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NOVEL COMPUTER VISION ANALYSIS OF NASAL SHAPE IN CHILDREN WITH UNILATERAL CLEFT LIP

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ABSTRACT

Background: Optimization of treatment of the unilateral cleft lip nasal deformity (uCLND) is hampered by lack of objective means to assess initial severity and changes produced by treatment and growth. The purpose of this study was to develop automated 3D image analysis specific to the uCLND; assess the correlation of these measures to esthetic appraisal; measure changes that occur with treatment and differences amongst cleft types.

Methods: Dorsum Deviation, Tip-Alar Volume Ratio, Alar-Cheek Definition, and Columellar Angle were assessed using computer-vision techniques. Subjects included infants before and after primary cleft lip repair (N=50) and children aged 8-10 years with previous cleft lip (N=50). Two expert surgeons ranked subjects according to esthetic nose appearance.

Results: Computer-based measurements strongly correlated with rankings of infants pre-repair ($r=0.8$, 0.75, 0.41 and 0.54 for Dorsum Deviation, Tip-Alar Volume Ratio, Alar-Cheek Definition, and Columellar Angle, $p<0.01$) while all measurements except Alar-Cheek Definition correlated moderately with rankings of older children post-repair ($r\sim0.35$, $p<0.01$). Measurements were worse with greater severity of cleft type but improved following initial repair. Abnormal Dorsum Deviation and Columellar Angle persisted after surgery and were more severe with greater cleft type.

Conclusions: Four fully-automated measures were developed that are clinically relevant, agree with expert evaluations and can be followed through initial surgery and in older children. Computer vision analysis techniques can quantify the nasal deformity at different stages, offering efficient and standardized tools for large studies and data-driven conclusions.

Keywords: Cleft Lip; Computer-Assisted Image Analysis; 3-D Image

INTRODUCTION

Cleft lip with or without palate occurs in 1 in 1000 births and results in complex 3-dimensional deformity of the nose (Figure 1). Although surgery can produce dramatic changes, the lack of objective measures and data-driven evaluations of different treatments result in decisions that are based on experience instead of scientific evidence. Conventional photography has been used to develop objective measures of cleft severity (*Mommaerts* and *Nagy*, 2008; *Fisher et al.*, 2008; *Fudalej et al.*, 2012) however, it suffers from parallax (*Oh et al.*, 2011) and fails to capture the complex 3D nature of the deformity. Traditional methods, such as direct anthropometry, CT scan, and dentofacial casts, provide richer information but are impractical in clinical settings or for routine use.

Advances in 3D stereo-photogrammetry, have allowed for acquisition of high-resolution 3D images with minimal burden to patients. Although the technology provides great opportunities to improve cleft care, its utility in research and clinical settings is still evolving. Prior studies have focused on the accuracy and reliability of indirect anthropometric analysis (*Ort et al.*, 2012; *Li et al.*, 2013; *Tse et al.*, 2014; *Othman* and *Aidil Koay*, 2016) and have used this type of analysis to compare children with clefts to controls (*Hood et al.*, 2004; *Krimmel et al.*, 2006; *Ayoub et al.*, 2011; *Othman et al.*, 2014), children with different types of clefts (*Yeow et al.*, 2002; *Bugaighis et al.*, 2013; *Bugaighis et al.*, 2014a), and children before and after surgery (*Huempfner-Hierl et al.*, 2009; *Okawachi et al.*, 2011; *Krimmel et al.*, 2013; *Alazzawi et al.*, 2017). Although anthropometric analysis is objective, it does not consider 3D shape and the manual landmarking can be tedious. More recent studies have measured surface asymmetry as a standard (*Hood et al.*, 2003; *Bilwatsch et al.*, 2006; *Nkenke et al.*, 2006; *Devlin et al.*, 2007; *Singh et al.*, 2007; *Stauber et al.*, 2008; *Weinberg et al.*, 2009; *Hoefert et al.*, 2010; *Meyer-Marcotty et al.*, 2010; *Bugaighis et al.*, 2013), however, as Fudalej has found, measurement of symmetry alone may only have weak association with esthetic rating (*Fudalej et al.*, 2012). An appropriate objective measure may therefore need to be based on specific and clinically relevant features. We define an objective measure as one that is not based upon a subjective appraisal and that is based upon mathematical measurement following a standardized and well-defined algorithm.

The goals of this study were to:

1. Develop automated objective measures of 3D nasal form that are specific and relevant to the unilateral cleft lip nasal deformity (uCLND)
2. Determine the correlation of the measures to subjective appraisals of nose appearance.
3. Assess changes in measures that occur with primary cleft lip repair
4. Assess differences in measures amongst children with different types of unilateral cleft lip and different age groups

Our plan is to use the methods and findings of this study to compare treatments and optimize outcomes of surgical care.

MATERIAL AND METHODS

This study was reviewed and approved by institutional review board of Seattle Children's Hospital. Consent was obtained from all subjects to participate in this project.

Subjects

Consecutive families presenting to our institution were recruited for this study. Group A included 45 infants with unrepaired cleft lip. Images before (Infant Pre-repair) and after (Infant Post-repair) primary cheiloplasty were collected. An additional 5 age-matched subjects with no craniofacial differences (Infant Control) were included in this group as control. Infants with clefts in Group A underwent repair by the senior author using the Anatomic Subunit Approximation Approach as described by Fisher (*Fisher*, 2005) and modified by Tse (*Tse* and *Lien*, 2015). Primary rhinoplasty was performed in the form of nasal floor closure, lateral sidewall reconstruction, and primary septoplasty (*Tse*, 2012).

To assess longer term and a wider variety of outcomes, Group B included 45 children aged 8-10 years old who had previously undergone repair (8-10 y Post-repair) and 5 control children aged 8-10 years old (8-10 y Control) with no craniofacial differences. Children with clefts in Group B underwent repair by any of 6 surgeons at our institution or by a surgeon at an outside institution. All had undergone variations of rotation-advancement repair (42% repaired at our institution and 58% repaired elsewhere). 53% had undergone surgical revision and 73% had undergone alveolar bone grafting. We had no pre-repair images for Group B subjects because 3D image capture was not yet available.

Imaging and preprocessing

3D facial images were captured by our center's professional imaging technologist using the 3dMD Cranial System (3dMD, Atlanta, GA). 3D images were preprocessed to extract the face and to correct alignment into a standard facial frontal plane using a previously described automated cleaning and pose normalization algorithm (*Wu et al.*, 2014). No manual image processing was performed. The images were then analyzed using the developed automated measures.

Computer-based quantification of cleft severity

Using a sample set of 3D images and computer vision techniques, we developed automated measurements to quantify specific features of the uCLND (Figure 1): dorsal deviation, columellar deviation, nasal tip asymmetry, and blunting of the alar-cheek junction (Figure 2A-B). Columellar angle has previously been found to be an important measure of initial cleft severity (*Fisher et al.*, 2008). The nasal form and nasal deviation domains of the Asher-McDade scale have previously been found to highly correlate with lay-person evaluations of post-operative nasal form via crowdsourcing (*Tse et al.*, 2016). The developed measures were designed to quantify these features. All of the steps in processing and analysis required no manual processing.

We defined the mid-facial reference plane as the geometric midline that ignores the nasolabial region. Based upon a previous study (*Wu et al.*, 2016a), the most valid automated method to produce a consistent reference plane was to identify the midline of calculated surface landmarks (*Liang et al.*, 2013) outside of the nasolabial region (Deformation method).

To more accurately differentiate dorsum from the tip region of the nose, the profile contour was extracted on the sagittal section containing the greatest projecting point of the nose (pronasale). Using local curvature contour analysis, the sellion, pronasale, and subnasale were defined (Figure 3A).

Horizontal contours were extracted by taking the intersection of the 3D surface mesh with an xz-plane at several y-coordinates (Figure 3B-C). For each contour, the curvature angle was calculated at all points by fitting lines to the neighboring 15 points on each side and calculating the angle between two lines (Figure 3E). On each contour, four points of interest were identified: two local minima of the curvature angle were detected as the nose corners, the global maximum of the curve was detected as the nasal dorsum, and the intersection of the contour with the mid-facial plane was identified for reference (Figure 3D-E). In doing so, the borders of the nose could be identified (Figure 3F).

Dorsum Deviation measures the deviation of the nasal dorsum from the mid-facial reference plane. The nasal dorsum was approximated by a line fitted to the highest points (detected through curvature analys) at 20 horizontal contours taken from pronasale to sellion. Dorsum Deviation was measured as the angle between the dorsum line and the mid-facial reference plane (Figure 2A and 2C). A perfectly symmetrical nose has a Dorsum Deviation of 0° while the Dorsum Deviation increases with asymmetry.

Tip-Alar Volume Ratio measures the volumetric asymmetry of the nasal tip-alar complex. The nasal tip was located between the subnasale and alar curvature. Figure 2A illustrates the nasal tip area where the Tip-Alar Volume Ratio is calculated. Horizontal contours were extracted, and the area under the horizontal contour line was calculated at each plane. Using the automatically calculated mid-facial reference plane, the area was divided into two parts (Figure 2D). As an approximation of the nose volume, the areas under the left and right sides were summed over all planes. The ratio of the volume of the larger side to the smaller side was calculated for each subject. A perfectly symmetrical nose produces a ratio of 1, and higher values of Tip-Alar Volume Ratio indicate asymmetry.

Alar-Cheek Definition measures alar-cheek definition and assesses the contour changes between the nasal ala and the cheek with the premise that this distinction tends to be blunted on the cleft side (Figure 1B and Figure 2B). 10 horizontal contours from the mid-point between the subnasale and pronasale to the alar curvature were extracted. Using the curvature analysis, nose corners were detected at each horizontal contour. A line was fitted to the 15 points from the nose corner towards the nasal tip and the curvature angle is the angle this line makes with the x-axis. Figure 2E demonstrates the curvature angles at two sides. Alar-Cheek Definition was measured as the mean of the absolute differences between the angles of the two nose corners. A perfectly symmetrical nose produces an Alar-Cheek Definition of 0°, and higher values Alar-Cheek Definition mean greater deformity.

Columellar Angle measures the deviation and deformation of the columella. Similar to the horizontal contours used for the measures above, a set of contours from the midpoint between the pronasale and subnasale to the subnasale that are parallel to the xy-plane were extracted. Using curvature analysis, the most prominent point on each contour was calculated and the columellar line was approximated by the line fitted to these points. Figure 2F demonstrates the points detected by curvature analysis. Figure 2B shows the columellar line and the columellar angle computed by the computer, while Figure 1B shows a columellar line drawn by a cleft surgeon. The Columellar Angle was defined as the angle between the columellar line and the yz-plane. A perfectly symmetrical nose has a Columellar Angle of 0°, and higher values of Columellar Angle mean greater deformity.

<u>Subjective appraisal of nasal form</u>

Expert surgeons have previously been found to reliably place images of infants with cleft lip in increasing order of nasal severity when allowed to perform side-by-side comparisons (*Fisher et al.*, 2008). Images from each group of subjects were assembled and randomly placed onto an electronic "sorting board" (*Wu et al.*, 2016b). Images could be selected and viewed in a 3D viewer that also displayed adjacent images for direct comparison. Pre-repair images of Group A and post-repair images of Group B were ranked in order of increasing nasal deformity by expert surgeons (CM and RT, respectively).

To compare rankings with measures, we ordered subjects in each group based on increasing Dorsum Deviation, Tip-Alar Volume Ratio, Alar-Cheek Definition and Columellar Angle. The correlation of measures to the expert rank order was determined by Pearson's correlation coefficients of the rank orders.

<u>Changes with primary repair and differences amongst cleft types and extents</u>

Subjects were grouped by cleft type and cleft extent. Changes in measures before and after surgery and differences in subject groups were assessed using t-test.

RESULTS

Subject demographics are summarized in Tables 1 and 2. Group A was consistent with the initial presentations normally seen at our institution. In Group B, there was a preponderance of subjects with complete cleft lip. Although this is not representative of initial presentations, it is consistent with visits in clinic by children at age 8-10 years who are returning for ongoing care.

Correlation of measures to subjective appraisals of nose deformity

Correlations of measures to expert ranking of uCLND are summarized in Table 3. In Group A, measures of Dorsum Deviation and Tip-Alar Volume Ratio were highly correlated with the expert rankings (0.8 and 0.75 respectively, $p < 0.01$) while Alar-Cheek Definition and Columellar Angle produced reasonable correlation coefficients (0.41 and 0.54 respectively, $p < 0.01$).

The raters did not feel that they could reliably differentiate the nasal appearance of subjects in Group A immediately after surgery because all the appearances were similar. Formal ranking of post-operative images of Group A was therefore abandoned.

The nasal appearances of subjects in Group B were distinct enough that raters could differentiate nasal appearance. The correlation of quantitative measures to the rank order of nasal appearance in Group B was moderate for all measures (correlation coefficient of ~0.35, $p < 0.01$), except for Alar-Cheek Definition (correlation coefficient of 0.18, $p \sim 0.2$). Apart from Alar-Cheek Definition, all correlations were statistically significant (see Table 3).

Changes with primary cleft lip repair

All 4 of the nasal measures were significantly reduced after repair and there were greater changes in measures with increasing initial severity (Table 4).

Pre-operative differences amongst cleft type and extent

In Group A, for all measures, except the Alar-Cheek Definition, the mean values decreased in the order of complete, complete with band, incomplete and control (Figure 4). The difference was statistically significant between infants with complete cleft and infants with incomplete cleft, and infants with complete cleft and controls. Mean Dorsum Deviation for infants with complete cleft was also significantly higher than for infants with complete cleft with band.

When grouped by extent of clefting, measures for infants with CLA and CLP were similar, however, measures of nasal deformity decreased for infants with CL and for control subjects. Those differences reached statistical significance for Dorsum Deviation and Tip-Alar Volume Ratio (Figure 5).

Post-operative differences amongst cleft type and extent

Following repair, measures of uCLND for children with clefts were worse than for control subjects (Table 4). In Group A the differences reached statistical significance for all measures. In Group B the differences approached significance for Dorsum Deviation ($p=0.06$) and Columellar Angle ($p=0.07$).

When grouped by cleft type, there was a trend toward worsening Columellar Angle with increasing cleft severity for both Group A and B. We also found worsening Dorsum Deviation with worsening cleft type in Group B but not in the younger Group A. Similar trends were not found for the Tip-Alar Volume Ratio or the Alar-Cheek Definition.

Other correlations

There were no significant differences between amongst ethnicities and the two sexes in any of the groups.

DISCUSSION

Advances in 3D stereophotogrammetry provide an opportunity for better assessment of cleft morphology. Whereas previous studies used traditional anthropometric analysis as a surrogate for 3D form, more recent studies have assessed surface data of 3D images to study facial and regional symmetry (*Hartmann et al.*, 2007; *Djordjevic et al.*, 2014). Dadakova and Bugaighis created average 3D images of subjects grouped by cleft type to illustrate differences in morphology and to produce "heat maps" that demonstrate regional differences in children 3 and 4.5 years (*Dadáková et al.*, 2016) and 8-12 years old (*Bugaighis et al.*, 2014b) respectively. Schwenzer-Zimmerer used a similar approach to visualize changes that occur with initial cleft lip repair performed in Cambodia for patients over 4 years old (*Schwenzer-Zimmerer et al.*, 2008). Heat maps have also been used to illustrate changes before and after both secondary alveolar bone grafting (*Kau et al.*, 2011) and secondary rhinoplasty (*Nakamura et al.*, 2011). Although these methods nicely illustrate differences and changes, they are qualitative, rely upon manually placed landmarks, and do not specifically address differences or changes of the nose.

Geometric morphometrics have been applied to assess 3D images. Bugaighis used Procrustes analysis and principal component analyses to assess differences amongst averaged faces for subjects grouped by cleft type at 8-12 years of age (*Bugaighis et al.*, 2010) and Bell used Procrustes analysis and facial curve analysis to compare regions of asymmetry amongst subjects grouped by cleft type at 10 years of age (*Bell et al.*, 2014). They found that different facial regions exhibited different degrees of asymmetry. Kuijpers examined a similar group of subjects using manual landmarks, mirror images and surface based registration and found that the nose was the most asymmetric region of the face (*Kuijpers et al.*, 2015). Their findings are consistent with the clinical notion that persistent nasal deformity is common and correction of the uCLND remains a significant challenge.

Only a few studies focus specifically on the nose. Singh used landmark-based geometric morphometrics to look at 3D nasal changes from nasoalveolar molding (*Singh et al.*, 2005). van Loon performed linear measurements and volumetric analysis of nasal symmetry in a group of 3 year-old children to demonstrate differences between children with repaired clefts and volunteers without clefts (*van Loon et al.*, 2011). In a similar manner, both Linden and van Loon manually isolated noses on 3D images and quantified overall symmetry for two methods of primary rhinoplasty (*Linden et al.*, 2016) and before and after secondary rhinoplasty (*van Loon et al.*, 2010), respectively. None of these studies have assessed infants before and after surgery and none of these examined specific features of the uCLND. Although overall symmetry may be an objective measure of form, as Fudalej has found, asymmetry alone may only partially account for esthetic ratings of form (*Fudalej et al.*, 2012; *Desmedt et al.*, 2015). In order to improve results of treatment, specific and clinically relevant measures of the uCLND nasal are required.

Our study differs from prior work in a number of ways. First, we developed measures based upon clinically relevant features of the uCLND that surgeons and lay people use to assess cleft severity and treatment outcome (*Fisher et al.*, 2008; *Meltzer et al.*, 2013; *Tse et al.*, 2016). Second, we assessed the correlation of these measures to esthetic appraisals of the unilateral cleft lip deformity and found strong agreement, thereby validating use of the measures for clinical and research purposes. Third, as opposed to evaluating a single age group, we examined subjects at 3 time points (pre-lip repair, post-lip repair, and at 8-10 years of age). Although the subjects in Group A and B were different, the same analysis may be used in the future for true longitudinal assessment. Finally, we used completely automated processes from image cleaning, registration and pose normalization (*Wu et al.*, 2014) to shape analysis. In contrast, previous methods require manual cropping or landmarks. By minimizing the burden of work on investigators, we hope to enable more centers to analyze and study their outcomes. Automation allows for study of large volumes of images in an efficient and practical manner. While these tools have considerable value in facilitating research, objective 3D analysis has also been found to be of clinical value for surgeons in planning and decision-making(*Trotman et al.*, 2013). Trotman et al. found that pre-operative systematic image analysis frequently resulted in alterations of surgical goals.

We found progressively worse measures of uCLND for worsening cleft types. Cleft lip repair and primary nasal correction improved all measures. Although we may have found similar relationships of appearance, cleft type, and changes with surgery using surgeon assessments, those assessments are tedious and time consuming. In addition, overall subjective appraisals by surgeons do not provide feedback on specific features that may contribute to an overall appearance. For infants post-repair, the Tip-Alar Volume Ratio and Alar-Cheek Definition were similar to that of controls, however Dorsum Deviation and Columellar Angle remained greater than that of controls. Similarly, for older children, the Tip-Alar Ratio was similar to that of control subjects, whereas the more specific measures of uCLND, Dorsum Deviation, Alar-Cheek Definition, and Columellar Angle, were greater for subjects with greater cleft severity. There may be several reasons why the Alar-Cheek Definition was worse in the older group than in the infant systepost-repair group including, recurrent deformity, differences in surgical technique, and a preponderance of subjects with complete clefts in the older group. Given that Group A underwent surgery by a single surgeon using one technique and that Group B underwent surgery by multiple surgeons using different techniques, inferences from direct comparison of the two groups is limited.. As we follow subjects in Group A over time with repeated images, analysis and true longitudinal assessment, we will gain further insights. For now, our results suggest that the treatment approaches in Group A and Group B leave residual dorsal deviation and columellar angulation but correct volumetric asymmetry of the nasal tip-alar region. Insights from these specific measures have potential value for both outcomes research and clinical feedback.

Although specific measures of the uCLND offer new opportunities, several features remain a challenge. We were unable to develop an automated method to measure nostril size and shape. While those can be measured manually (*Stauber et al.*, 2008), the sparse mesh resolution in the nasal cavity results in inaccurate representation of form, data holes, and artifacts that prevent accurate automated detection. With improvements in imaging of these regions, we may be able to more accurately detect and measure nostril shapes. We were also unable to detect the two pronasale landmarks that an expert may recognize as part of the uCLND. Computer vision still lacks the complex human perception of form and can't detect these by computation. We therefore defined a single pronasale point based mathematically as the greatest projecting point along the z-axis.

Our future plans include producing a user-friendly interface that would allow clinicians and non-computer science researchers to use the developed tools for automated image cleaning, normalization, and analysis. Ultimately we plan to use similar analysis to study nasal morphology following primary septoplasty, tip rhinoplasty, secondary tip rhinoplasty, and secondary septorhinoplasty. We may not be able to fully correct the uCLND in a single stage, however we may be able to optimize care by producing stepwise improvements that minimize the number of procedures a patient undergoes. Quantitative methods of measurement are necessary to assess changes in the setting of varying initial cleft severity, multi-stage treatment, and changes or relapse that occur with time and growth.

CONCLUSION

We have developed four specific and objective measures of the uCLND that can be generated by automated computer analysis. Those measures had tight correlation with expert assessments of initial cleft severity and moderate correlation with expert assessments of treatment outcome.

In our study population, we found that primary cleft lip repair resulted in improved nasal form as determined by the objective measures, however, residual Dorsum Deviation and Columellar Angulation persisted. Similar residual deformities of Dorsum Deviation and Columellar Angulation were found in an older population of children age 8-10 years of age who previously underwent treatment. Further work is needed to specifically measure other residual features of the uCLND and to determine the best strategies for treatment over the course of longitudinal care.

3D stereo-photogrammetry provides a unique opportunity to develop automated and specific measures that can facilitate large-scale analysis and minimize barriers to outcomes assessment. In turn, the objective data may be used to directly or indirectly improve patient care.

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REFERENCES

Alazzawi O, Morioka D, Miyabe M, Tosa Y, Ohkubo F, Yoshimoto S: Nasolabial Growth in Individuals With Unilateral Cleft Lip and Palate. J Craniofac Surg. 28(5):e449e451, 2017.

Ayoub A, Garrahy A, Millett D, Bowman A, Siebert JPP, Miller J, Ray A: Three-Dimensional Assessment of Early Surgical Outcome in Repaired Unilateral Cleft Lip and Palate: Part 2. Lip Changes. Cleft Palate-Craniofacial J. 48(5):578-583, 2011.

Bell A, Lo T-WR, Brown D, Bowman AW, Siebert JP, Simmons DR, Millett DT, Ayoub AF: Three-Dimensional Assessment of Facial Appearance Following Surgical Repair of Unilateral Cleft Lip and Palate. Cleft Palate-Craniofacial J. 51(4):462-471, 2014.

Bilwatsch S, Kramer M, Haeusler G, Schuster M, Wurm J, Vairaktaris E, Neukam FW, Nkenke E: Nasolabial symmetry following Tennison-Randall lip repair: A three-dimensional approach in 10-year-old patients with unilateral clefts of lip, alveolus and palate. J Cranio-Maxillofacial Surg. 34(5):253-262, 2006.

Bugaighis I, Mattick CR, Tiddeman B, Hobson R: 3D asymmetry of operated children with oral clefts. Orthod Craniofac Res. 17(1):27-37, 2013.

Bugaighis I, Mattick CR, Tiddeman B, Hobson R: 3D Facial Morphometry in Children With Oral Clefts. Cleft Palate-Craniofacial J. 51(4):452-461, 2014a.

Bugaighis I, O'Higgins P, Tiddeman B, Mattick C, Ben Ali O, Hobson R: Three-dimensional geometric morphometrics applied to the study of children with cleft lip and/or palate from the North East of England. Eur J Orthod. 32(5):514-521, 2010.

Bugaighis I, Tiddeman B, Mattick CR, Hobson R: 3D comparison of average faces in subjects with oral clefts. Eur J Orthod. 36(4):365-372, 2014b.

Dadáková M, Cagáňová V, Dupej J, Hoffmannová E, Borský J, Velemínská J: Three-dimensional evaluation of facial morphology in pre-school cleft patients following neonatal cheiloplasty. J Cranio-Maxillofacial Surg. 44(9):1109-1116, 2016.

Desmedt DJ, Maal TJ, Kuijpers MA, Bronkhorst EM, Kuijpers-Jagtman AM, Fudalej PS: Nasolabial symmetry and esthetics in cleft lip and palate: analysis of 3D facial images. Clin Oral Investig. 19(8):1833-42, 2015.

Devlin MF, Ray A, Raine P, Bowman A, Ayoub AF: Facial symmetry in unilateral cleft lip and palate following alar base augmentation with bone graft: a three-dimensional assessment. Cleft Palate Craniofac J. 44(4):391-395, 2007.

Djordjevic J, Toma AM, Zhurov AI, Richmond S: Three-dimensional quantification of facial symmetry in adolescents using laser surface scanning. Eur J Orthod. 36(2):125-32, 2014.

Fisher DM: Unilateral cleft lip repair: an anatomical subunit approximation technique. Plast Reconstr Surg. 116(1):61-71, 2005.

Fisher DM, Tse R, Marcus JR: Objective Measurements for Grading the Primary Unilateral Cleft Lip Nasal Deformity. Plast Reconstr Surg. 122(3):874-880, 2008.

Fudalej P, Katsaros C, Hozyasz K, Borstlap WA, Kuijpers-Jagtman AM: Nasolabial symmetry and aesthetics in children with complete unilateral cleft lip and palate. Br J Oral Maxillofac Surg. 50(7):621-625, 2012.

Hartmann J, Meyer-Marcotty P, Benz M, Häusler G, Stellzig-Eisenhauer A: Reliability of a Method for Computing Facial Symmetry Plane and Degree of Asymmetry Based on 3D-data. J Orofac Orthop.

68(6):477-90, 2007.

Hoefert CS, Bacher M, Herberts T, Krimmel M, Reinert S, Hoefert S, Göz G: Implementing a superimposition and measurement model for 3D sagittal analysis of therapy-induced changes in facial soft tissue: a pilot study. J Orofac Orthop. 71(3):221-34, 2010.

Hood CA, Bock M, Hosey MT, Bowman A, Ayoub AF: Facial asymmetry - 3D assessment of infants with cleft lip & palate. Int J Paediatr Dent. 13(6):404-410, 2003.

Hood CA, Hosey MT, Bock M, White J, Ray A, Ayoub AF: Facial characterization of infants with cleft lip and palate using a three-dimensional capture technique. Cleft Palate Craniofac J. 41(1):27-35, 2004.

Huempfner-Hierl H, Hemprich A, Hierl T: Results of a Prospective Anthropometric and Functional Study About Aesthetics and Nasal Respiration After Secondary Rhinoplasty in Cleft Lip and Palate Patients. J Craniofac Surg. 20(Suppl 2):1863-1875, 2009.

Kau CH, Medina L, English JD, Xia J, Gateno J, Teichgraber J: A comparison between landmark and surface shape measurements in a sample of cleft lip and palate patients after secondary alveolar bone grafting. Orthodontics (Chic). 12(3):188-195, 2011.

Krimmel M, Kluba S, Bacher M, Dietz K, Reinert S: Digital surface photogrammetry for anthropometric analysis of the cleft infant face. Cleft Palate Craniofac J. 43(3):350-355, 2006.

Krimmel M, Kluba S, Breidt M, Bacher M, Müller-Hagedorn S, Dietz K, Bülthoff H, Reinert S: Three-Dimensional Assessment of Facial Development in Children With Unilateral Cleft Lip With and Without Alveolar Cleft. J Craniofac Surg. 24(1):313-316, 2013.

Kuijpers MA, Desmedt DJ, Nada RM, Bergé SJ, Fudalej PS, Maal TJ: Regional facial asymmetries in unilateral orofacial clefts. Eur J Orthod. 37(6):636-642, 2015.

Li G, Wei J, Wang X, Wu G, Ma D, Wang B, Liu Y, Feng X: Three-dimensional facial anthropometry of unilateral cleft lip infants with a structured light scanning system. J Plast Reconstr Aesthetic Surg. 66(8):1109-1116, 2013.

Liang S, Wu J, Weinberg SM, Shapiro LG: Improved detection of landmarks on 3D human face data. Conf Proc . Annu Int Conf IEEE Eng Med Biol Soc IEEE Eng Med Biol Soc Annu Conf. 2013:6482-6485, 2013.

Linden OE, Taylor HO, Vasudavan S, Byrne ME, Deutsch CK, Mulliken JB, Sullivan SR: Three-Dimensional Analysis of Nasal Symmetry Following Primary Correction of Unilateral Cleft Lip Nasal Deformity. Cleft Palate-Craniofacial J. 0(0):16-73, 2016.

van Loon B, Maal TJ, Plooij JM, Ingels KJ, Borstlap WA, Kuijpers-Jagtman AM, Spauwen PH, Bergé SJ, Berg?? SJ, Bergé SJ: 3D Stereophotogrammetric assessment of pre- and postoperative volumetric changes in the cleft lip and palate nose. Int J Oral Maxillofac Surg. 39(6):534-540, 2010.

van Loon B, Reddy SG, van Heerbeek N, Ingels KJAO, Maal TJJ, Borstlap WA, Reddy RR, Kuijpers-Jagtman A-MM, Bergé SJ: 3D stereophotogrammetric analysis of lip and nasal symmetry after primary cheiloseptoplasty in complete unilateral cleft lip repair. Rhinology. 49(5):546-553, 2011.

Meltzer NE, Vaidya D, Capone RB: The Cleft-Columellar Angle: A Useful Variable to Describe the Unilateral Cleft Lip-Associated Nasal Deformity. Cleft Palate-Craniofacial J. 50(1):82-87, 2013.

Meyer-Marcotty P, Alpers GW, Gerdes ABM, Stellzig-Eisenhauer A: Impact of facial asymmetry in visual perception: A 3-dimensional data analysis. Am J Orthod Dentofac Orthop. 137(2)2010.

Mommaerts MY, Nagy KK: Analysis of the cleft lip-nose in the submental-vertical view. Part II. Panel study: Which is the most important deformity? J Cranio-Maxillofacial Surg. 36(6):315-320, 2008.

Nakamura N, Sasaguri M, Okawachi T, Nishihara K, Nozoe E: Secondary correction of bilateral cleft lip nose deformity - Clinical and three-dimensional observations on pre- and postoperative outcome. J Cranio-Maxillofacial Surg. 39(5):305-312, 2011.

Nkenke E, Lehner B, Kramer M, Haeusler G, Benz S, Schuster M, Neukam FW, Vairaktaris EG, Wurm J: Determination of facial symmetry in unilateral cleft lip and palate patients from three-dimensional data: technical report and assessment of measurement errors. Cleft Palate Craniofac J. 43(2):129-137, 2006.

Oh TS, Choi JW, Koh KS: Upper Lip Asymmetry Perception Using Three-Dimensional Anthropometry in Patients With Unilateral Cleft Lip Deformity. J Craniofac Surg. 22(6):2080-3, 2011.

Okawachi T, Nozoe E, Nishihara K, Nakamura N: 3-Dimensional Analyses of Outcomes Following Secondary Treatment of Unilateral Cleft Lip Nose Deformity. J Oral Maxillofac Surg. 69(2):322-332, 2011.

Ort R, Metzler P, Kruse AL, Matthews F, Zemann W, Grätz KW, Luebbers H-T: The Reliability of a Three-Dimensional Photo System- (3dMDface-) Based Evaluation of the Face in Cleft Lip Infants. Plast Surg Int. 2012(3):1-8, 2012.

Othman SA, Ahmad R, Asi SM, Ismail NH, Rahman ZAA: Three-dimensional quantitative evaluation of facial morphology in adults with unilateral cleft lip and palate, and patients without clefts. Br J Oral Maxillofac Surg. 52(3):208-213, 2014.

Othman SA, Aidil Koay NA: Three-dimensional facial analysis of Chinese children with repaired unilateral cleft lip and palate. Sci Rep. 6(1):418, 2016.

Schwenzer-Zimmerer K, Chaitidis D, Berg-Boerner I, Krol Z, Kovacs L, Schwenzer NF, Zimmerer S, Holberg C, Zeilhofer H-FF: Quantitative 3D soft tissue analysis of symmetry prior to and after unilateral cleft lip repair compared with non-cleft persons (performed in Cambodia). J Cranio-Maxillofacial Surg. 36(8):431-438, 2008.

Singh GD, Levy-Bercowski D, Santiago PE: Three-dimensional nasal changes following nasoalveolar molding in patients with unilateral cleft lip and palate: geometric morphometrics. Cleft Palate Craniofac J. 42(4):403-409, 2005.

Singh GD, Levy-Bercowski D, Yáñez MA, Santiago PE: Three-dimensional facial morphology following surgical repair of unilateral cleft lip and palate in patients after nasoalveolar molding. Orthod Craniofac Res. 10(3):161-166, 2007.

Stauber I, Vairaktaris E, Holst A, Schuster M, Hirschfelder U, Neukam FW, Nkenke E: Three-dimensional analysis of facial symmetry in cleft lip and palate patients using optical surface data. J Orofac Orthop. 69(4):268-82, 2008.

Trotman C-A, Phillips C, Faraway JJ, Hartman T, van Aalst JA: Influence of Objective Three-Dimensional Measures and Movement Images on Surgeon Treatment Planning for Lip Revision Surgery. Cleft Palate-Craniofacial J. 50(6):684-695, 2013.

Tse R: Unilateral cleft lip: Principles and practice of surgical management. Semin Plast Surg.2012.

Tse R, Booth L, Keys K, Saltzman B, Stuhaug E, Kapadia H, Heike C: Reliability of Nasolabial Anthropometric Measures Using Three-Dimensional Stereophotogrammetry in Infants with Unrepaired Unilateral Cleft Lip. Plast Reconstr Surg. 133(4):530e–542e, 2014.

Tse R, Lien S: Unilateral Cleft Lip Repair Using the Anatomical Subunit Approximation. Plast Reconstr Surg. 136(1):119-130, 2015.

Tse RW, Oh E, Gruss JS, Hopper RA, Birgfeld CB: Crowdsourcing as a Novel Method to Evaluate

Aesthetic Outcomes of Treatment for Unilateral Cleft Lip. Plast Reconstr Surg. 138(4):864-874, 2016.

Weinberg SM, Naidoo SD, Bardi KM, Brandon CA, Neiswanger K, Resick JM, Martin RA, Marazita ML: Face shape of unaffected parents with cleft affected offspring: combining three-dimensional surface imaging and geometric morphometrics. Orthod Craniofac Res. 12(4):271-281, 2009.

Wu J, Heike C, Birgfeld C, Evans K, Maga M, Morrison C, Saltzman B, Shapiro L, Tse R: Measuring Symmetry in Children With Unrepaired Cleft Lip: Defining a Standard for the Three-Dimensional Midfacial Reference Plane. Cleft Palate-Craniofacial J. 53(6):695-704, 2016a.

Wu J, Liang S, Shapiro L, Tse R: Measuring symmetry in children with cleft lip. Part 2: Quantification of nasolabial symmetry before and after cleft lip repair . Cleft Palate Craniofac J. 53(6):1-2, 2016b.

Wu J, Tse R, Shapiro LG: Automated Face Extraction and Normalization of 3D Mesh Data. IEEE EMBS Conf .:1-4, August 2014.

Yeow VKL, Huang MHS, Lee ST, Fook Chong SMC: An anthropometric analysis of indices of severity in the unilateral cleft lip. J Craniofac Surg. 13(1):68-74, 2002.

Table 1 Subject demographics.

		Group A		Group B	
		Infant Pre-/Post-repair	**Infant Control**	**8-10 y Post-repair***	**8-10 y Control**
Mean age		7.5 / 10 months	5.5 months	9.5 years	9 years
Sex	Male	32	4	27	2
	Female	13	1	17	3
Ethnicity	Caucasian	27	2	17	4
	Asian	4	1	19	0
	Latino	0	0	0	1
	Native American	0	0	1	0
	Mixed Caucasian	4	2	3	0
	Other	7	0	2	0
	Did not indicate	3	0	2	0

* For Group B, pre-repair images were not available. One subject was excluded from the study due to an image quality problem, resulting in 44 subjects for 8-10 y Post-repair.

Table 2 Statistics for cleft type, side, extent and surgical interventions.

		Infant Pre-/Post-repair	8-10 y Post-repair
Cleft Side	Left	25	33
	Right	20	11
Cleft Type	Complete	15	41
	Complete + band*	6	2
	Incomplete	24	1
Cleft Extent	Cleft Lip	15	6
	Cleft Lip and Alveolus	5	2
	Cleft Lip and Palate	25	36
Associated Syndrome		4	2‡
Interventions (in house)	Primary repair	45 (45)	44 (19)
	Secondary revision	0 (0)	23 (23)
	Tip rhinoplasty	0 (0)	8 (7)
	Septorhinoplasty	0 (0)	3 (2)
	Alveolar bone graft	0 (0)	32 (32)

* Band (a.k.a. Simonart band) was defined as any soft tissue found across the cleft in the presence of a complete cleft of alveolus.
† Popliteal pterygium syndrome, bilateral hand and foot syndactyly, cardiac anomalies, EEC.
‡ Van der Woode syndrome.

Table 3 Mean values of severity measures before and after primary cleft repair.

		Dorsum Deviation	Tip-Alar Volume Ratio	Alar-Cheek Definition	Columellar Angle
Group A	**Infant Pre-repair**	9.63*	1.59*	14.65	19.49*
	Infant Post-repair	2.87†	1.20†	8.29†	11.85†
	Infant Control	2.00	1.11	8.09	8.90
Group B	**8 - 10 y Post-repair**	2.94	1.18	11.92	9.15
	8 - 10 y Control	1.37	1.15	5.88	2.19

* Significant difference compared with infant control ($p<0.05$).
† Significant difference compared with infant pre-repair ($p<0.05$).

Table 4: Pearson correlation coefficients and p-values of the computational measures to the expert consensus rankings.

	Dorsum Deviation	Tip-Alar Volume Ratio	Alar-Cheek Definition	Columellar Angle
Group A*	0.8 ($p < 0.01$)	0.75 ($p < 0.01$)	0.41 ($p<0.01$)	0.54 ($p<0.01$)
Group B	0.38 ($p<0.01$)	0.38 ($p<0.01$)	0.18 ($p=0.20$)	0.37 ($p<0.01$)

* Only the pre-repair and control images are ranked in Group A.

Figure 1 A patient with cleft lip nasal deformity: A. Asymmetry and deviation of nasal tip and dorsum relative to midline **B.** Deviation of columella and blunting of nasal ala-cheek junction on the cleft side on the cleft side.

Figure 2 Shape analysis based measurements: A. Frontal view of a 3D mesh. Dorsal Deviation is defined as the angle between the dorsal line (red) and mid-facial reference plane (blue), whereas Tip-Alar Volume Ratio is the ratio of volumes of the two halves of the nose divided by the mid-facial reference plane, indicated by green and red shades. **B.** Basal view of a 3D mesh. Alar-Cheek Definition is defined as the difference between angles (green) at the two sides of the nose, and Columellar Deviation is the angle columella (red) makes with the yz-plane. **C.** The highest points of the nose at the contours taken between pronasale and sellion were used to fit the dorsal line. **D.** The area under each horizontal contour was divided into two by using the mid-facial reference plane (blue dot). The sum of these areas on all contours approximated the nose volume, and the ratio of the larger sum to the smaller sum was calculated as Tip-Alar Volume Ratio. **E.** Curvature angles were calculated at two nose corners by fitting lines (green) to the neighboring points towards nose tip. **F.** The most prominent points on contours between the subsanale and the midpoint between the subnasale and pronasale were used to fit the columellar line.

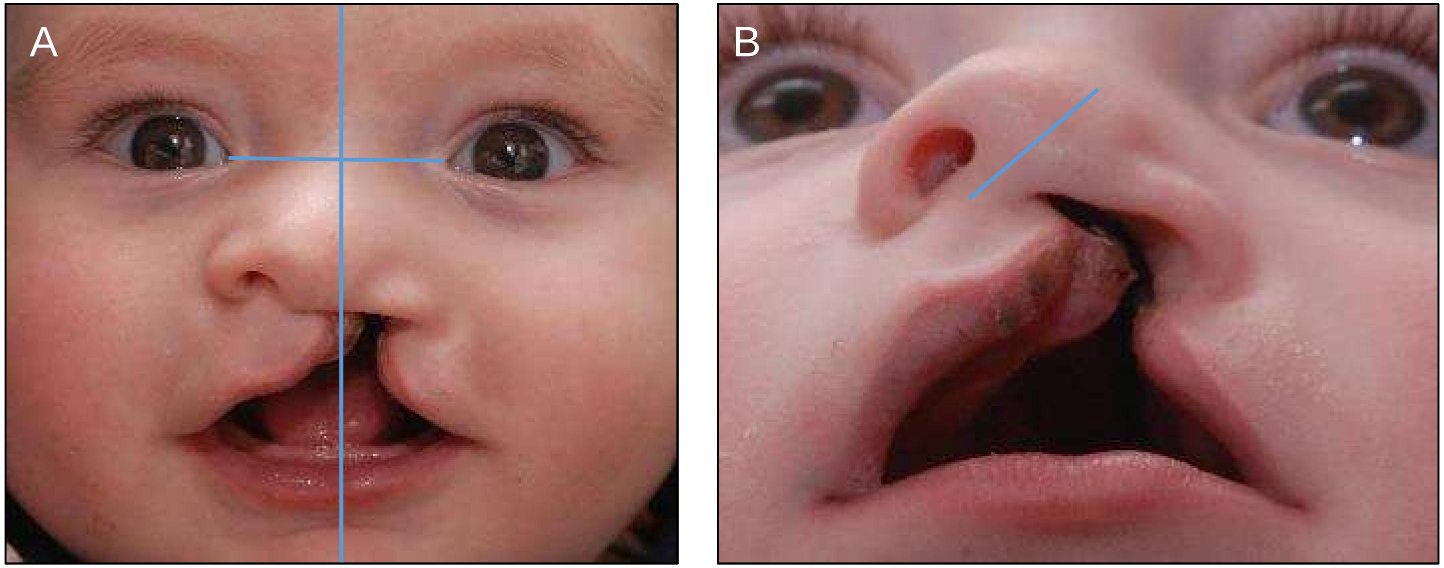
Figure 3 Horizontal contours and curvature analysis: A. The profile contour is used to detect subnasale (sn), pronasale (pn) and sellion (se). **B.** The horizontal contours from a frontal view. **C.** Horizontal contours from a basal view. **D.** Several points of interest including nose corners (green), nose tip (red) and mid-facial reference plane were noted on a horizontal contour. **E.** Plot of curvature angle at each point in horizontal contour in D. The highest point of the nose (red) and two corners of the nose where nasal ala meets the cheek (green) were detected through curvature analysis. **F.** Nose corners reflected on the 3D surface for visualization. They follow the crease of the nose.

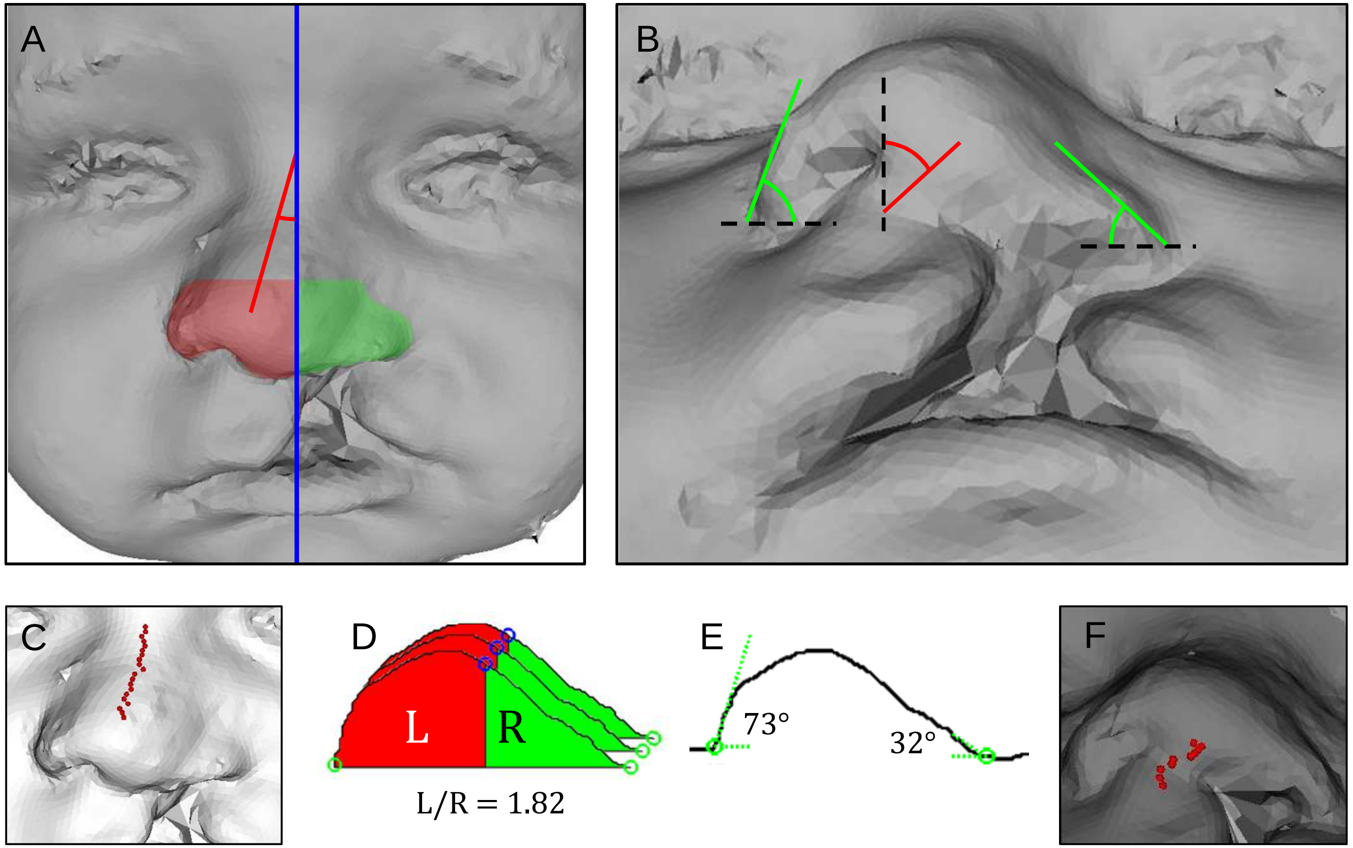
Figure 4 Mean values of severity measures by cleft type: For Infants Pre-repair, all measurements followed a decreasing trend with less severe cleft types. The differences reached significance for complete clefts and variably for complete clefts with band and incomplete clefts. There were more significant differences amongst groups for Dorsum Deviation and Tip-Alar Volume Ratio. All measures improved after surgery and were similar amongst groups except for persistent trends of worse Columellar Angle for more severe cleft types in both the Infant Post-Repair and the 8-10 year old group. The Alar-Cheek definition was similar amongst groups for Infants post-repair but seemed to follow a trend of worse measures with more severe clefts for children in the older group.

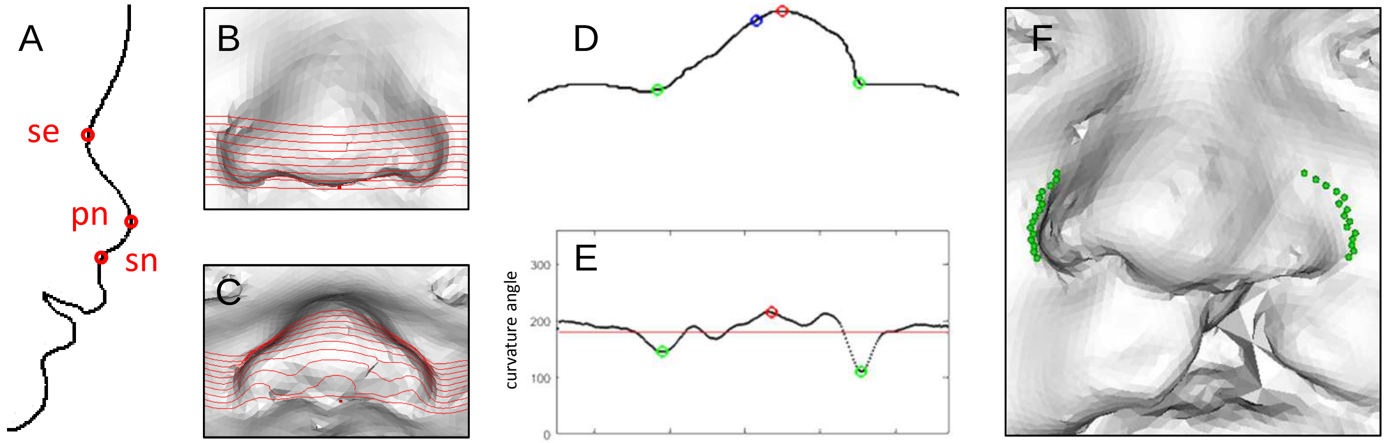
* Significant difference compared with Control Infants ($p<0.05$).
† Significant difference compared with Pre-repair Infants with incomplete cleft ($p<0.05$).
‡ Significant difference compared with Pre-repair Infants with complete cleft with band ($p<0.05$).

Figure 5: Mean values of severity measures for different cleft extent: For Infants Pre-repair, all measurements were similar for CLP and CLA but they decreased for CL and further for control. All measurements decreased after repair. For Infants Post-repair, there were significant differences in Dorsum Deviation amongst groups but not for the other measures. For Children 8-10 years old, most measurements amongst groups were similar, however, there were few subjects with CL only.

***** Significant difference compared with infant control ($p<0.05$).
† Significant difference compared with infant pre-repair CL ($p<0.05$).
‡ Significant difference compared with infant post-repair CL ($p<0.05$).
§ Significant difference compared with 8-10 y control ($p<0.05$).


A
B


A
B
C
D
L
R
L/R = 1.82
E
73°
32°
F


A
se
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B
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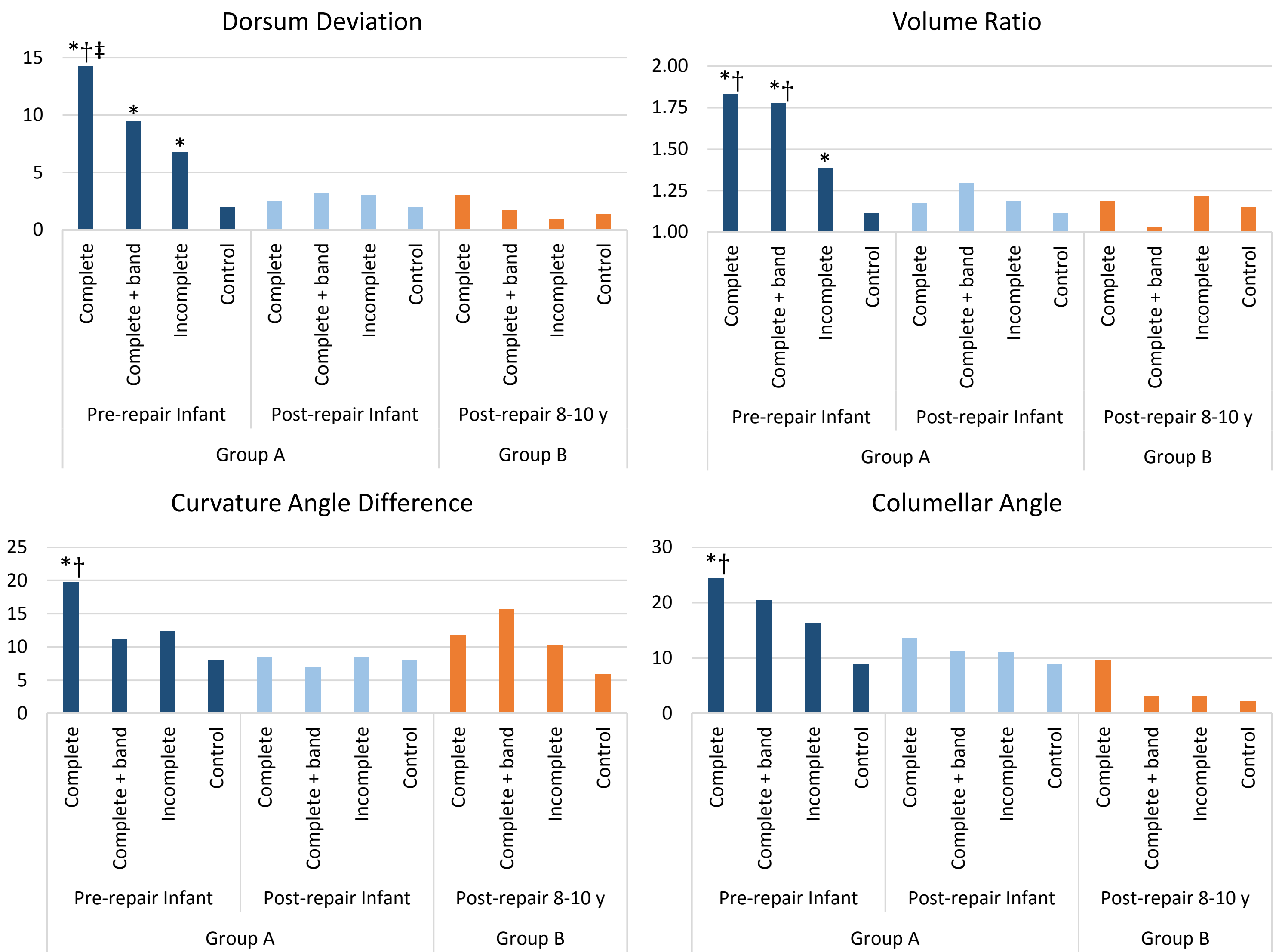
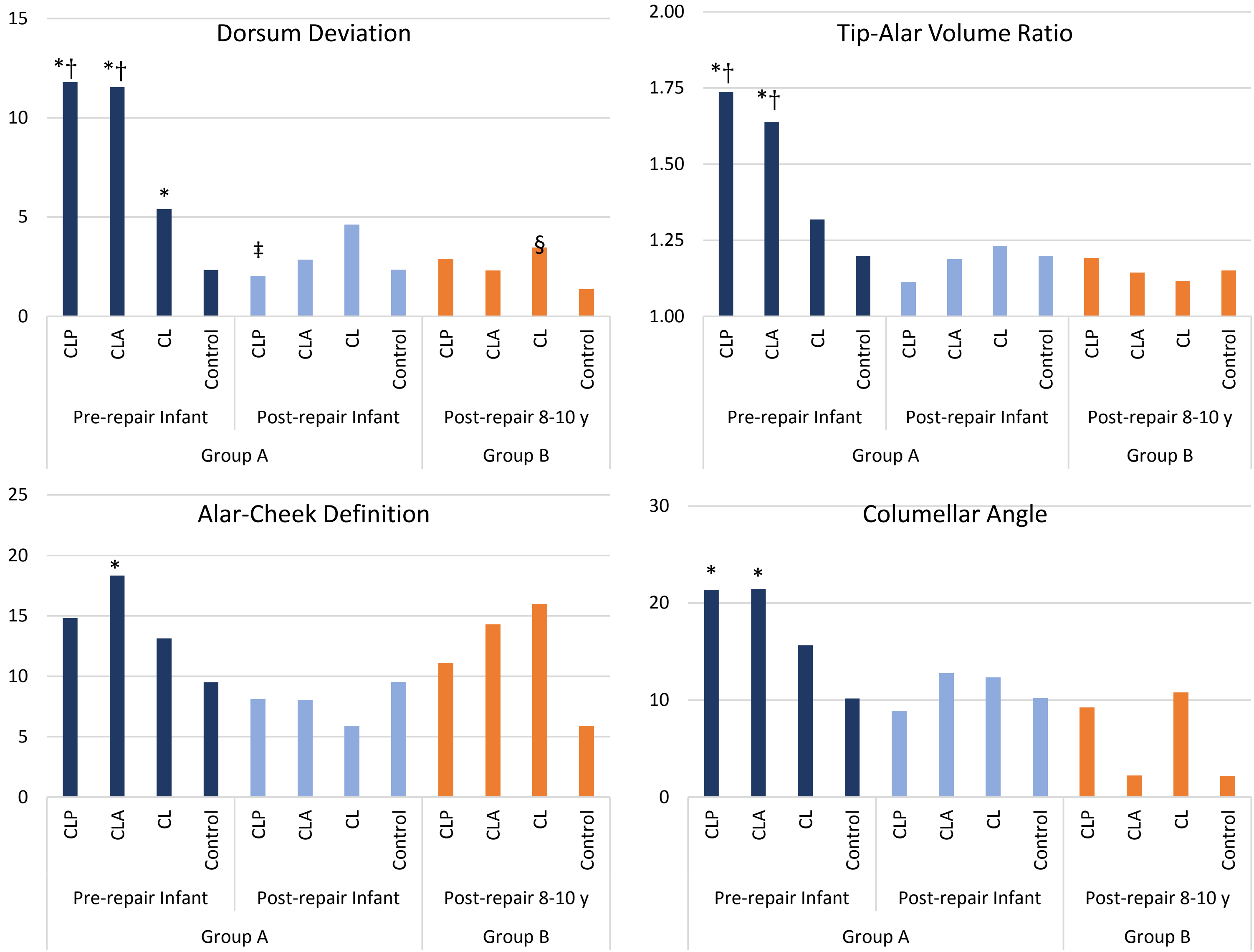
curvature angle
300
200
100
0
F



Dorsum Deviation
15
10
5
0
*†‡
*
*
Volume Ratio
2.00
1.75
1.50
1.25
1.00
*†
*†
*
Curvature Angle Difference
25
20
15
10
5
0
*†
Columellar Angle
30
20
10
0
*†
Complete
Complete + band
Incomplete
Control
Pre-repair Infant
Post-repair Infant
Post-repair 8-10 y
Group A
Group B


Dorsum Deviation
Tip-Alar Volume Ratio
Alar-Cheek Definition
Columellar Angle
CLP
CLA
CL
Control
Pre-repair Infant
Post-repair Infant
Post-repair 8-10 y
Group A
Group B