



Al-Rudainy, D. , Ju, X., Mehendale, F. V. and Ayoub, A. (2018)
Longitudinal 3D assessment of facial asymmetry in unilateral cleft lip and
palate. *Cleft Palate: Craniofacial Journal*,
(doi: [10.1177/1055665618780108](https://doi.org/10.1177/1055665618780108))

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Deposited on: 12 June 2018

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Longitudinal 3D assessment of facial asymmetry in Unilateral Cleft Lip and Palate (UCLP)

Abstract

Objective: longitudinal evaluation of asymmetry of the surgically managed UCLP to assess the impact of facial growth on facial appearance.

Design: Prospective study.

Setting: Glasgow Dental Hospital and School, University of Glasgow, U.K.

Patients: 15 UCLP infants.

Method: This study was carried out on 15 UCLP cases (mean age 3.8 ± 0.7 months old), 3D facial images were captured for each infant before surgery, 4 months after surgery and at four years follow-up using stereophotogrammetry. A generic mesh, a mathematical facial mask that consists of thousands of points, was conformed on the 3D images. Using Procrustean analysis, average facial meshes were obtained for each age group. A mirror image was mathematically obtained for each average mesh for the analysis of facial dysmorphology. Facial asymmetry was assessed by measuring the discrepancies between corresponding vertices of the original and mirror conformed meshes and was displaced using colour coded map. The asymmetry was further examined in each of the three directions, horizontal, vertical and anteroposterior.

Results: There was clear improvement of facial asymmetry following the primary repair of cleft lip. Residual asymmetry was detected around the nasolabial region. Facial growth accentuated the underlying facial asymmetry in three directions, the philtrum of the upper lip was deviated towards the scar tissue on the cleft side. Asymmetry of the nose was significantly worse at four-year follow-up.

Conclusion: Residual asymmetry of UCLP was more pronounced at four years following the surgical repair of UCLP in all three directions. Dense correspondence analysis is a reliable and innovative tool for the comprehensive analysis of facial morphology.

Keywords: longitudinal study, facial asymmetry, dense correspondence analysis, cleft children, 3D images, directions of asymmetry.

Introduction

One of the aims of the primary surgery of cleft lip and palate is to improve facial appearance, where restoring facial symmetry is of paramount importance (Nadjmi et al., 2016). Unfortunately, the surgically managed cleft cases can be left with residual facial asymmetry, and secondary surgery may be necessary. Objective quantification of facial asymmetry following primary cleft lip repair is an important outcome measure for successful surgery (Bell et al., 2014). Stereophotogrammetry is an excellent choice for facial imaging of cleft patients, especially children, due to its safety and short acquisition time, which is about 1 millie second. The first attempt for the assessment of cleft-related facial asymmetry using stereophotogrammetry was by Ras et al. in 1994. Since then, several studies have evaluated facial asymmetry related to cleft lip and palate (Stauber et al., 2008; Meyer-Marcotty et al., 2011; Bugaighis et al., 2013; Djordjevic et al., 2014; Kuijpers et al., 2015). The evaluation of facial asymmetry was carried out a few years after primary surgery, though the surgical repair is usually performed in the early months of life.

There is also limited information in the literature regarding the impact of facial growth on the residual facial asymmetry following cleft repair. Consequently, It is unclear whether the harmony between the groups of facial muscles will or could improve with time. Such uncertainty could have an impact on the timing of lip revision surgery to deal with the residual scarring which contributes to facial asymmetry. However, the longitudinal evaluation of facial asymmetry of the surgically managed cleft cases is rare. Most of the published data on of facial morphology of cleft cases are based on the analysis of few facial landmarks (Hood et al., 2003). This landmraks based analysis provided a limited and sparse informtaion on fcaial morhology and the salient features of facial forms are overlooked

(Thomas 2005). The comprehensive analysis that includes the entire 3D facial surface which is recorded by stereophotogrammetry has yet to be carried out.

Various methods have been considered for the analysis of facial morphology, the most common one is to divide the face into right and left halves and the analysis of each side is usually achieved using a set of linear and angular measurements (Ferrario et al 2001). However, this approach fails to describe the spatial characteristics of facial morphology and the identification of the mid-sagittal plane to divide the face into two halves may not be possible in deformed faces (Thomas 2005, Slice 2007).

The most common method of assessing facial asymmetry, without dividing it into hemifaces, is the mirror image technique, whereby the superimposition of the original 3D facial image and its mirror copy allows the quantification of the asymmetry which is illustrated in a colour map to reflect the disparities between the right and left sides of the face. The main drawback of this method is that the registration process is usually performed by Iterative Closest Point (ICP) algorithm software which is based on minimising the distances between the two images. The mathematical superimposition of the two surface "original and mirrored one" does not take into consideration the anatomical correspondence between the points in both images. The method only iterates the closest points to each other regardless if there are anatomical related or not which underestimates the quantification of facial asymmetry (Verhoeven et al., 2016). The method is only sensitive to large differences and under estimates subtle asymmetries "Pinocchio effect" (Zelditch et al 200). To overcome this problem, the generic facial mesh has been introduced. The conformation of the generic facial mesh on the 3D facial morphology is a mathematical "wrapping" of the mesh on the morphology of the 3D image has proved accurate (Cheung et al., 2016). This

allows the superimposition of the anatomical corresponding points of the two images (Claes et al., 2012). This method goes further to achieve dense correspondence between the vertices for a group of images for in-depth facial analysis (Mao et al., 2006). The method provides a novel asymmetry score which is ideal for the longitudinal analysis of facial morphology and the cross sectional evaluation of various populations.

Aim of the study

The aim of this study was the longitudinal evaluation of the asymmetry of the surgically managed UCLP cases to assess the impact of facial growth on facial appearance.

Material and methods

Ethical approval (15/SW/0095) was obtained from the REC and R&D committees for the conduction this study. Fifteen surgically managed UCLP patients participated in this study, all were of Caucasian origin, and were treated according to the same surgical protocol by the same surgeon; a Modified Millard cheiloplasty and McComb primary rhinoplasty were carried out at about three months, and palatal surgery was performed at about eighteen months. A set of four 3D facial images were captured before the surgical repair of cleft lip, 4 months postoperatively, and at a four-year follow-up (Figure 1). All the images were captured at rest position.

All the images of the patients were captured by the same professional photographer using the same stereophotogrammetric device; the 3dMDface System (3dMD Inc., Atlanta, GA, USA). During image capturing, the patients were seated on a raised seated chair about 1.5 metres from the capturing system, and they were looking slightly above the midpoint of the camera pods so that a clear picture of the nose could be obtained. Three stereo pair cameras and a flashing system were working simultaneously to capture the face from ear to

ear within 1.5 millisecond. The captured 3D image consisted of six images: four black and white images under structured light condition and two-coloured images. A computer connected to the capturing system was used to construct a 3D model of the face by processing the stereo images. The obtained 3D model was saved in obj file format.

Assessment of facial asymmetry

A generic mesh was utilised in this study for the assessment of the residual facial asymmetry (Figure 2). This mesh had 7,190 vertices which were symmetrically distributed and were indexed to be mathematically identified. This mesh was conformed on each 3D image to match the 3D characteristics of facial morphology. The first step of the conformation process is to identify a set of anatomical landmarks on both the 3D surface image and the generic mesh to guide the rigid superimposition followed by elastic deformation of the mesh to wrap on the 3D facial morphology (Almukhtar et al., 2016). During the conformation process, the geometry surface shapes of the individual patients were obtained, while maintaining the mesh topology of the generic model. The generic mesh represented the children's faces by a fixed number of indexed vertices (dense mathematical landmarks). Within the 3D images, the images of the right cleft were reflected into the images of the left cleft. Using this conformation, the generic mesh was conformed into three meshes, one to the preoperative 3D facial morphology, one to the postoperative face, one to the four years facial morphology were constructed. Mirror images (Figure 3) of each conformed image was created by reflecting the mesh on an arbitrary plane. Partial Procrustes Analysis (PPA) was applied to align the original and mirror conformed meshes; this alignment process was based on minimising the distances between the corresponding indexed vertices. Facial asymmetry score was quantified by measuring the difference between the conformed original and mirror meshes. In perfect symmetry, this score will be

zero. The discrepancies in corresponding distances between the original regions and its mirrors were displayed in colours. In addition to the assessment of the general facial asymmetry, this was further stratified and analysed in three directions: medio-lateral, vertical and antero-posterior. Asymmetry scores of the whole face, nose and upper lip were quantified (before surgery, after surgery and four years after surgery) by extracting the nose and upper lip from the generic mesh. Wilcoxon Signed ranked test was applied to assess the changes of asymmetry scores preoperatively, postoperatively and at 4 years follow-up.

Errors of the method

The conformation process was repeated on 10 randomly selected preoperative cases and 10 postoperative cases to investigate the impact of digitisation errors of facial landmarks on this process. The differences were statistically analysed using Student-t-test ($p < 0.05$).

Results

The mean age of the infants before surgery was 3.8 ± 0.7 months, 8.5 ± 1.9 months at the postoperative 3D facial capture, and 4.2 ± 1.1 years at the final imaging. There were no statistically significant differences between the repeated conformation process (p -value > 0.05). The mean absolute differences between corresponding vertices of the repeated preoperative conformed meshes were 0.39 mm for X direction, 0.33 mm for Y direction and 0.33 mm in Z direction. For the postoperative conformed meshes, the mean absolute differences were 0.31 mm, 0.27 mm and 0.29 for X, Y, and Z directions respectively.

Wilcoxon Signed ranked test for longitudinal changes for asymmetry scores of the whole face, nose and upper lip is shown in Table 1.

The total facial asymmetry before primary lip repair is displayed in Figure 3. It is clear that the nasolabial region was the most asymmetrical region of the face; the philtrum, columella,

and the vermillion border of the upper lip showed the maximum asymmetry which was more than 5 mm (red). The asymmetry was clear at the alar cartilage and the base of the nose.

The average postoperative asymmetry is demonstrated in Figure 1. Unsurprisingly, there was an obvious improvement of facial asymmetry postoperatively. However, residual asymmetries were identified mainly at the tip of the nose. Figures 3, 4, and 5 show the directions of postoperative asymmetries in the mediolaterally (X direction), vertically (Y direction) and anteroposteriorly (Z direction) respectively. In Figure 3, the nose was deviated toward the non-cleft side, while the philtrum and the cupid bow were shifted toward the scar tissue of the cleft side. The vertical asymmetry (Figure 4) was minimal postoperatively. The anteroposterior asymmetry was demonstrated at the alar base, upper lip and the cheek of the cleft side (Figure 5).

Figure 1 illustrates the average total facial asymmetry at four years of age. The asymmetries were minimum and were identified at the vermillion of the upper lip and at the nares. Asymmetry in the mediolateral direction is demonstrated in Figure 3, the philtrum of the upper lip was considerably deviated towards the scar tissue on the cleft side (red colour), while the light blue colour of the nose represents the deviation towards the non-cleft side. The upper lip and corner of the mouth and the cheeks of the cleft side showed vertical deficiencies (Figure 4). The anteroposterior deficiencies, and the associated asymmetries, of the nares, upper lip, and paranasal areas have increased at the four-year follow-up (Figure 5). The overall asymmetry of the nose was statistically significantly worse at 4 years follow-up (Table 1).

Discussion

This is the first study in the literature which applied dense correspondence analysis for longitudinal evaluation of facial asymmetry of the surgically managed UCLP cases. It overcame the shortage of landmark- dependant analysis and described the morphology of whole facial surfaces which provided a more comprehensive and meaningful assessment of facial asymmetry. The method provided an in-depth understanding of the cause of residual dysmorphology by identifying the direction of facial asymmetry in relation to three main cartesian directions.

This study shows that facial asymmetry improved after primary lip surgery; the maximum asymmetry of the nasolabial region before surgery has significantly improved postoperatively. The surgical repair restored the balance between the forces of the perioral and perinasal muscles (Campbell et al., 2010) which improved facial asymmetry. However, residual asymmetry was noticed following surgery mainly at the tip of the nose rather than the upper lip, while at the four years follow up assessment, the anatomical location of residual asymmetry has changed to involve both the philtrum and the nares. Such findings contradict that of Hood et al. (2003); who reported that the improvements after surgery were significant only at the landmarks of the nose. Furthermore, their results show that at a two-year follow up, the asymmetry improved at the landmarks of the lip rather than the nose. This contradiction is attributed to the methodological differences; the landmark-based analysis by Hood et al. (2003) was limited in describing the full morphology of the surfaces of the nasolabial region.

The perfect repair of nasal deformity is challenging due to the complex anatomical structure of the nose. The results of this study show that the asymmetry of the nose was identifiable and the main residual deformity after lip repair.

Despite the fact that no obvious differences could be detected between the general asymmetry immediately following lip repair and at 4 years follow-up, the details assessment showed clear worsening of this dysmorphology. Medio-laterally the asymmetry was more pronounced at 4 years and was mainly localised at the philtrum. The scar tissue of this region has contributed to the unequal lateral growth of the upper lip. One could argue that the surgical repair of cleft palate may have contributed to the noticed mediolateral

asymmetry. However, the pattern of the noted dysmorphology, which did not affect the lateral side of the lip or the cheek emphasises the impact of the lip scarring on this asymmetry.

The maximum mediolateral asymmetry of the philtrum of the upper lip, columella and tip of the nose were satisfactorily addressed by the primary surgery. The minimum deviation of the nose towards the non-cleft side postoperatively was noted at four years following surgery. The surgical repositioning of the lower border of the nasal septum to its correct position at the anterior nasal spine helped to support the initial correction of primary surgery of the nose in the mediolateral direction. Adequate mobilisation of the lateral alae nasi muscle and its approximation toward the non-cleft side during the primary surgery reduced the residual mediolateral asymmetry. At 4 years follow-up, the lip showed a significant shift towards the scar tissue of the cleft side. We believe this is due to inadequate approximation of the orbicularis oris muscle fibres during primary surgery. Anatomically, the superficial fibres of this muscle are decussated in the midline, passing from one side and inserting into the skin of the contralateral side forming the philtral ridge, there are no muscle fibres inserted into the skin of the philtral dimple (Latham and Deaton, 1976). The lack of approximation leads to the development of tension forces on the skin and the formation of scar tissue during the healing process, which can pull the lip toward the scar tissue of the cleft side.

The vertical asymmetry of the upper lip was restored after primary lip surgery. However, residual asymmetry at the corner of the mouth was noted at four-years following surgery. Adequate rotation of the orbicularis oris muscle during the primary surgery was necessary, and an incision anterior to the inferior turbinate that extends superiorly along the pyriform rim can help to overcome this deficiency.

Residual asymmetries were noted postoperatively at the nares, paranasal area and at the upper lip which had increased at the four years postoperative assessment. The asymmetries could be related to incomplete dissection of the lateral nasal muscle in the primary surgery. Complete dissection of this muscle and subperiosteal undermining that extends around the pyriform fossa and nasal bone up to the infraorbital foramen and maxillary-zygomatic suture are necessary.

Anteroposterior growth deficiency at four years follow-up can be related to two factors, the genetically programmed growth deficiency, or iatrogenic factor produce by palatal surgery. Intrinsic factors responsible for developmental deficiency is responsible for the formation of a cleft and the growth potential deficiency (Liao and Mars, 2005). Growth deficiency could be related to palatal surgery, denuded bone and subsequent scar tissue formation after palatal surgery inhibits the growth of the maxilla (Ross, 1987; Kuijpers-Jagtman and Long, 2000). We appreciate that mild asymmetry is common with typical facial growth (Ercan et al., 2008). The analysis of the facial morphology of non-cleft cases infants of the same country, during the first two years of life showed that there was a tendency for the asymmetry of the face to be reduced with age. Paired t-test showed no significant change in the asymmetry scores for the face from 3 to 6 months, 6 months to one year or 1 to 2 years. More specifically, there was no significant difference in the asymmetry of the nasal rim with age, the asymmetry of the nostrils did not change consistently with age, there was slight reduction of the asymmetry of the upper lip with age (White et al 2004, White 2005). On the other hand, this study on the surgically managed UCLP cases confirmed the increase of facial asymmetry in the anteroposterior direction with age. There was significant statistical deficiency of the forward growth of the nasal and paranasal area of the cleft side. This extended to involve the upper lip and the anterior part of the cheek. The impact of lip scar and the surgical repair of the cleft palate have contributed to the noted anteroposterior deficiency of the nasolabial growth of the cleft side (Naqvi et al., 2015). It is not possible to separate the effect of these two factors without radiographic analysis to assess maxillary growth. The other variable is the programmed growth deficiency in cleft cases which is one of the phenotypic characteristics of cleft deformities.

In summary, facial growth accentuated the underlying facial asymmetry in three directions, specifically anteroposteriorly. The scarring of the lip and the palate are responsible for the noted anteroposterior asymmetry at 4 years following primary lip surgery. The pattern of facial asymmetry was different from what was noticed immediately following lip repair. Patients and their parents should be notified of the potential deterioration of facial asymmetry mainly at the nasolabial region in the anteroposterior direction with age. It is not unreasonable to predict further deterioration of facial growth as the children get older and

the disparity or facial asymmetry becomes more pronounced. It is, therefore, logical to suggest the delay of any other surgical intervention to improve on facial appearance until the cessation of growth.

Conclusion

Residual asymmetry of UCLP was more pronounced at four years following the surgical repair of UCLP in all three directions. The dense correspondence analysis is a reliable and innovative tool for comprehensive facial analysis.

Acknowledgement

We would like to thank all children and families who enrolled in this study. We would like to thank the Children's Clinical Research Facility CRF Edinburgh for their help in this study. I would like to thank in particular Mrs Orla Duncan and Mr Steve Stanton, Royal Hospital for Sick Children Edinburgh for their unlimited help and support to this study.

Legends of the figures:

Figure 1: 3D facial images and the surface mesh of an infant preoperatively (left), postoperatively (middle), at the four-year follow-up (right). The green colour represents no symmetry, the dark blue colour indicates minimum asymmetry; the dark red indicates maximum asymmetry which is > 5 mm distance between the corresponding points.

Figure 2: (a) Conformation of the generic mesh on 3D postoperative facial image of cleft infant. (b) Postoperative conformed mesh. (c) Mirror image of the conformed mesh.

Figure 3: Colour map of the average preoperative asymmetry (left), postoperative (middle) and at 4 years follow up (left) in the X direction (medio-lateral asymmetry). The blue colour represents a deviation towards the non-cleft side. The red colour represents a deviation towards the cleft side.

Figure 4: Colour map of the average postoperative asymmetry (left) and at 4 years follow up (right) in the Y direction. The red colour represents asymmetry in an upward direction. The blue colour represents asymmetry in a downward direction.

Figure 4: Colour map of the average postoperative asymmetry (left) and at 4 years follow up (right) in the Y direction. The red colour represents asymmetry in an upward direction. The blue colour represents asymmetry in a downward direction.

References

- Almukhtar, A., Ayoub, A., Khambay, B., McDonald, J., Ju, X., 2016. State-of-the-art three-dimensional analysis of soft tissue changes following Le Fort I maxillary advancement. *Br J Oral Maxillofac Surg* 54, 812–817.
- Ayoub, A., Garrahy, A., Millett, D., Bowman, A., Siebert, J.P., Miller, J., Ray, A., 2011. Three-dimensional assessment of early surgical outcome in repaired unilateral cleft lip and palate: part 2. Lip changes. *Cleft Palate Craniofac J* 48, 578–83.
- Bell, A., Lo, T.-W.R., Brown, D., Bowman, A.W., Siebert, J.P., Simmons, D.R., Millett, D.T., Ayoub, A.F., 2014. Three-Dimensional Assessment of Facial Appearance Following Surgical Repair of Unilateral Cleft Lip and Palate. *Cleft Palate-Craniofacial J.* 51, 462–471.
- Bugaighis, I., Mattick, C.R., Tiddeman, B., Hobson, R., 2014. 3D asymmetry of operated children with oral clefts. *Orthod Craniofac Res* 17, 27–37.
- Campbell, A., Costello, B.J., Ruiz, R.L., 2010. Cleft Lip and Palate Surgery: An Update of Clinical Outcomes for Primary Repair. *Oral Maxillofac Surg Clin North Am* 22, 43–58.
- Cheung, M.Y., Almukhtar, A., Keeling, A., Hsung, T.-C., Ju, X., McDonald, J., Ayoub, A., Khambay, B.S., 2016. The Accuracy of Conformation of a Generic Surface Mesh for the Analysis of Facial Soft Tissue Changes. *PLoS One* 11, e0152381.
- Claes, P., Walters, M., Clement, J., 2012. Improved facial outcome assessment using a 3D anthropometric mask. *Int J Oral Maxillofac Surg* 41, 324–330.
- Djordjevic, J., Lewis, B.M., Donaghy, C.E., Zhurov, A.I., Knox, J., Hunter, L., Richmond, S., 2014. Facial shape and asymmetry in 5-year-old children with repaired unilateral cleft lip and/or palate: an exploratory study using laser scanning. *Eur J Orthod* 36, 497–505.
- Ercan ST, Ozdemir A, Etoz D, Sigirli RS, Tubba M, et al., 2008. Facial asymmetry in young healthy subjects evaluated by statistical shape analysis. *J Ant* 213, 663-669.
- Farkas, L., 1994. *Anthropometry of the Head and Face.*, 2nd ed. ed. New York: Raven Press.

- Ferrario VH, Sforza C, Ciusa V, et al., 2001. The effect of sex and age on facial asymmetry in healthy subjects: a cross-sectional study from adolescence to mid adulthood. *J Oral Maxillofac Surg* 59, 82-388.
- Hood, C.A., Bock, M., Hosey, M.T., Bowman, A., Ayoub, A.F., 2003. Facial asymmetry - 3D assessment of infants with cleft lip & palate. *Int J Paediatr Dent*. 13, 404–410.
- Hood, C.A., Hosey, M.T., Bock, M., White, J., Ray, A., Ayoub, A.F., 2004. Facial Characterization of Infants With Cleft Lip and Palate Using a Three-Dimensional Capture Technique. *Cleft Palate Craniofac J*. 41, 27–35.
- Kuijpers-Jagtman, A.M., Long, R.E., 2000. The Influence of Surgery and Orthopedic Treatment on Maxillofacial Growth and Maxillary Arch Development in Patients Treated for Orofacial Clefts. *Cleft Palate Craniofacial J*. 37, 527–527.
- Kuijpers, M.A., Desmedt, D.J., Nada, R.M., Bergé, S.J., Fudalej, P.S., Maal, T.J., 2015. Regional facial asymmetries in unilateral orofacial clefts. *Eur J Orthod*. 37, 636–642.
- Latham, R. a, Deaton, T.G., 1976. The structural basis of the philtrum and the contour of the vermilion border: a study of the musculature of the upper lip. *J. Anat*. 121, 151–60.
- Liao, Y.-F., Mars, M., 2005. Long-Term Effects of Clefts on Craniofacial Morphology in Patients With Unilateral Cleft Lip and Palate. *Cleft Palate Craniofac J*. 42, 601–609.
- Mao, Z., Ju, X., Siebert, J.P., Cockshott, W.P., Ayoub, A., 2006. Constructing dense correspondences for the analysis of 3D facial morphology. *Pattern Recognit. Lett*. 27, 597–608.
- Meyer-Marcotty, P., Kochel, J., Boehm, H., Linz, C., Klammert, U., Stellzig-Eisenhauer, A., 2011. Face perception in patients with unilateral cleft lip and palate and patients with severe Class III malocclusion compared to controls. *J. Cranio Maxillofac Surg*. 39, 158–163.
- Nadjmi, N., Amadori, S., Van de Castele, E., 2016. Secondary Cleft Lip Reconstruction and the Use of Pedicled, Deepithelialized Scar Tissue. *Plast Reconstr Surg Glob. Open* 4, e1061.
- Nakamura, N., Suzuki, A., Takahashi, H., Honda, Y., Sasaguri, M., Ohishi, M., 2005. A

Longitudinal Study on Influence of Primary Facial Deformities on Maxillofacial Growth in Patients With Cleft Lip and Palate. *Cleft Palate Craniofacial J.* 42, 633–640.

Naqvi, Z., Ravi, S., Shivalinga, B., Munawwar, S., 2015. Effect of cleft lip palate repair on craniofacial growth. *J. Orthod. Sci.* 4, 59.

Ras, F., Habets, L.L.M.H., Van Ginkel, F.C., Prah-Andersen, B., 1994. Three-Dimensional Evaluation of Facial Asymmetry in Cleft Lip and Palate. *Cleft Palate Craniofacial J.* 31, 116–121.

Ross, R.B., 1987. Treatment variables affecting facial growth in complete unilateral cleft lip and palate. *Cleft Palate J.* 24, 5–77.

Slice D, 2007. Geometric morphometrics. *Annu Rev Anthropol.* 36, 261-281.

Stauber, I., Vairaktaris, E., Holst, A., Schuster, M., Hirschfelder, U., Neukam, F.W., Nkenke, E., 2008. Three-dimensional Analysis of Facial Symmetry in Cleft Lip and Palate Patients Using Optical Surface Data. *J. Orofac. Orthop. / Fortschritte der Kieferorthopädie* 69, 268–282.

Thomas CDL., 2005. Three-dimensional quantification of facial shape. In Clement JG, Marks MK, editors. *Computer-Graphic Facial Reconstruction*. London: Elsevier Academic Press; 55-78.

Verhoeven, T., Xi, T., Schreurs, R., Bergé, S., Maal, T., 2016. Quantification of facial asymmetry: A comparative study of landmark-based and surface-based registrations. *J. Cranio Maxillofac Surg.* 44, 1131–1136.

White J, Ayoub AF, Mosey MT, Bock M, Bowman A., Bowman J, Siebert PJ, Ray A, 2004. 3D facial characteristics of non-cleft Caucasian infants and correlation with body measurements. *Cleft Palate Craniofac J.* 41, 593-602.

White, Jill Elizabeth (2005) A longitudinal study of facial growth in infants using a three-dimensional imaging technique. PhD thesis. <http://theses.gla.ac.uk/2058/>

Zelditch ML, Swiderski DL, Sheets HD, et al. *Geometric morphometrics for biologists: a Primer*. New York: Elsevier Academic Press, 2004.

