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Title: Facial thirds-based evaluation of facial asymmetry using stereophotogrammetric devices: application on facial palsy subjects

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Keywords: Facial Asymmetry; Photogrammetry; Facial Paralysis

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Abstract: Many conditions can compromise facial symmetry, resulting in an impairment of the affected people from both aesthetical and functional points of view. For these reasons a detailed, focused and objective evaluation of facial asymmetry is advised, both for surgical planning and treatment evaluation.
In this study we present a new quantitative method to assess symmetry in different facial thirds, objectively defined on the territories of distribution of trigeminal branches.
Seventy subjects (40 healthy controls and 30 patients, affected by unilateral facial palsy) were acquired with a stereophotogrammetric system and the level of asymmetry of their hemi-facial thirds was evaluated, comparing the root mean square of the distances (RMSD) between their original and mirrored facial surfaces.
Results show a high average reproducibility of area selection (98.8%) and significant differences in RMSD values between controls and patients ($p=0.000$) for all the facial thirds. No significant differences were found on different thirds among controls ($p>0.05$), while significant differences were found for upper, middle and lower thirds of patients ($p=0.000$).
The presented method provides an accurate, reproducible and local facial symmetry analysis, that can be used for different conditions, especially when only part of the face is asymmetric.

Milan, 07 June, 2016

Professor J. Wiltfang, Klinik fur Mund, Kiefer-. und Gesichtschirurgie, Universitätsklinikum Schleswig – Holstein, Campus Kiel, Arnold-Hellerstr. 16, 24105, Kiel, Germany,

Editor in-Chief, *Journal of Cranio-Maxillo-facial Surgery*

Dear professor **Wiltfang**,

Please find enclosed the MS "Facial thirds-based evaluation of facial asymmetry using stereophotogrammetric devices: application on facial palsy subjects" by Marina Codari, Valentina Pucciarelli, Fabiano Stangoni, Matteo Zago, Filippo Tarabbia, Federico Biglioli, and Chiarella Sforza", which I would like to submit as original MS to the *Journal of Cranio-Maxillo-facial Surgery*.

The authors certify that

- the current "Guide for Authors" has been read, the text has been written in compliance with those instructions and we accept the conditions posed;
- they have seen and agreed to the submitted version of the paper, and bear responsibility for it;
- the material is original, and it has been neither published elsewhere nor submitted for publication simultaneously.

If accepted, the paper will not be published elsewhere in the same or similar form, in English or in any other language, without written consent of the copyright holder.

Thank you for your kind attention.
Sincerely

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Professor Jörg Wiltfang, MD, DMD, PhD
Editor-in-Chief
Journal of Cranio-Maxillofacial Surgery

Milan, 27 September 2016

Dear professor Wiltfang,

Please find enclosed the revised version of MS # JCMS-D-16-00546 "Facial thirds-based evaluation of facial asymmetry using stereophotogrammetric devices: application on facial palsy subjects" by Marina Codari, Valentina Pucciarelli, Fabiano Stangoni, Matteo Zago, Filippo Tarabbia, Federico Biglioli, and Chiarella Sforza.

The title page was modified as kindly requested, and all modifications are highlighted in yellow.

We would like to thank you and the reviewer for all the time and expertise you are devoting to our submission. I trust that the present version of the MS will be suitable for publication in the Journal of Cranio-Maxillofacial Surgery.

Thank you for your kind attention.

Sincerely

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Facial thirds-based evaluation of facial asymmetry using stereophotogrammetric devices: application on facial palsy subjects.

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Summary:

Many conditions can compromise facial symmetry, resulting in an impairment of the affected people from both aesthetical and functional points of view. For these reasons a detailed, focused and objective evaluation of facial asymmetry is advised, both for surgical planning and treatment evaluation.

In this study we present a new quantitative method to assess symmetry in different facial thirds, objectively defined on the territories of distribution of trigeminal branches.

Seventy subjects (40 healthy controls and 30 patients, affected by unilateral facial palsy) were acquired with a stereophotogrammetric system and the level of asymmetry of their hemi-facial thirds was evaluated, comparing the root mean square of the distances (RMSD) between their original and mirrored facial surfaces.

Results show a high average reproducibility of area selection (98.8%) and significant differences in RMSD values between controls and patients ($p=0.000$) for all the facial thirds. No significant differences were found on different thirds among controls ($p>0.05$), while significant differences were found for upper, middle and lower thirds of patients ($p=0.000$).

The presented method provides an accurate, reproducible and local facial symmetry analysis, that can be used for different conditions, especially when only part of the face is asymmetric.

Keywords: Facial Asymmetry, Photogrammetry, Facial Paralysis

1. **INTRODUCTION**

Many pathologies can result in facial asymmetry. Among those, hemifacial microsomia, cleft lip/ palate, mandibular osteochondroma, trauma and infections, untreated mandibular fractures and damage to facial nerves are mentionable. In particular, facial nerve palsy, which can be due to different etiologies, from neoplasm to infective, traumatic, congenital and metabolic causes, can strongly alter facial harmony (Melvin and Limb 2008). Furthermore, environmental factors, as chewing and sucking habits, or craniofacial syndromes, can compromise facial symmetry (Bishara, Burkey and Kharouf 1994; Avelar *et al.* 2010). The amount of asymmetry of the face can vary among subjects, ranging from unperceived or subclinical cases to evident and clear ones. In those cases, aesthetics, appearance and functionality of the orofacial district can be severely affected, leading to discomfort and dissatisfaction of the patients for their own facial appearance (Kim *et al.* 2015; Thiesen *et al.* 2015).

To both improve aesthetics and correct functional defects, an objective, quantitative assessment of facial asymmetry is advised. The quantification of asymmetry can be especially useful during surgical treatment planning, but it can also be performed during follow up examinations, allowing surgeons and dentists to evaluate the progressive reduction of asymmetry, therapy progression and achieved results (Claes, Walters and Clement 2012; Chatrath *et al.* 2016; Verhoeven *et al.* 2016).

The evaluation of facial morphology evolved during the last decades, passing from the direct measurement to an indirect assessment of the face, through two- and three-dimensional imaging systems (Smeets *et al.* 2010). These technologies can allow not only a facial analysis based on landmarks, but also the investigation of the whole surface (Richtsmeier, DeLeon and Lele 2002). Surface assessments have already been found to be more sensitive than landmark measurements (Verhoeven *et al.* 2016). Currently, facial asymmetry is mainly evaluated using the entire facial surface, thus providing measurements that give only general information about facial morphology (Ostwald *et al.* 2015; Verhoeven *et al.* 2016). In contrast, several pathologies affecting facial appearance are localized in selected parts of the face (Avelar *et al*. 2010; Djordjevic *et al*. 2014a), and a local assessment can provide helpful information for clinical decisions.

In this study, we introduce a new method that combines surface and landmarks based approaches to assess facial asymmetry, taking different facial thirds into account, in order to provide local information. The intra-operator repeatability of the method was assessed, and a practical application in patients with unilateral facial palsy was made.

2. MATERIAL AND METHODS

2.1. Sample:

Seventy adult Caucasian subjects were voluntarily recruited for this study. This sample was composed of 40 healthy subjects (21 females; 19 males; average age 39 ± 12 years) and 30 patients with diagnosed unilateral facial palsy (15 females; 15 males; average age 44 ± 15 years). All healthy subjects had no history of facial trauma, maxillofacial surgery and craniofacial syndromes or deformities. Among the patients, the etiology of the facial nerve palsy was: oncological surgery (71%), Bell's palsy (18%), trauma (7%) and brainstem embolus due to arterio-venous malformations (4%).

2.2. Image acquisition:

All the involved subjects were acquired using the VECTRA M3 stereophotogrammetric system (Canfield Scientific Inc., Fairfield, NJ), which allows to scan their faces in a fast and non-invasive way (Sforza, de Menezes and Ferrario 2013). Before the acquisition, 50 soft tissue facial landmarks were marked using black liquid eyeliner; following a protocol that was previously developed, tested and validated by our research group (Ferrario *et al.* 1998; De Menezes *et al.* 2010). During the acquisition, subjects were asked to have a neutral facial expression of the face, with teeth in loose contact and closed mouth. The institutional review board of the University of Milan (approval n. 92/2014) approved all the described procedures and all patients gave their written informed consent to them.

After the acquisition process, the facial landmarks were digitally marked on each surface, to delimit the portions of the face used for asymmetry evaluation, using the manufacturer's software (Mirror Vectra; Canfield Scientific Inc., Fairfield, NJ).

2.3 Asymmetry quantification:

In order to define the portion of face used to evaluate the asymmetry of the subject, 10 facial landmarks were selected. A detailed list of these landmarks is provided in Table 1. Landmark selection allows to delimit the facial surface in a standard and repeatable way, thus reducing operator dependency. An example of the selected surface is depicted in Figure 1.

Intra-operator repeatability of facial area (FA) selection was evaluated on a training sample of 20 facial surfaces. One experienced operator selected the different facial thirds and the FA twice with a two week interval. The repeatability was assessed on facial surface selection since it is the main cause of variability in surface mirroring approaches, as further image processing steps are automated. After landmark identification, the Mirror Vectra software (Canfield Scientific Inc., Fairfield, NJ) automatically computed the surface area.

The selected surface was then used to calculate the plane of maximum symmetry, this process allowed to automatically find the midline plane of symmetry using only a previously selected area on the acquired facial surface. In this study, the selected area was defined in order to minimize the regions that can affect asymmetry quantification, such as hairs and neck region, and to take all the craniofacial structures of interest for maxillofacial morphometric analysis into account. This processing step was carried out using the Mirror imaging software (Canfield Scientific Inc., Fairfield, NJ).

Once the plane of maximum symmetry was obtained, it was used as mirroring plane to obtain the reflected face of each subject.

The original facial surface was then divided in two hemi-face surfaces, that were subsequently subdivided into three different facial thirds: upper (UT), middle (MT) and lower third (LT). In the proposed method, facial thirds division was based on the territories of distribution of trigeminal branches, which correspond to different embryological origins (Holmes, 2016). Each third was defined using anatomical landmarks, thus providing a standard and repeatable selection criterion. The list of landmarks used to define each facial third is provided in Table 1 while an example of facial third selection is depicted in Figure 2.

Finally, to quantify the asymmetry of each facial third in each subject, the root mean square deviation (RMSD) between original and reflected surfaces was calculated. A color-coded surface map displayed the local values of the distances between the two surfaces, as it can be seen in Figure 3. The RMSD has already proved to be a reproducible and accurate way to measure facial asymmetry, using three-dimensional photogrammetric systems (Taylor *et al.* 2014).

2.4. Statistical Analysis

Chi square test was used to check differences in sex distribution between control and patient groups, while unpaired Student's t-test was used to check age difference.

The repeatability in surface area selection was tested using Bland and Altman analysis for both the total facial area and each facial third. For repeated area measurements, the bias value, that corresponds to the systematic error, and the repeatability coefficient (RC), that represents the least detectable difference among measurements and it is twice the standard deviation of measurement differences (Bland and Altman 1986), were calculated.

Boxplot were used for representing RMSD values of different facial thirds in different subject groups. Normality distribution of the data was tested using the Kolmogorov-Smirnov-test. RMSD of different facial thirds in both control and pathological subject were positively skewed; so logarithmic transformation of the data was performed in order to obtain normal distributions. After this transformation, a two-way ANOVA analysis was performed in order to check if there were statistical significant differences among groups and facial thirds. Post hoc analyses were performed using Fisher's LSD test. The statistical level of significance was set to $p<0.05$ for all tests.

3. RESULTS

In this study, 40 control subjects and 30 patients with diagnosed unilateral facial palsy were analyzed. No statistically significant differences were found in age ($p = 0.1$, Student's t) and sex distribution ($p = 0.84$, chi-square).

The statistical analysis of the repeated area measurements showed high level of reproducibility. Bland and Altman plots and the values of bias, standard deviation (SD), repeatability coefficient and reproducibility are respectively reported in Figure 4 and Table 2.

Values of RMSD in control subjects and patients, divided for each facial third, are presented in Figure 5. Overall, patients had a larger asymmetry in all facial thirds than control subjects; the difference appears particularly evident for the middle and lower thirds.

Two-way ANOVA showed a statistically significant difference in RMSD values between control subjects and patients ($p = 0.000$). A significant effect of facial third was also found ($p = 0.0014$), together with a significant group x third interaction ($p = 0.0012$). Among different thirds, the RMSD values of the UT resulted significantly different from the ones of the MT ($p = 0.005$) and LT ($p = 0.003$). Post hoc analysis showed that among control subject there was no significant difference between different thirds ($p > 0.05$). On the other hand, in patients there was a significant difference between UT and MT ($p = 0.001$) and between UT and LT ($p = 0.000$). Comparing the same third between control and patient groups, statistically significant differences were found in all occasions ($p = 0.000$).

4. DISCUSSION

The evaluation and quantification of facial asymmetry is a key task in maxillofacial surgery and orthodontics, since a lot of conditions can alter it, thus compromising the patient quality of life from functional, aesthetic and social points of view (Berlin *et al.* 2014).

The introduction of noninvasive and inexpensive imaging procedures, e.g. laser scan and stereophotogrammetry, speeded up the research in this field and, in the last years, a lot of works were published on this topic, suggesting different approaches to assess facial asymmetry (Berssenbrügge *et al.* 2014; Alqattan *et al.* 2015; Kornreich *et al.* 2016; Verhoeven *et al.* 2016). Unfortunately, none of them is universally accepted from the scientific community, thus demonstrating that is still necessary to improve these procedures (Djordjevic *et al.* 2014a).

In the proposed method, we analyzed symmetry comparing original and mirrored facial surfaces and calculating the RMSD of the distances between their corresponding points. This approach is well known in the literature and it has proved to be a potentially powerful method to analyze facial symmetry (Djordjevic *et al.* 2014b; Taylor *et al.* 2014; Ostwald *et al.* 2015).

Traditionally, the whole face is used to measure the asymmetry level of the subject, thus providing only a global evaluation of facial morphology (Kornreich *et al.* 2016; Verhoeven *et al.* 2016). In this study, we divided each hemi-face in thirds, based on trigeminal branches distribution territories for somatic sensitivity. Other studies tried to provide a local subdivision of the face using horizontal planes, thus obtaining irregular edges of selected thirds due to subjective selection of the facial area (Djordjevic *et al.* 2014a; Taylor *et al.* 2014; Ozsoy 2016).

In the proposed method, facial area selection is the only manual image processing step needed to quantify the asymmetry of the face using surface mirroring approaches. To obtain a standardized imaging method it is essential to reduce the variability among different measurements as low as possible. For this reason, the selection of the FA plays a key role in asymmetry assessment on 3D facial surfaces. In the proposed method, the standardized definition of thirds allowed to reach a very high level of reproducibility during area selection, which is the main source of variability in asymmetry quantification. Repeatability analysis shows an average RC value (± SD) equal to 1.2% ± 0.005%, proving a high level of agreement between repeated measurements. As shown by the Bland and Altman plot in Figure 4, the bias is always near to 0% (average bias value 0.03% ± 0.001%), thus demonstrating the absence of systematic errors during repeated measurements. Moreover, the division of the face in thirds allows to focus treatment planning and follow up evaluations on the most asymmetric region.

To validate the proposed method, both patients with diagnosed unilateral facial palsy and control subjects, matched for gender and age, were enrolled. Unilateral facial palsy causes an evident asymmetry of the facial soft tissues, so it can be considered a perfect condition for testing this method within a clinical context. Other investigations used artificial, mathematically originated facial asymmetries that can be difficulty translated into daily practice (Verhoeven *et al.* 2016).

In all subjects, the asymmetry was quantified calculating the RMSD of corresponding points belonging to mirrored hemi-facial thirds. The results show that patients had a significantly less asymmetric UT compared to the middle and lower thirds. Indeed, the UT is mainly composed by the frontal region, which is the area less affected by facial palsy. On the other hand, despite the fact that this third is less asymmetric than the other two, it is still more asymmetrical in patients than in control subjects. That can also be explained by the fact that the upper eyelid/ superior orbital region, which is strongly altered in facial nerve palsy, is part of our UT. Among control subjects, there was no significant difference in RMSD values of different thirds, thus confirming the recent observations of Djordjevic et al. (Djordjevic *et al.* 2014b).

These results proved the accuracy of the proposed method in asymmetry quantification, both in physiological and pathological conditions, allowing clinicians to use it in different kind of pathologies. Moreover, the strong reproducibility of this method makes it suitable for follow up evaluations in different craniofacial conditions.

5. CONCLUSION

With this study a facial third-based method for the analysis of facial asymmetry is provided. The method showed high reproducibility and accuracy in evaluating differences between control subjects and patients. Moreover, it is applicable for diagnosis, treatment planning and evaluation in patients with altered craniofacial morphology. In particular, the method appears suitable for pathologies that alter only part of the face, providing quantitative local information about facial symmetry.

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Table 1. Landmarks used to define facial area and the different facial thirds.

Landmarks	
Facial area (FA)	trichion (tr); frontotemporale (ft); zygion (zy); tragion (t); gonion (go); gnation (gn)
Upper third (UT)	trichion (tr); glabella (g); nasion (n); pronasale (prn); columella (c); alare (al); endocantion (en); exocantion (ex); frontotemporale (ft)
Middle third (MT)	endocantion (en); alare (al); upper terminal of the nostril (stn); columella (c); subnasale (sn); labiale superius (ls); stomion (sto); chelion (ch); zygion (zy); frontotemporale (ft); exocantion (ex)
Lower third (LT)	Stomion (sto), labiale inferius (li); sublabiale (sl); pogonion (pg); gnation (gn); gonion (go); tragion (t); zygion (zy); cheilion (ch)

Table 2. Results of Bland and Altman analysis. Bias, SD and RC of area measurements are reported for upper (UT), middle (MT) and lower (LT) thirds and the whole facial area (FA)

	UT		MT		LT		FA
	Left	**Right**	**Left**	**Right**	**Left**	**Right**	
Bias [cm^2]	- 0.003	-0.051	-0.039	-0.028	0.097	0.043	0.075
SD [cm^2]	0.319	0.372	0.393	0.329	0.340	0.267	0.479
RC [%]	0.9	1.1	1.7	1.4	1.4	1.1	0.6

Figure 1. Facial area (FA) selected to evaluate asymmetry, based on the more external anthropometric landmarks of the face. Landmarks that are not visible from the frontal view are shown in white; r and l indicate right and left side of the face, respectively.

Figure 2. (a) Upper facial third (UT); (b) Middle facial third (MT); (c) Lower facial third (LT); each one defined by the respective anatomical landmarks, chosen to follow the territories of distribution of trigeminal branches.

Figure 3. Color coded maps for the local distances between the original and mirrored facial areas. (a) Upper third; (b) Middle third; (c) Lower third.

Figure 4. Bland and Altman plots for the area repeated measurements. Continuous line indicates the average; dashed lines indicate the interval of agreement.

Figure 5. Box plots, representing Root Mean Square (RMS) values of controls subjects and patients for upper, middle and lower facial third.

*Title Page

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No grants were obtained for this investigation.

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Figure 1

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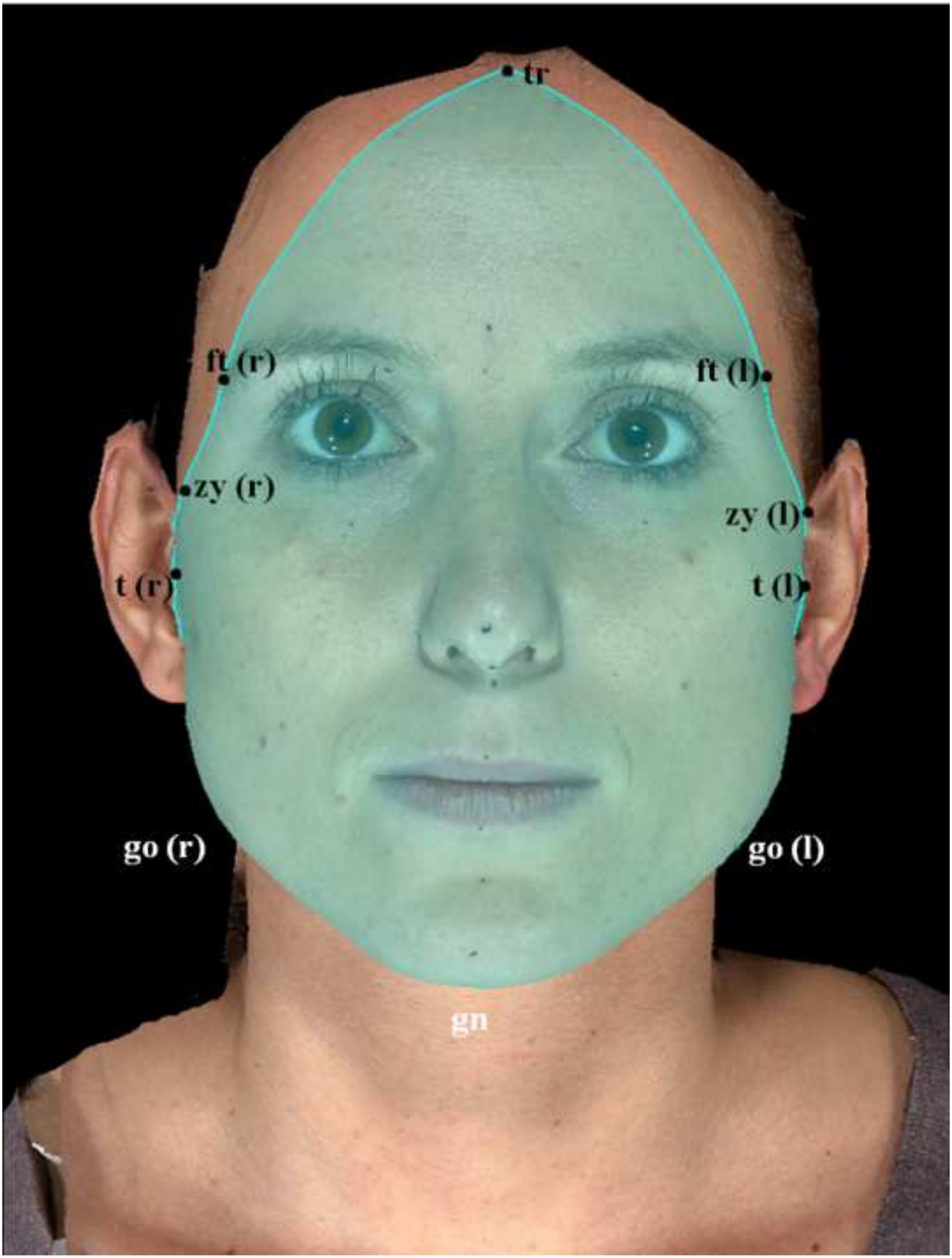

Figure 2

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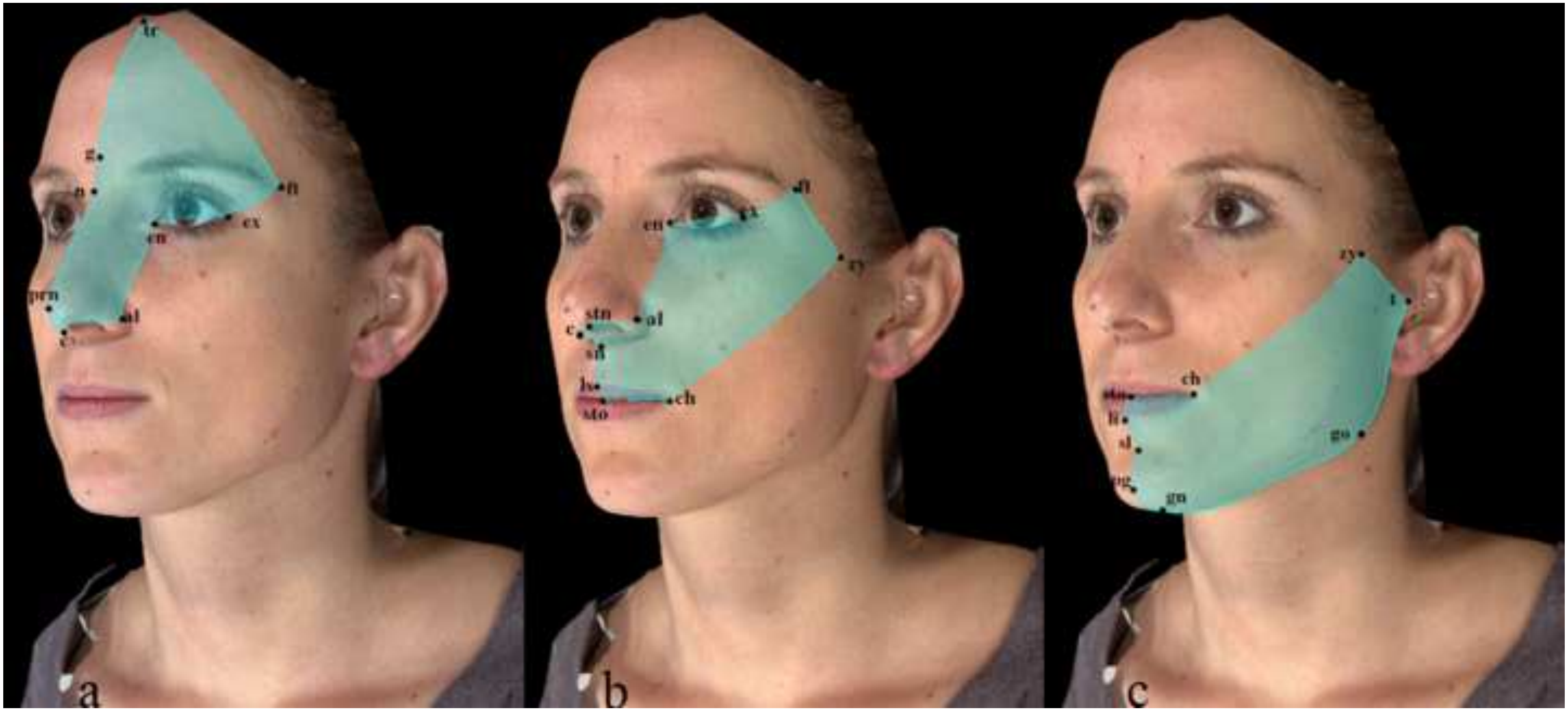

Figure 3
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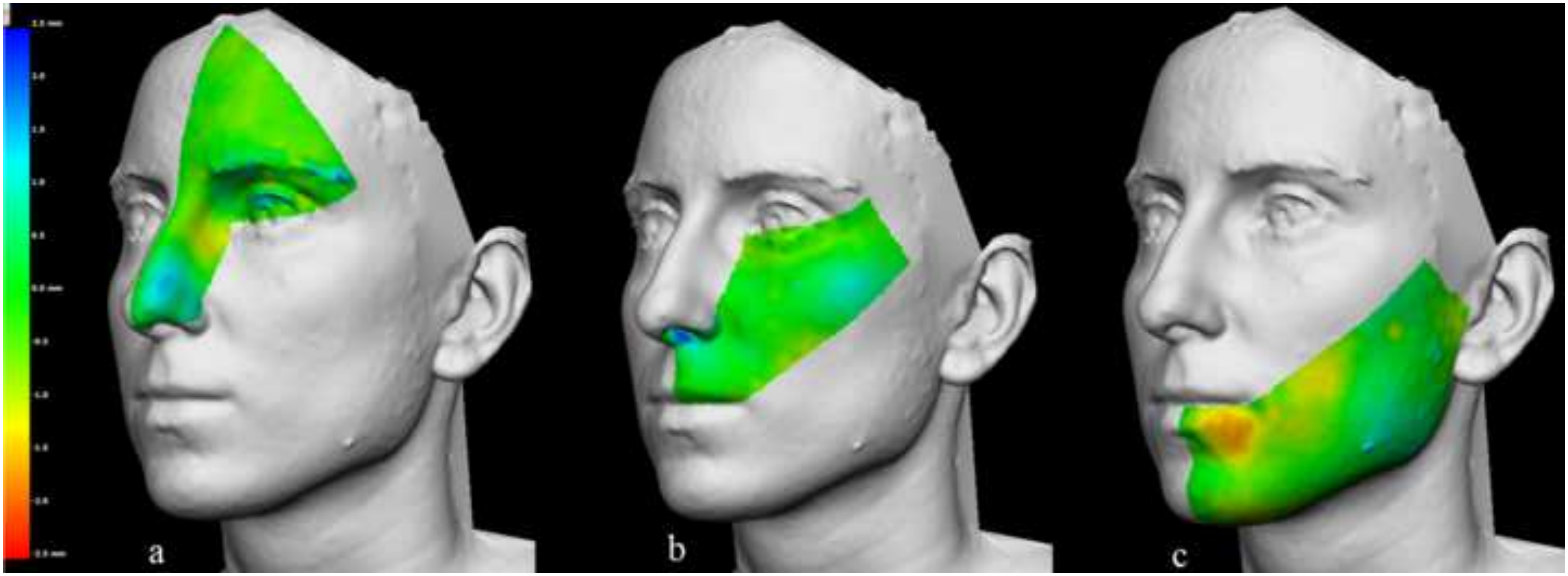

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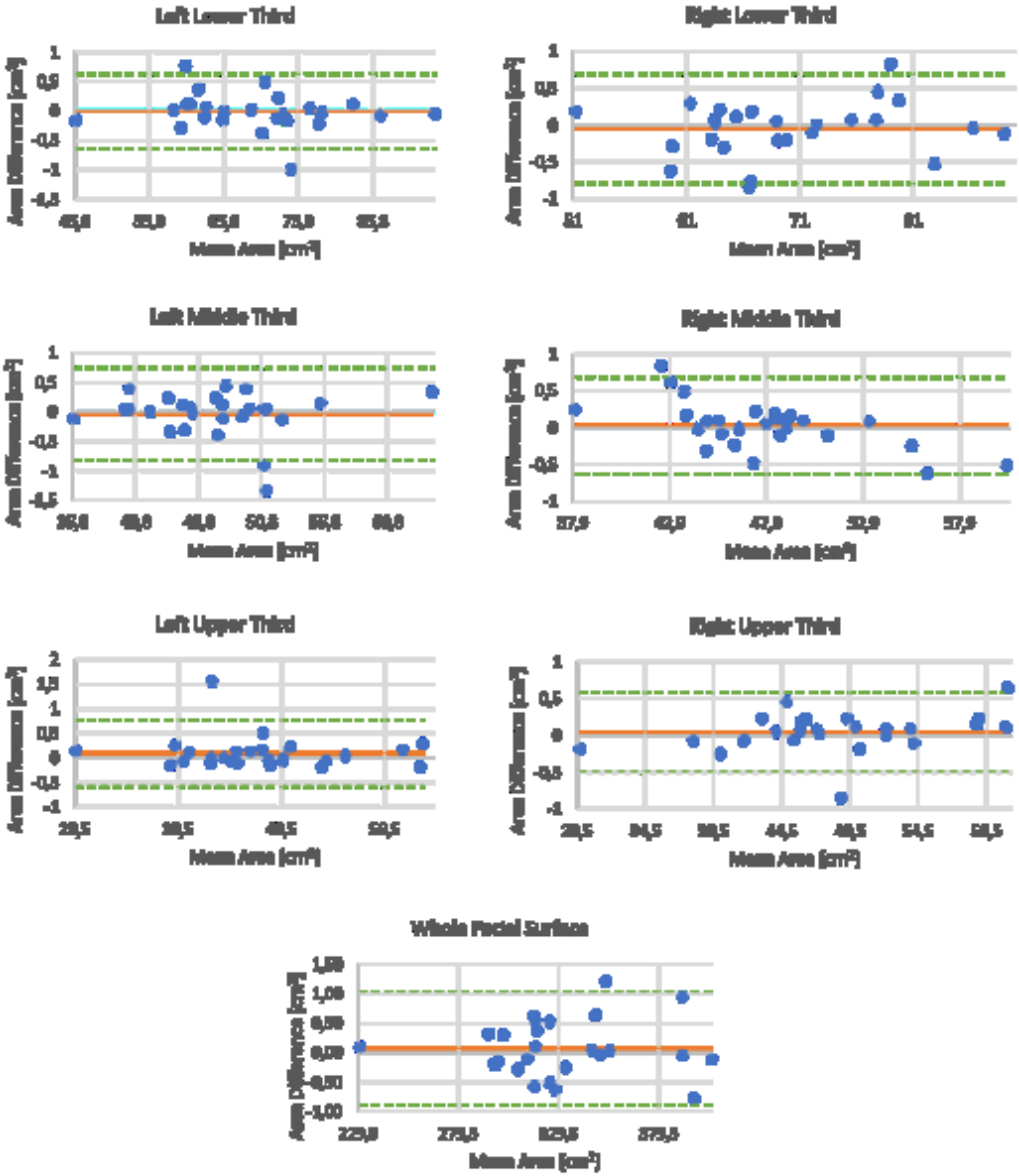

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