can be found in MM, Discussion and Figure legends.

**The effect of orthognathic surgery on soft-tissue facial asymmetry: a longitudinal three-dimensional analysis.**

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**ABSTRACT**

In modern orthognathic surgery, the functional results cannot disregard a good aesthetic outcome. In this study, a stereophotogrammetric longitudinal analysis of the symmetry of facial thirds was performed in 18 patients affected by Class III skeletal malocclusion, with clinical asymmetry, treated with a bimaxillary osteotomy. Their 3D facial images were acquired in the preoperative phase and 6, 12 and 24 months after surgery, and compared to those obtained in a control group of 23 subjects with Class I skeletal occlusion, without clinical asymmetry and no history of traumas or alterations at the maxillo-facial area. Images of the hemi-faces of the subjects were divided into thirds (upper, middle, lower), mirrored and superimposed to their contralateral ones; soft-tissue facial symmetry was obtained as the Root Mean Square Distance (RMSD) between the hemi-faces in the three thirds.

In patients, no significant differences in facial symmetry (RMSD) were found among the study time points (ANOVA, $p > 0.05$); the lower facial third was more asymmetric than the upper one (Tukey's HSD $p < 0.05$). Patients were significantly more asymmetric than the control subjects (Student's t, $p < 0.05$). In conclusion, patients with Class III malocclusion exhibited a higher level of facial asymmetry than control subjects; their asymmetry did not change significantly in the different phases of the surgical and orthodontic treatment and throughout a 24-month follow-up. In skeletal Class III patients, bimaxillary osteotomy did not modify the level of asymmetry in any facial third.

**KEY WORDS:** orthognathic surgery, facial symmetry, bimaxillary osteotomy, stereophotogrammetry.

## INTRODUCTION

Aesthetic issues and facial symmetry are crucial parameters in modern orthognathic surgery. An essential part of the surgical treatment of dentoskeletal dysmorphism is the restoration of the normal occlusal and skeletal relationships. However, the surgeon's and the patient's attention is increasingly focused on the results obtained on the soft tissues, the restoration of the correct proportions between the thirds of the face, and its physiological symmetry[1,4].

Nevertheless, a slight facial asymmetry is always present and it can be defined as physiological or structural[5,6]. Delimiting the boundary for which the asymmetry turns from physiological to pathological is not always an easy task. When the level of asymmetry becomes more severe, the overall aesthetics of the face can be compromised[7,8].

In recent years, the evaluation of facial morphology increasingly evolved, moving from direct anthropometry to indirect assessments, through two- and three-dimensional (3D) radiographic and optical imaging systems[2,3,9-11]. These instruments permit not only a facial analysis based on landmarks, but also a more complete assessment of the whole surface[12]. In particular, 3D facial surface analyses have been applied to the qualitative and quantitative evaluation of orthognathic surgery[2,3].

In this field, the first 3D longitudinal studies focused on the assessment of sets of selected landmarks[13,14], while more recently facial surfaces were analyzed as well[2,4]. For surface analysis, optical devices were used, with follow-up times ranging from 6 to 24 months[4,15-18]. Among the others, patients affected by Class III skeletal malocclusion[2,16], jaws asymmetry[2,3,17] and obstructive sleep apnoea syndrome requiring maxilla-mandible advancement[18], were investigated; classic anthropometric measurements, evaluations of facial symmetry, and assessments of facial mimicry were performed[2,3,15-19].

In general, orthognathic surgery reduced 3D soft-tissue facial asymmetry, especially in patients with evident right-left side imbalances in facial proportions[3,4,17]. Nonetheless, the medium-long term effects of surgery in patients with a moderate facial asymmetry are still to be investigated. A recent investigation compared data collected in more than 100 patients one day before orthognathic surgery with those obtained one day before removal of osteosynthesis material[2], but no other follow-up evaluations were performed. In a longitudinal study, Ostwald et al.[3] found a significant correlation between measured (objective) and perceived (subjective) asymmetry; on average, both increased after surgery.

These last investigations assessed the effect of orthognathic surgery on total facial asymmetry, even if the interventions mainly interest the middle and lower facial thirds that should be analyzed separately. The purpose of the current longitudinal research was to analyze the response of facial soft tissues to orthognathic surgery, focusing on the degree of local facial asymmetry. To the scope, 18 patients undergoing a combined surgical-orthodontic treatment to correct a Class III dento-skeletal malocclusion were followed up for 24 months. Morphometric measurements were performed on 3D stereophotogrammetric images.

## MATERIAL AND METHODS

*Patients*

The evaluation involved 18 patients with a diagnosis of dentoskeletal Class III facial dysmorphosis, subjected to orthodontics and bimaxillary osteotomy at the Maxillo-Facial Surgery Unit of Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico of Milan, Università degli Studi di Milano). Data about some of the patients were previously published[19].

After conventional clinical and radiographic assessments, including posteroanterior, lateral and sub-chin-vertex projections, all patients underwent a Le Fort I osteotomy and an Obwegeser/Dal Pont bilateral sagittal split osteotomy[19]; three patients also underwent a genioplasty. Furthermore, all patients had a diagnosis of facial asymmetry based on the clinical evaluation and surgical planning, and needed a compensatory rotation of the jaw and/or the maxilla on the frontal plane (**Table 1**). The research was carried out in four different stages (preoperative, at the end of orthodontic treatment; and postoperative, 6, 12 and 24 months after surgery) through 3D stereophotogrammetric images obtained using the VECTRA M3 3D system (Canfield Scientific, Fairfield, NJ, USA).

Images were taken from October 2013 to September 2016, and nine women and nine men aged 21 to 51 years (mean age 28 years, SD 7 years) were analyzed. Twenty-three subjects formed the control group (13 women and 10 men, mean age 26 years, SD 6.8 years); they all had a diagnosis of dentoskeletal Class I without clinical asymmetry and no history of traumas or alterations at the maxillo-facial area.

Acquisitions were obtained after patients' written informed consent and did not involve any invasive, painful or dangerous procedure. In addition, all procedures were carried out in accordance with the Helsinki Declaration and with the approval of the Local Ethics Committee (Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Milan, Italy #843 03 April 2012).

*Image acquisition*

The VECTRA system uses three pairs of coordinated, high-definition digital cameras configured in a Cartesian reference system; they simultaneously shot the analyzed object from different perspectives and accurately calculate its 3D position in the space. The technique is safe, fast, and not invasive[20-23].

The first step in the acquisition of the facial images was the identification, by an experienced and qualified operator, of 50 anthropometric landmarks on the patient's facial surface detected by facial palpation and inspection. The landmarks were highlighted with a biocompatible and easily removable black eyeliner[20,23]. Marking the points of interest before the acquisition increases the precision of the measurements without affecting the quality of the image[24]. Where needed, the patient's hair was tied with a disposable elastic band. The procedure lasted a few minutes and it was completely painless and minimally disturbing. During image acquisition, the patient remained seated in front of the instrument, in a relaxed posture and with a natural expression, closed mouth and teeth in slight contact[21].

*Image analysis*

For each patient four stereophotogrammetric reconstructions of the entire face surface, one for each evaluation (before surgery and after 6, 12, and 24 months), were obtained. All manually marked landmarks were digitized in the 3D reconstructions, using Mirror® software (Canfield Scientific, Fairfield, NJ, USA).

Afterwards, the facial portion to be used for the analysis was outlined, with 10 landmarks chosen between the ones previously identified: trichion (tr); frontotemporal (ft); zygion (zy); tragion (t); gonion (go); gnathion (gn). The procedure is reproducible, standardized and non-operator dependent[21]. For each 3D reconstruction, the Mirror® software automatically detected the maximum symmetry plane, which was used to split each face into two halves. Then, each half-face was divided into three thirds (lower, middle and upper part) according to the areas of trigeminal nerve innervation[21].

Using the Mirror® software, the left side (conventionally chosen) of each subject's face was reflected around the maximum symmetry plane. The software automatically calculated the root mean square distance (RMSD) between the original and reflected surfaces, and this value was used to quantify the asymmetry of each facial third in each subject. The higher the value, the higher the asymmetry[21]. The procedure was repeated for every time point of the patients follow-up (before surgery and 6, 12, 24 months after), and for each subject of the control group. The procedure was tested in our laboratory, and found to be highly reproducible, with Bland-Altman repeatability coefficients ranging from 0.9% to 1.7%, and relevant mean biases of area measurements comprised between -0.003 and 0.097 $cm^2$[21].

The software also produced colorimetric maps which highlight the variations in an intuitive way.

*Statistical analysis*

Statistically significant differences, in sex and age distribution between patients and the control group, were respectively checked with Chi square and Student's t tests.

Jarque Bera's test was used to evaluate the normality of the RMSD values. A two-way ANOVA was performed to compare the RMSD values obtained for each third of the face at different times (factors: time, facial third; the time x facial third interaction was also calculated). Where necessary, Tukey's HSD test was applied to post-hoc comparisons. To assess the practical effect of the differences, partial eta squared statistics were obtained; values larger than 0.01 were considered small, larger than 0.09 medium, and larger than 0.25 large[25].

For each part of the face, RMSD values (mean and SD) obtained for the control group were used to calculate a set of z-scores for the patients, before and 2 years after surgery. Student's t test was used to compare the z-score values of patients with those of control subjects (=0 for definition), and to compare z-scores obtained before surgery and 24 months after.

Cohen's d statistics (effect size) for paired and unpaired t tests were obtained to evaluate the practical effect of differences: values larger than 0.2 were considered small, larger than 0.5 medium, and larger than 0.8 large[25].

For all statistical analyses, the significance level was established at $p < 0.05$.

## RESULTS

The patient and control groups had similar sex and age distributions (p Chi square = 0.09, p t test = 0.2). RMSD values were normally distributed.

On average, the RMSD of the lower third of the face obtained from the overlap of the pre-surgical images of the two hemifaces was 1.05 mm; this value remained practically unchanged for the acquisitions at 6, 12 and 24 months (on average, 1.09±0.47 mm). RMSD values for the middle and upper thirds of the face were somewhat smaller (respectively, 1.00±0.38 and 0.92±0.3 mm, **Table 2**). Two-way ANOVA did not reveal statistically significant differences in symmetry over time ($p = 0.98$). Among facial thirds there was a significant p value ($p = 0.04$): the lower facial third was more asymmetric than the upper one (Tukey's HSD $p < 0.05$). No significant time x facial third interaction was found. Partial eta squared statistic was small for both factors and the relevant interaction (facial third, $\eta^2 = 0.031$; time, $\eta^2 < 0.001$; interaction, $\eta^2 = 0.007$).

However, even though the statistical significance was not reached over time in any third of the face, it was possible to notice, for some patients, a trend of symmetry improvement at the 24 months follow-up for the lower, middle and upper thirds **(Figure 1)**. The patients are sorted by their pre-surgical asymmetry (RMSD values) in ascending order: patients F02, F06, F08, M02, and M03 are always among those with a low asymmetry, while patients F04, F07, M05 and M07 are always in top levels of asymmetry of the group.

In the upper facial third, all the patients who had a pre-surgical asymmetry larger than 1.3 mm, showed an improvement after 24 months; in contrast, among patients with low asymmetry, M03 and F02 had an increment of 46-65%. In the middle and lower facial thirds, facial asymmetry increased in about half of the patients, independently from the original situation; in the middle third, the largest increment was observed in patient F06 (83%), the largest decrement in patient M07 (-37%); in the lower third, M02 (108%) and F04 (-36%) had the largest variations. Overall, in patients F03, F04, M04, M07 post-surgical asymmetry reduced in all facial thirds, while in patients F02 and F08 it increased everywhere. Patients F01 had negligible variations of her facial asymmetry.

Z-score values (mean and SD) calculated before and 24 months after surgery are reported in **Table 3.** On average, patients z-scores differed less than 1 SD from the control values; they were significantly larger than those of the control group in all occasions except for the upper third in the 24 months follow-up ($p = 0.07$; Student's t test). For all the significant p values, a medium Cohen's effect size was found. In all facial thirds, no significant variations in z-score values were observed during the follow-up ($p > 0.05$), and all effect sizes were small.

## DISCUSSION

A crucial objective in maxillofacial surgery is the evaluation of the soft tissues and the estimation of facial asymmetry over time, since it may severely influence the patient's quality of life from a functional, aesthetic, and social prospect[1].

In the present study, the effect of bimaxillary surgery on the soft-tissue facial asymmetry of patients with skeletal Class III malocclusion was examined longitudinally. On average, the patients were more asymmetric than control subjects, both before and 24 months after surgery: the combined orthodontic and orthognathic treatment did not modify this aspect.

Acquisitions were made at different stages of treatment: in the pre-surgical phase and 6, 12 and 24 months after surgery. Following-up until 24 months after surgery allowed to obtain (possibly) definitive facial images of the patients, without alterations of soft tissues caused by edema and post-surgical orthodontic treatment, which in part affect the 6-month analysis[26,27].

Despite the numerous studies on 3D facial asymmetry assessment after orthognathic surgery, few were longitudinal, based on 3D optical devices, and considered a follow up longer than 12 months[2,13,15,16,28]. With regards to the imaging technique, stereophotogrammetry proved to be effective for obtaining accurate, reproducible and objective data on soft tissue changes and facial symmetry[21]. To ensure an accurate and reliable procedure, technical errors were controlled through the recalibration of the instruments before each data collection. The primary source of operator error was the correct identification and digitization of the landmarks of interest, as the following analyses were performed by the computer with algorithms that had negligible errors. The accurate identification and marking of facial landmarks was reviewed before data analysis[20,21,23].

Among the different mathematical methods proposed to investigate facial symmetry, the calculation of RMSD values had proved to be reproducible and accurate, also allowing a synthetic representation of results that may help patient's communication[2,3,21]. In particular, the portion of the facial surface evaluated in the study included the craniofacial components of interest for morphometric analyses, excluding hair, ears, and the neck. The subjects' face was divided into three thirds[21] (upper, middle and lower), following the distribution territories of the three major branches of the trigeminal nerve. Most of the studies that evaluated facial asymmetry considered only the entire patient's face[2,3,12,15]. The "whole face" approach does not accurately account for variations in symmetry that are majorly concentrated in different areas of the face. Conversely, the current method of facial division allows to study individually the level of symmetry in different facial portions. Such approach helps the surgeon in performing a more accurate patient analysis and may provide better clinical outcomes. Furthermore, colorimetric map generated by the software shows surgical results in an intuitive way **(Figure 2)**, thus enhancing increasing compliance in carrying out the treatment[22]. To better assess soft-tissue asymmetry in the facial lower third, patients were also analyzed by using sub-chin-vertex projections, as shown in **Figure 3** for one of the most asymmetric women. After surgery, the blue area (asymmetric part) decreased, with an increment in the green one (symmetric part).

In conformity with several researches, the present results confirm how the degree of asymmetry of patients with maxillary dysmorphism is, on average, larger than that of healthy patients[13,14,29,30].

In the current group of patients, the lack of significant differences in symmetry over time may be explained by their moderate pre-surgical asymmetry, as shown by their small or medium effect sizes relative to the control subjects values and the reduced z-scores. Considering individual patients, several factors may be analyzed to partly explain the variations in soft-tissue asymmetry: additional surgical procedures (three patients were submitted to genioplasty), intra- or postoperative complications (seven patients), amount of surgical movements, that could partly explain the variations in soft-tissue asymmetry.

The treatment of patient F06 included genioplasty: in her facial middle third, she had the largest increment in asymmetry (83%), but practically no variations in lower third symmetry. Also patient F05 underwent genioplasty; additionally, after surgery she had a temporary inferior alveolar nerve hypoesthesia and cervical pain. Overall, her 24-months soft-tissue asymmetry increased in the middle and lower facial thirds, and reduced in the upper one. The last patient who received genioplasty was F08, who unfortunately had a complication in her left side sagittal split osteotomy: her facial asymmetry, low before treatment, increased especially in the lower facial third (+55%).

Patient F02 had a pre-operative low asymmetry, that increased after surgery in all parts of the face: she underwent the largest maxillary advancement and mandibular rotation of the group, and lamented a temporomandibular joint disorder. A temporary inferior alveolar nerve hypoesthesia was lamented by patients F06, F01 and M02. F01 had negligible variations of facial asymmetry, while M02 had high increments in asymmetry (+108%). This patient underwent the largest mandibular set-back of the group.

Patients M06 and M08 had a severe bleeding after their Le Fort I osteotomy; at the 24 months evaluation, soft-tissue facial asymmetry was reduced in all facial thirds in M06, but increased in M08, especially in the middle third. This last patient had the largest maxillary advancement of the group. Patient M09 underwent the largest mandibular advancement: his soft tissue asymmetry increased in the middle and lower facial thirds.

Overall, in patients F03, F04, M04 and M07 post-surgical asymmetry reduced in all facial thirds, even if the surgical movements were of different amounts: low-moderate in M07 and F04; massive in F03, and with the second largest mandibular set-back of the group in M04. In synthesis, patients with pre-surgical low-moderate soft-tissue facial asymmetry had variable modifications that were partially explained by operative complications and additional surgical procedures.

Constraints stemming from the limited number of patients in this study must be taken into account. A larger group sample would indeed improve the clinical value of the results. Furthermore, it is important to consider that the first acquisition was obtained after the pre-surgical orthodontic treatment: the orthodontic correction may have influenced the actual facial asymmetry. Finally, we did not assess the effect of treatment on facial attractiveness and perceived symmetry, as recently done by Ostwald et al.[3]. It should be mentioned that the levels of asymmetry of the current group of patients were low-moderate, and possibly not perceived subjectively.

The present study illustrated a detailed longitudinal analysis of the impact of bimaxillary osteotomy surgery on the level of soft-tissue facial asymmetry in patients with Class III skeletal malocclusion.

The patients showed, on average, a larger asymmetry than healthy controls, that was maintained even at the 24 months follow-up. The analyzed data show that surgery did not improve facial asymmetry, except for those patients with an evident pre-surgical asymmetry degree. Bimaxillary surgery, however, did not worsen significantly the degree of asymmetry of patients with mild deviations from the norm.

**REFERENCES**


1. Cheong YW, Lo LJ. Facial asymmetry: etiology, evaluation, and management. Chang Gung Med J. 2011;34(4):341-51.
2. Wermker K, Kleinheinz J, Jung S et al. Soft tissue response and facial symmetry after orthognathic surgery. J Craniomaxillofac Surg. 2014;42(6):e339-45.
3. Ostwald J, Berssenbrügge P, Dirksen D, et al. Measured symmetry of facial 3D shape and perceived facial symmetry and attractiveness before and after orthognathic surgery. J Craniomaxillofac Surg. 2015;43(4):521-527.
4. Cullati F, Mapelli A, Beltramini G, et al. Surface electromyography before and after orthognathic surgery and condylectomy in active laterognathia: a case report. Eur J Paediatr Dent. 2017;18(2):131-138.
5. Ferrario VF, Sforza C, Dellavia C, et al. A quantitative three-dimensional assessment of soft tissue facial asymmetry of cleft lip and palate adult patients. J Craniofac Surg. 2003;14(5):739-46.
6. Sforza C, Laino A, D'Alessio R, et al. Soft-tissue facial characteristics of attractive Italian women as compared to normal women. Angle Orthod. 2009;79(1):17-23.
7. Thiesen G, Gribel BF, Freitas MP. Facial asymmetry: a current review. Dental Press J Orthod. 2015;20(6):110-25.
8. Kim JY, Kang MH, You JY, et al. Natural head postures of patients with facial asymmetry in frontal view are corrected after orthognathic surgeries. J Oral Maxillofac Surg. 2016;74(2):392-398.
9. Smeets D, Claes P, Vandermeulen D, et al. Objective 3D face recognition: Evolution, approaches and challenges. Forensic Sci Int. 2010;201(1-3):125-32.
10. Akhil G, Senthil Kumar KP, Raja S, et al. Three-dimensional assessment of facial asymmetry: A systematic review. J Pharm Bioallied Sci. 2015;7(Suppl 2):S433-7.
11. Kogou T, Takaki T, Shibahara T. Three-dimensional Analysis and Evaluation in Orthognathic Surgical Cases with Facial Asymmetry. Bull Tokyo Dent Coll. 2018;59(3):147-161.
12. Verhoeven T, Xi T, Schreurs R, et al. Quantification of facial asymmetry: A comparative study of landmark-based and surface-based registrations. J Craniomaxillofac Surg. 2016;44(9):1131-6.
13. Ferrario VF, Sforza C, Schmitz JH, et al. Three-dimensional facial morphometric assessment of soft tissue changes after orthognathic surgery. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1999;88(5):549-56.

14. Sforza C, Peretta R, Grandi G, et al. Three-dimensional facial morphometry in skeletal Class III patients. A non-invasive study of soft-tissue changes before and after orthognathic surgery. Br J Oral Maxillofac Surg. 2007;45(2):138-44.
15. Hajeer MY, Ayoub AF, Millett DT. Three-dimensional assessment of facial soft-tissue asymmetry before and after orthognathic surgery. Br J Oral Maxillofac Surg. 2004;42(5):396-404.
16. Verzé L, Bianchi FA, Dell'Acqua A, et al. Facial mobility after bimaxillary surgery in class III patients: a three-dimensional study. J Craniofac Surg. 2011;22(6):2304-7.
17. Verzé L, Bianchi FA, Schellino E, et al. Soft tissue changes after orthodontic surgical correction of jaws asymmetry evaluated by three-dimensional surface laser scanner. J Craniofac Surg. 2012;23(5):1448-52.
18. Verzé L, Bianchi FA, Barla N, et al. Facial Mobility after Maxilla-Mandibular Advancement in Patients with Severe Obstructive Sleep Apnea Syndrome: A Three-Dimensional Study. Int J Dent. 2017;2017:1574304.
19. Cullati F, Rusconi FME, Mapelli A, et al. Three-dimensional longitudinal evaluation of facial mimicry in orthognathic class III surgery. Int J Oral Maxillofac Surg. 2018 Oct 9. pii: S0901-5027(18)30374-6.
20. De Menezes M, Rosati R, Ferrario VF, et al. Accuracy and reproducibility of a 3-dimensional stereophotogrammetric imaging system. J Oral Maxillofac Surg. 2010;68(9):2129-35.
21. Codari M, Pucciarelli V, Stangoni F, et al. Facial thirds-based evaluation of facial asymmetry using stereophotogrammetric devices: Application to facial palsy subjects. J Craniomaxillofac Surg. 2017;45(1):76- 81.
22. Pucciarelli V, Tarabbia F, Codari M, et al. Stereophotogrammetric Evaluation of Labial Symmetry After Surgical Treatment of a Lymphatic Malformation. J Craniofac Surg. 2017;28(4):e355-8.
23. Gibelli D, Pucciarelli V, Cappella A, et al. Are Portable Stereophotogrammetric Devices Reliable in Facial Imaging? A Validation Study of VECTRA H1 Device. J Oral Maxillofac Surg. 2018;76(8):1772-84.
24. Sforza C, de Menezes M, Ferrario V. Soft- and hard-tissue facial anthropometry in three dimensions: what's new. J Anthropol Sci. 2013;91:159-84.
25. Cohen, J, Cohen, P, West, SG and Aiken, LS (2003) Applied multiple regression/correlation analysis for the behavioral sciences. Third Edition. Routledge: New York.
26. Proffit W.R. White R.P. Sarver D.M. Contemporary treatment of dentofacial deformity. Mosby. Chicago. 2003.

27. Aydemir H, Efendiyeva R, Karasu H, Toygar-Memikoğlu U. Evaluation of long- term soft tissue changes after bimaxillary orthognathic surgery in Class III patients. Angle Orthod. 2015;85(4):631-7.
28. Kobayashi T, Ueda K, Honma K, et al. Three-dimensional analysis of facial morphology before and after orthognathic surgery. J Cranio-Maxillofacial Surg. 1990;18(2):68–73.
29. Severt TR, Proffit WR. The prevalence of facial asymmetry in the dentofacial deformities population at the University of North Carolina. Int J Adult Orthodon Orthognath Surg. 1997;12(3):171-6.
30. Chew MT. Spectrum and management of dentofacial deformities in a multiethnic Asian population. Angle Orthod. 2006;76(5):806-9.

## FIGURE LEGENDS

**Figure 1:** RMSD values of the lower, middle and upper facial third of the analyzed 18 patients; blue striped bars: before surgery; red solid bars: 24 months follow-up. The patients are sorted by their pre-surgical asymmetry (RMSD values) in ascending order (the black horizontal lines show the mean RMSD values of the control group: upper third 0.77 mm, middle third 0.76 mm, lower third 0.81 mm).

**Figure 2**: Colorimetric maps showing the symmetry degree in the three facial thirds, before surgery (on the left) and 24 months after bimaxillary osteotomy (on the right), in a 26 years old woman. Green indicates a low level of asymmetry; red and blue indicate a high level of asymmetry. RMSD values: upper third 1.43 mm pre, 0.74 mm post 24 months; middle third 0.94 mm pre, 0.60 mm post 24 months; lower third 1.51 mm pre, 0.96 mm post 24 month.

**Figure 3:** Colorimetric maps showing the symmetry degree in the sub-chin-vertex projection, before surgery (on the left) and 24 months after bimaxillary osteotomy (on the right). The patient is the same of figure 2. Green indicates a low level of asymmetry; red and blue indicate a high level of asymmetry. RMSD values: 1.11 mm pre, 0.95 post 24 months.

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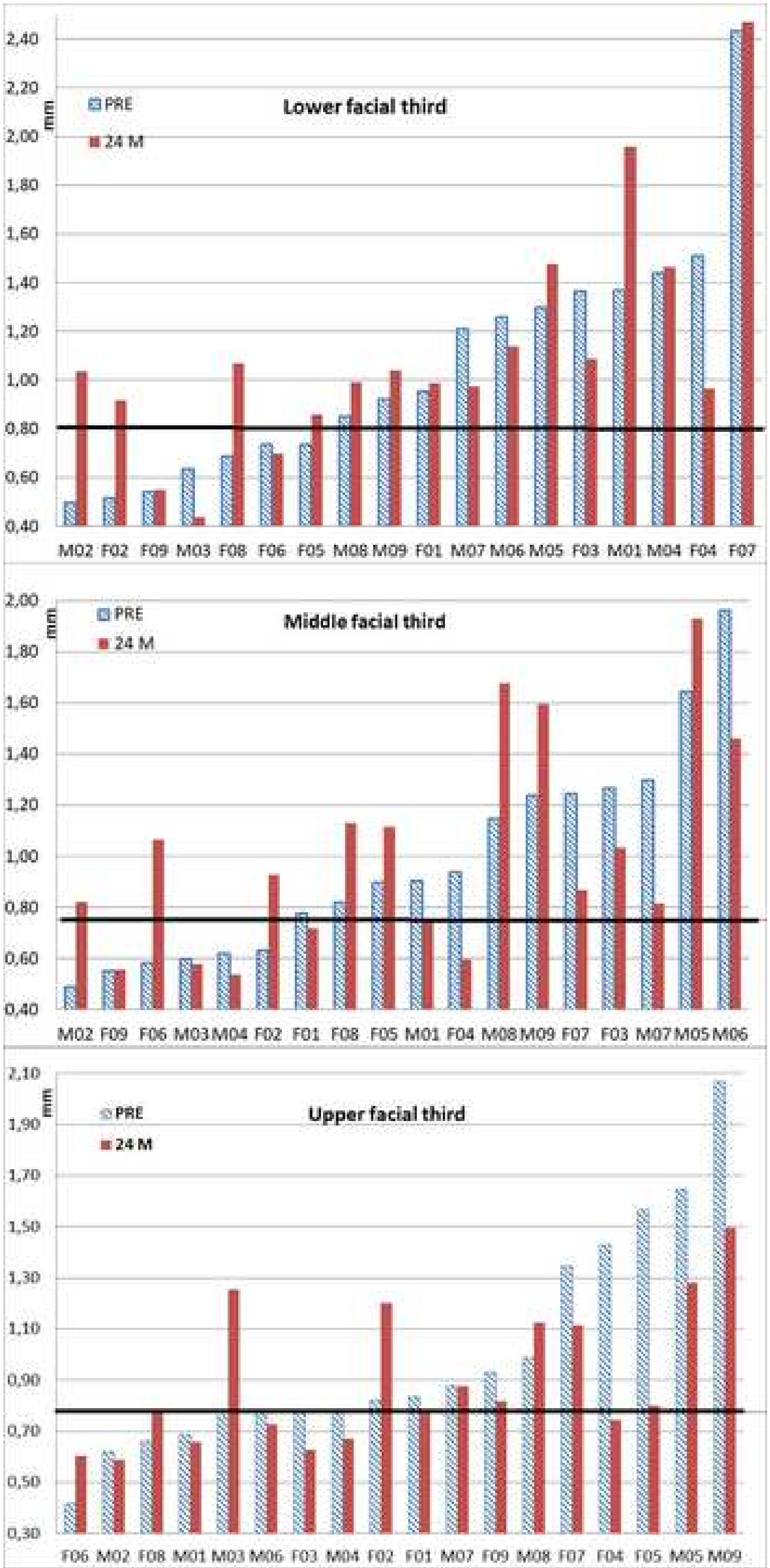

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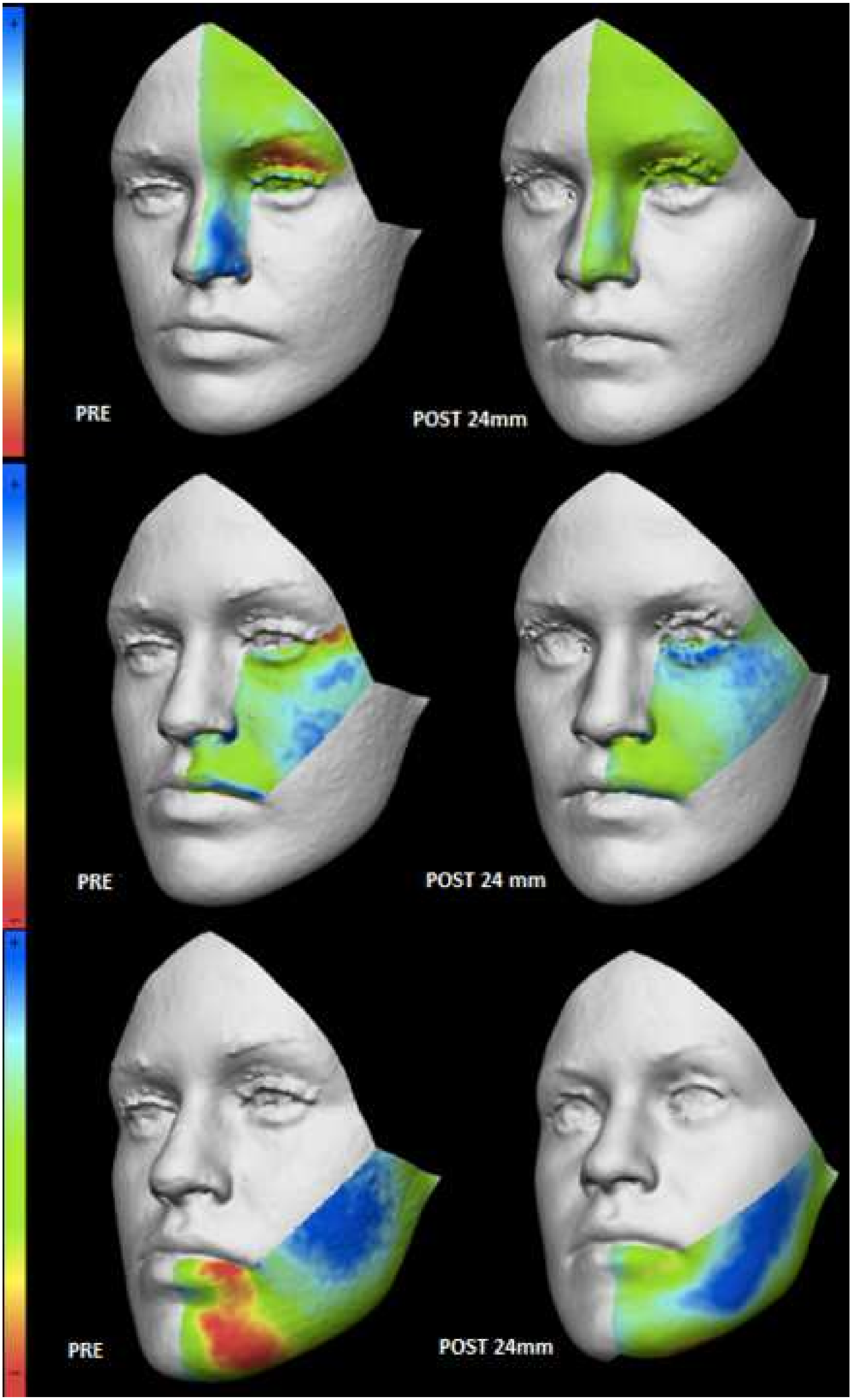

Figure 3



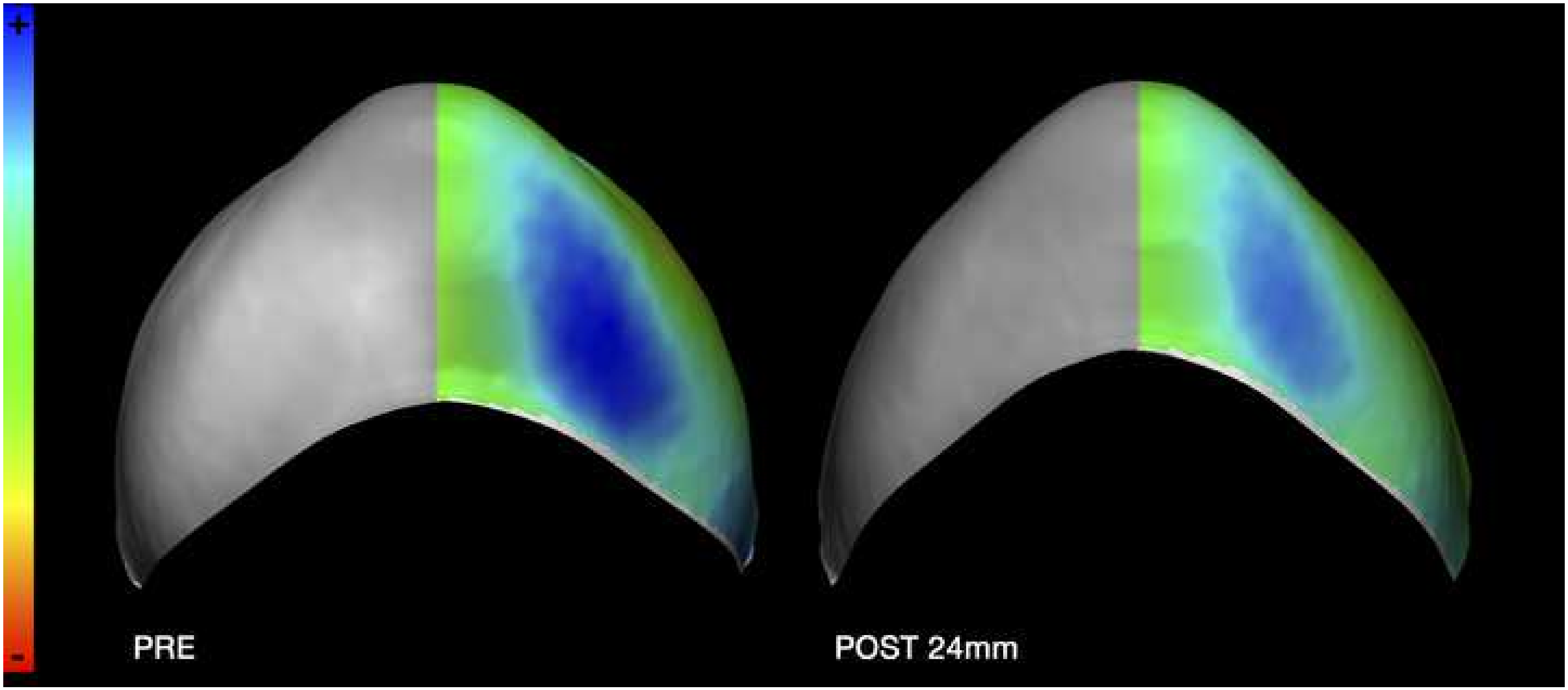

Table (one Table Per File. WORD format only)

**Table 1.** Analyzed patients and surgical interventions.

| | | **Maxillary movements (mm)** | | | **Mandibular movements (mm)** | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Patient** | **Age (y)** | Advancement | Impaction | Rotation | Advancement (+)/ setback (-) | Impaction | Rotation | **Additional surgical techniques** | **Complications** |
| **F01** | 34 | 3.0 | 2.6 | -- | -- | 4.9 | 1.0 Left | -- | Left IAN hypoesthesia (2 months) |
| **F02** | 24 | 5.1 | -- | 1.7 Left | -2.8 | 0.8 | 5.0 Left | -- | Right TMD |
| **F03** | 28 | 4.0 | 2.9 | 1.2 Left | -2.6 | 6.4 | 1.6 Left | -- | - |
| **F04** | 26 | 4.3 | 0.2 | -- | 3.4 | 0.7 | 0.6 Right | -- | - |
| **F05** | 29 | 1.2 | 1.3 | 1.2 Right | 1.1 | 1.7 | 2.4 Right | Genioplasty | Bilateral IAN hypoesthesia (8 months) |
| **F06** | 21 | 2.0 | 2.0 | -- | -1.6 | 3.5 | 0.5 Left | Genioplasty | - |
| **F07** | 23 | -- | 0.8 | 3.2 Left | -2.7 | 3.0 | 3.1 Left | -- | - |
| **F08** | 26 | 2.7 | 0.6 | -- | -1.5 | -- | 0.6 Left | Genioplasty | Left bad split in SSO |
| **F09** | 21 | 2.8 | 5.2 | 2.5 Left | | | 1.0 Left | -- | -- |
| **M01** | 28 | 4.1 | 1.9 | -- | 0.5 | 3.1 | 3.0 Left | -- | - |
| **M02** | 30 | 3.4 | -- | 1.6 Left | -7.0 | -- | 2.3 Right | -- | Left IAN hypoesthesia (6 months) |
| **M03** | 25 | 4.1 | -- | -- | -0.8 | 1.8 | 2.0 Left | -- | - |
| **M04** | 34 | 2.1 | -- | 1.3 Left | -5.8 | 0.5 | 1.4 Right | -- | - |
| **M05** | 33 | 4.3 | 2.0 | -- | -1.4 | 2.6 | 2.4 Right | -- | - |
| **M06** | 30 | 3.1 | -- | 1.4 Left | -3.4 | 1.9 | 4.3 Right | -- | Le Fort I osteotomy severe bleeding |
| **M07** | 23 | 3.0 | 0.2 | 1.7 Left | -2.8 | 1.96 | -- | -- | - |
| **M08** | 51 | 5.2 | 4.1 | 3.1 Left | 2.3 | -- | -- | -- | Le Fort I osteotomy severe bleeding |
| **M09** | 23 | 1.6 | 4.0 | -- | +6.9 | 2.4 | 3.2 Left | -- | -- |

Age at surgery. All patients underwent an Obwegeser/Dal Pont bilateral sagittal split osteotomy and Le Fort I osteotomy.
IAN, inferior alveolar nerve; SSO, sagittal split osteotomy; TMD, temporomandibular joint disorder.

**Table 2:** Mean and SD of the RMSD values for the different facial thirds, before surgery and 6, 12 and 24 months after surgery.

| | Upper third | | | | Middle third | | | | Lower third | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | PRE | 6 M | 12 M | 24 M | PRE | 6 M | 12 M | 24 M | PRE | 6 M | 12 M | 24 M |
| Mean | 1.00 | 0.90 | 0.89 | 0.90 | 0.98 | 0.99 | 1.02 | 1.01 | 1.05 | 1.07 | 1.14 | 1.12 |
| SD | 0.43 | 0.26 | 0.25 | 0.28 | 0.41 | 0.38 | 0.39 | 0.41 | 0.49 | 0.49 | 0.49 | 0.48 |

**Table 3:** Mean and SD of the z-score values for the different facial thirds, before surgery and 24 months after surgery.

| | Upper Third | | Middle Third | | Lower Third | |
|---|---|---|---|---|---|---|
| | PRE | 24 M | PRE | 24 M | PRE | 24 M |
| Mean | 0.82 | 0.44 | 0.72 | 0.83 | 0.78 | 0.98 |
| SD | 1.54 | 0.97 | 1.35 | 1.37 | 1.54 | 1.53 |
| *P value control* | 0.037* | 0.07 | 0.04* | 0.02* | 0.05* | 0.015* |
| *Cohen d* | 0.533 M | 0.455 S | 0.535 M | 0.603 M | 0.504 M | 0.639 M |
| *P value time* | 0.193 | | 0.984 | | 0.741 | |
| *Cohen d* | 0.297 S | | 0.078 S | | 0.132 S | |

P values are from Student's t test (*significantly different from control group values).
Cohen d: S, Small effect; M, Medium effect; L, Large effect [25].