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ORIGINAL ARTICLE

Measuring Symmetry in Children With Unrepaired Cleft Lip: Defining a Standard for the Three-Dimensional Mid-facial Reference Plane

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Objective: **Quantitative measures of facial form to evaluate treatment outcomes for cleft lip (CL) are currently limited. Computer-based analysis of three-dimensional (3D) images provides an opportunity for efficient and objective analysis. The purpose of this study was to define a computer-based standard of identifying the 3D mid-facial reference plane of the face in children with unrepaired cleft lip for measurement of facial symmetry.**

Participants: **The 3D images of 50 subjects (35 with unilateral CL, 10 with bilateral CL, five controls) were included in this study.**

Interventions: **Five methods of defining a mid-facial plane were applied to each image, including two human-based (Direct Placement, Manual Landmark) and three computer-based (Mirror, Deformation, Learning) methods.**

Main Outcome Measure: **Six blinded raters (threes cleft surgeons, two craniofacial pediatricians, and one craniofacial researcher) independently ranked and rated the accuracy of the defined planes.**

Results: **Among computer-based methods, the Deformation method performed significantly better than the others. Although human-based methods performed best, there was no significant difference compared with the Deformation method. The average correlation coefficient among raters was .4; however, it was .7 and .9 when the angular difference between planes was greater than 6° and 8°, respectively.**

Conclusions: **Raters can agree on the 3D mid-facial reference plane in children with unrepaired CL using digital surface mesh. The Deformation method performed best among computer-based methods evaluated and can be considered a useful tool to carry out automated measurements of facial symmetry in children with unrepaired cleft lip.**

KEY WORDS: *3D stereophotogrammetry; cleft lip; outcomes; symmetry*

Treatment of cleft lip (CL) can produce dramatic changes in nasolabial form; however, understanding the relative effect of individual interventions, techniques, or protocols is challenging given our lack of ideal methods to quantify longitudinal changes with treatment and growth. Recent advances in three-dimensional (3D) stereophotogrammetry have made rapid 3D digital capture of infants with unrepaired CL possible (Heike et al., 2010; Tse et al., 2014), and the use of this technology by treatment centers is likely to become more common (Al-Omari et al., 2005; Mosmuller et al. 2013). The application of computer vision techniques to the analysis of these 3D images provides an opportunity to quantify changes in a convenient and practical manner.

Our eventual goal is to develop an automated process to accurately assess nasolabial symmetry given that symmetry is a major component of facial attractiveness (Gorney and Harries, 1974; Little and Jones, 2003; Jones et al., 2007; Komori et al., 2009; Little et al., 2011) and a major goal of cleft treatment. To do so, a mid-facial reference plane (henceforth referred to as the *mid-facial plane*) needs to be defined so that 3D differences mirrored across this reference

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plane can be quantified. Ideally, this plane should divide the face into two halves, ignore the nasolabial region, and remain consistent throughout the course of cleft treatment. The mid-facial plane is not the plane of greatest symmetry of the entire face, as the latter would change in patients with changes in nasolabial form before and after an intervention. Given our objective of automation, this plane should be defined based solely on 3D surface images.

Nkenke et al. (2006) previously described a "mirror method" of determining the plane of greatest facial symmetry for children who have already undergone CL repair. We have developed two computer-based methods of defining a plane that vertically splits the face (using deformation and machine learning algorithms), ignores the nasolabial region, and can be applied to children who have unrepaired CL. Our objective was to determine which of these automated methods of defining a reference plane most closely approximates the mid-facial plane and is thus best for measuring facial symmetry in infants with unrepaired CL.

Methods

This study was approved by the Seattle Children's Hospital Institutional Review Board, and informed consent to participate was obtained for each subject. We assembled the 3D images of 50 subjects on whom reference planes were defined using five different methods. Thus, the data set included 250 defined planes. Six raters were provided with the possible reference planes for each subject so that the accuracy of each method could be assessed. The overall rating and ranking related to each method was used to determine the standard. Details are described below.

Cleft/Control Subjects

We enrolled 50 subjects into this study: 35 infants with unrepaired unilateral cleft lip (UCL), 10 infants with unrepaired bilateral cleft lip (BCL), and five infants without craniofacial differences. We approached parents of consecutive patients with CL who were receiving treatment by the senior author (R.T.) to participate. Patients with associated anomalies or syndromes were not excluded. Cleft characteristics were documented as part of the surgeon's standard clinical care using a modified LAHSHAL notation (Kriens, 1989). He also documented the presence or absence of a soft tissue band (previously known as Simonart band) across a complete cleft lip and alveolus (Semb and Shaw, 1991). The surgeon directly measured the columellar angle (Fisher et al., 2008) from the worm's eye view using a clear protractor at the time of lip repair. We used the columellar angle as an objective indicator of cleft nasal severity for unilateral cleft lip (Fisher et al., 2008) and as a measure of asymmetry for bilateral cleft lip.

Mid-facial Reference Planes Using Five Different Methods

All images were reviewed and met our image quality standards. We removed structures other than the face and head and corrected alignment into a standard facial frontal plane. We created five 3D images for each of the 50 subjects using each of the following five methods of defining the reference plane:

1. Direct Placement: An experienced cleft surgeon (R.T.) examined each 3D facial image and used Rapidform XOR3 software (Rock Hill, SC) to place a plane on what he considered to be the geometric vertical midline of the face that ignored the nasolabial region. Placement of a plane took approximately 20 minutes per subject.
2. Manual landmark: An experienced craniofacial pediatrician (C.H.) placed indirect landmarks on 3D images using 3dMD Vultus (Atlanta, GA). Landmarks included bilateral endocanthion points and the midline of the chin. A plane was determined by calculating the vertical geometric midline of these points. The reference plane was perpendicular to the plane defined by the three landmarks. Placement of landmarks took approximately 5 to 10 minutes per subject.
3. Mirror method: The 3D facial data were mirrored across an arbitrary plane. The original mesh and the mirrored mesh were then registered using an iterative-closest-point algorithm until the best mirrored plane was found according to the methods put forth by Nkenke et al. (2006).
4. Deformation method: We used a previously described tool that automatically locates 20 facial landmarks via a deformable registration algorithm. A template mesh, which includes the defined landmarks, is deformed to fit a target mesh using a geometric point detector (Liang et al., 2013). Once the landmarks were detected, we removed the nasolabial landmarks from the algorithm so that the geometric midline of the face could be calculated based on eye and chin points.
5. Learning method: This involves "artificial intelligence" that automatically recognizes specific facial regions. With the regions defined, the geometric midline of the face can be calculated. We have previously found that this method is less prone to error from artifacts (i.e., additional objects captured in an image, etc.) and errors in initial pose positioning (i.e., a subject positioned in a slanted position) than the mirror method in noncleft subjects (Wu et al., 2011). For this project, we modified the Learning method (Wu et al., 2011) so that the nasolabial region was ignored when defining a reference plane.

Evaluation of Reference Planes

We converted the full textured images to mesh images and created a software module (written in C++ and using VTK, http://www.vtk.org/) in which six facial meshes (all representing the same subject) could be displayed and rotated synchronously by the user (Fig. 1a and 1b). One image (upper left) had no defined plane and controlled the rotation of all six images; the other five images displayed a reference plane defined by each of the five methods. For each subject, images were arranged in random order so that raters were blind to the method used to define the displayed planes. We presented subjects to raters in a random order and in batches of 10 to avoid rater fatigue.

Six raters (three cleft surgeons, two craniofacial pediatricians, one craniofacial morphology researcher) evaluated the five planes generated for each of the 50 subjects (total of 250 images) to determine the relative success or accuracy of each method in defining the mid-facial plane. Three-dimensional images were displayed on a 27-inch computer monitor to ensure sufficient image quality to examine facial characteristics. We defined the mid-facial plane as the plane that best divided the face in into symmetric halves, ignoring the nasolabial region and the overall head shape. Raters were instructed to use the forehead, eyes, ears, commissures, and chin as reference for the overall face. For each subject, raters rotated the 3D meshes to ensure they could appreciate the full 3D facial form before positioning the mesh into what they felt was the best frontal orientation. To determine the relative performance of one method to another, images were ranked in order of best to worst approximation of the mid-facial plane. If two planes could not be discerned, raters could assign the same ranking. Raters were also asked to rate the accuracy of planes according to a 1 to 7 numeric scale (Table 1) with the aid of a visual guide (Fig. 2). These ratings evaluated the deviation (in degrees) from each rater's imagined best mid-facial plane, as well as the lateral displacement. The rating scale and a visual guide (Fig. 2) were developed through consensus by the raters who examined defined by the five methods on five nonstudy subjects. Raters were asked to indicate if the mid-facial plane could not be determined and why.

Statistical Analysis

We used *t* tests to evaluate whether differences between each method's rating and ranking were significant according to a 95% threshold and analysis of variance to evaluate differences in the ranking of various methods. We used Pearson correlation coefficients to evaluate interrater reliability.

Results

Subject Characteristics

Subject characteristics, cleft severity, and type of cleft lip are summarized in Table 2. There was a wide range of columellar angle reflecting a broad spectrum of severity for subjects with UCL (Fig. 3) and of asymmetry for subjects with BCL (Fig. 4).

Evaluation of Planes Defined by Five Methods: Ranking

Planes were ranked from 1 to 5 (best to worst). Results are summarized in Table 3. The two manual methods, received better mean rankings (2.43 and 2.54 for Direct Placement and Manual Landmark, respectively) than the three automated methods (3.27, 2.66, and 3.15 for Mirror, Deformation, and Learning methods, respectively). The manual methods also received better rankings for each of the subject types (UCL, BCL, and control). Among computer-based methods, the Deformation method performed the best overall and for each subject type (UCL, BCL, and control).

There was no significant difference in rankings assigned to the Deformation method compared with each of the two manual methods (P values of .10 and .41 for Direct Placement and Manual Landmark methods, respectively). In contrast, the Deformation method performed significantly better than the other two computer-based methods (P values were $<.01$ and $<.01$ for the Mirror method and Learning method, respectively).

The distribution of rankings assigned for each of the five methods is displayed in Figure 5. The Deformation method received the best ranking more often than all the other methods. The Mirror method was most frequently ranked the worst.

Evaluation of Planes Defined by Five methods: Rating of Accuracy

Planes were rated for accuracy according to the developed scale (Table 1; Fig. 2) from 1 to 7 (best to worst). Results are summarized in Table 3. The two manual methods received the best ratings. Among computer-based methods, the Deformation method received the best ratings for subjects with UCL and BCL; however, the Mirror method performed best for the control group (Table 3).

There was no significant difference in the ratings of the Deformation method compared with each of the two manual methods (P values of .08 and .37 for Direct Placement and Manual Landmark methods, respectively). In contrast, the Deformation method performed significantly better than the other two computer-based

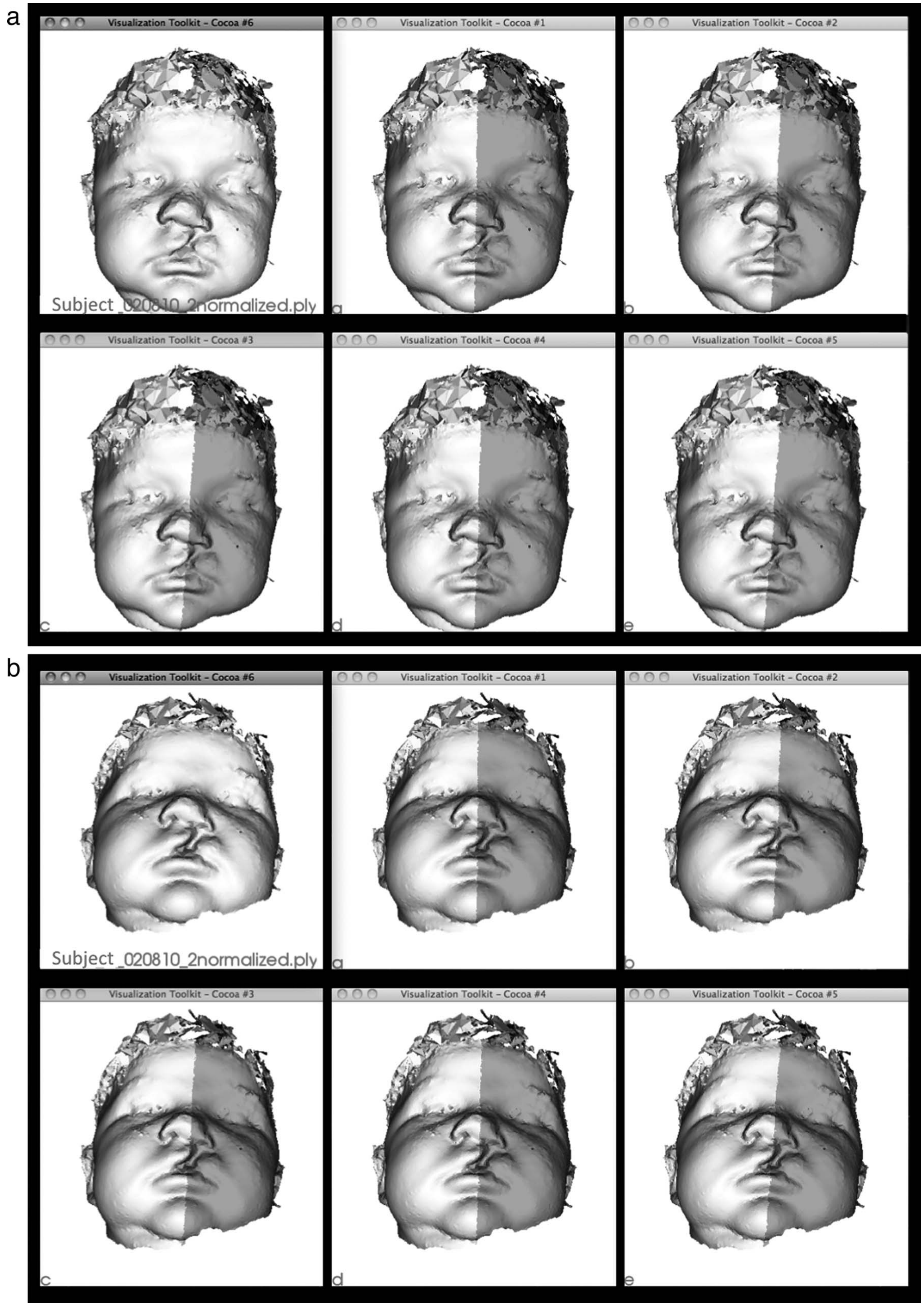

FIGURE 1 **a: Screenshot of survey module used to evaluate the accuracy of planes produced by each of the five methods of defining a reference plane. Six raters assessed how well each plane approximated the mid-facial plane of the face for measurement of symmetry. Raters were blinded to the method used to produce each plane, and planes were arranged in random order. The upper left mesh was for reference and had no plane on it. b: The facial meshes could be rotated synchronously to allow examination from different views.**

TABLE 1 Rating Scale for Approximation of a Plane to the Midfacial Plane

Scale	*Definition*	
1	Absolute match	No difference in planes
2	Probably	Within 1° of rotation and 1/128 facial width of translation
3	Very close	Within 2° of rotation and 1/64 facial width of translation
4	Slightly off	Within 3° of rotation and 1/32 facial width of translation
5	Moderately off	Within 5° of rotation and 1/16 facial width of translation
6	Severely off	Within 10° of rotation and 1/8 facial width of translation
7	Unacceptable	Greater than 10° of rotation or 1/8 facial width of translation

methods (P values were <.01 and <.01 for the Mirror method and Learning method, respectively).

The distribution of ratings for the five methods is illustrated in Figure 6. The two manual methods (Direct and Manual Landmark) were rated perfectly (score of 1) more often than the other automated methods and rarely receive ratings lower than 4. The Deformation method received the best scores among automated methods. The distribution of rating scores for the Deformation method was similar to the manual human-based methods.

Rater Reliability

The average Pearson correlation coefficient comparing rating scores assigned by each rater was .43 (Table

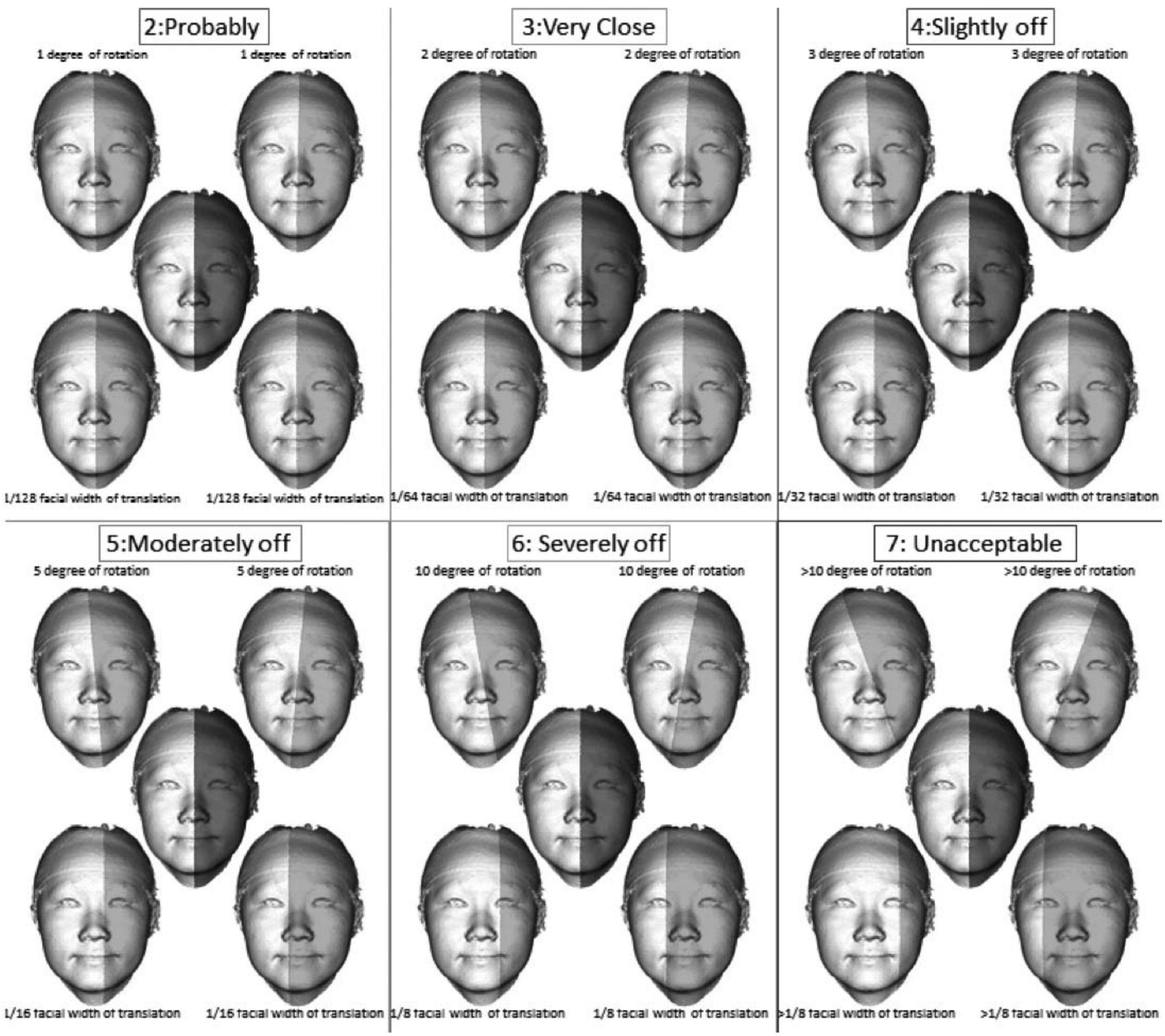

FIGURE 2 Visual guide for rating scale defined in Table 1.

TABLE 2 Characteristics of Patients Whose Images Were Used in This Study

	Unilateral Cleft Lip n = 35	*Bilateral Cleft Lip n = 10*	*No Cleft n = 5*
Mean age at photo, mo	5.8	6.7	3.2
Male:female	4:3	3:2	4:1
Laterality of cleft (left:right)	19:16	n/a	n/a
Syndrome	2*	1†	n/a
Cleft extent			
Cleft lip	6 (17%)	1 (10%)	
Cleft lip and alveolous	16 (46%)	1 (10%)	
Cleft lip and palate	13 (37%)	8 (80%)	
Cleft lip type			
Microform	1 (3%)	1 (10%)	
Incomplete	17 (49%)	0 (0%)	
Complete + soft tissue band‡	8 (23%)	5 (50%)	
Complete	9 (26%)	4 (40%)	

* One child with craniofacial microsomia and one with popliteal pterygium.
† One child with ectrodactyly ectodermal dysplasia.
‡ Differentiated from incomplete cleft lip by presence of a complete cleft alveolus.

4). None of the raters indicated that a mid-facial reference plane could not be identified. All of the raters noted that the angular difference between planes was often very small. To determine if rater reliability would change with the magnitude of this difference, we calculated Pearson correlation coefficients for assigned ratings within categories defined by increasing angular differences between defined planes (Fig. 7). When there was a difference between planes of more than 6°, the average Pearson correlation coefficient increased to .66, while for more than 8°, the average Pearson score was .9.

Discussion

"Despite modern technological attempts to reproduce the first-hand experience, there is no perfect substitute for human, stereoscopic, three-dimensional vision in evaluating appearance" (Lu and Bartlett, 2014).

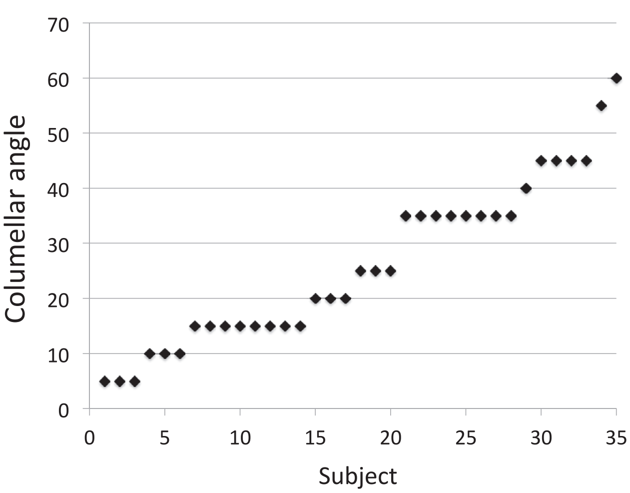

FIGURE 3 Distribution of columellar angle as a reflection of cleft severity for subjects with UCL.

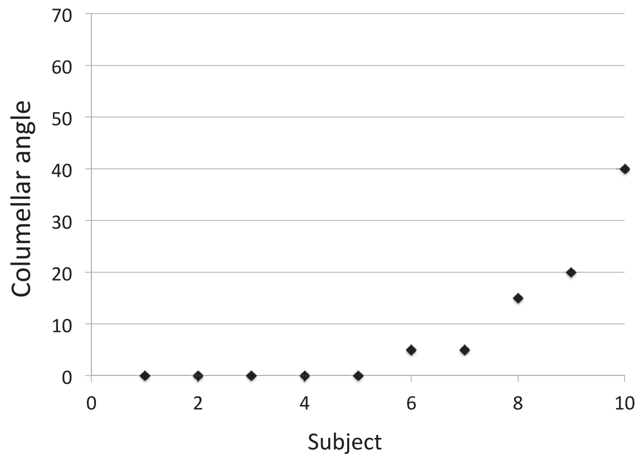

FIGURE 4 Distribution of columellar angle as a reflection of asymmetry for subjects with BCL.

Assessment of surgical severity and outcomes is often based on subjective evaluation of 2D images for treatment of cleft lip and other areas of plastic surgery. Three-dimensional stereophotogrammetry provides an opportunity for objective, 3D-based assessment of form. Given that image capture is rapid, is noninvasive, bears no direct patient burden beyond the time required to obtain the image, and avoids errors from parallax, 3D sterephotogrammetry might offer significant advantages over computed tomography (Kane et al., 2007), direct anthropometrics (Yeow et al., 2002), facial casts (Dusková et al., 2006; Ferrario et al., 2007), and 2D photography (Oh et al., 2011). Although laser scanning is accurate, the capture time is too slow for use with young children who are prone to impatience and quick movements (Mori et al., 2005; Schwenzer-Zimmerer et al., 2008). The reliability of 3D sterephotogrammetry has been documented in children with unrepaired cleft lip (Krimmel et al., 2006; Li et al., 2013; Tse et al., 2014), and facial analysis has typically involved landmark-based anthropometric measurement (Hood et al., 2004; Krimmel et al., 2006; Schwenzer-Zimmerer et al., 2008; Li et al., 2013; Tse et al., 2014). These measurements can be tedious and time-consuming, making them impractical for most surgeons and researchers. Advances in computer vision techniques and the application to 3D stereophotogrammetry provide opportunities for novel and convenient approaches for analysis.

Characterization of symmetry in the treatment of CL has been of great interest. Traditionally, anthropometric analysis on 3D images has involved comparison of interlandmark distances, and this approach has been applied after nasoalveolar molding (Yamada, 2003; Simanca et al., 2011), prior to cleft lip repair (Schwenzer-Zimmerer et al., 2008), after cleft lip repair (Hoefert et al., 2010; Bugaighis et al., 2013), and after secondary cleft

TABLE 3 Rankings and Rating Scores for All Methods

	All *n = 50*	*Unilateral Cleft Lip* *n = 35*	*Bilateral Cleft Lip* *n = 10*	*Control* *n = 5*
Ranking score*				
Manual				
Direct plane placement	2.43	2.62	2.03	1.90
Landmark placement	2.54	2.52	2.79	2.13
Automated				
Mirror	3.27	3.32	3.44	2.47
Deformation	2.66	2.70	2.66	2.36
Learning	3.15	3.17	3.36	2.63
Rating score*				
Manual				
Direct plane placement	2.45	2.60	2.16	2.00
Landmark placement	2.53	2.57	2.56	2.20
Automated				
Mirror	3.07	3.15	2.64	2.37
Deformation	2.61	2.63	2.64	2.37
Learning	2.93	2.99	3.04	2.30

* Lower numbers indicate better approximation to the best midfacial reference plane for measuring facial symmetry.

surgery (Devlin et al., 2007; van Loon et al., 2010). This approach is limited in that it considers only linear distances as surrogate indicators of 3D form and requires manual placement of each landmark.

Further attempts at measuring symmetry have involved defining a mid-sagittal plane and measuring distances to specific landmarks across this plane (Bilwatsch et al., 2006; Nkenke et al., 2006; Stauber et al., 2008). More recent analyses use all available facial data about the "plane of symmetry" to characterize asymmetry and have been applied in the study of the normal population (Hartmann et al., 2007; Djordjevic et al., 2013, 2014; Alqattan et al., 2015), of patients following cleft lip repair (Singh et al., 2007; Nakamura et al., 2010), and of patients before and after cleft surgery (Hood et al., 2003; Schwenzer-Zimmerer et al., 2008; van Loon et al., 2010). These latter studies require the placement of multiple landmarks to define the "plane of symmetry." The time-intensive and tedious nature of such analysis hampers wide adoption in the assessment of outcomes.

Our goal is to develop automated quantitative measures of 3D facial symmetry for children with cleft lip that can be easily used to evaluate treatment outcomes. To do so, an automated method of defining the mid-facial reference plane is needed. In a perfectly symmetric face, this plane would be the same as the plane of symmetry and would equally divide the two halves. However, most human faces are not perfectly symmetric. Asymmetry of the nasolabial region in a child with an unrepaired cleft lip (Hajnis, 1978; Farkas et al., 1993) will alter the plane of symmetry relative to the other unaffected parts of the face (Wu et al., 2011). As such, the plane of symmetry will change before and after cleft treatment. We wanted to define a mid-facial plane representing the midline of the face that would remain constant, regardless of changes that occurred in the nasolabial region. This mid-facial plane would allow measurement of changes and symmetry with sequential changes in the treatment of CL. The convergence of the

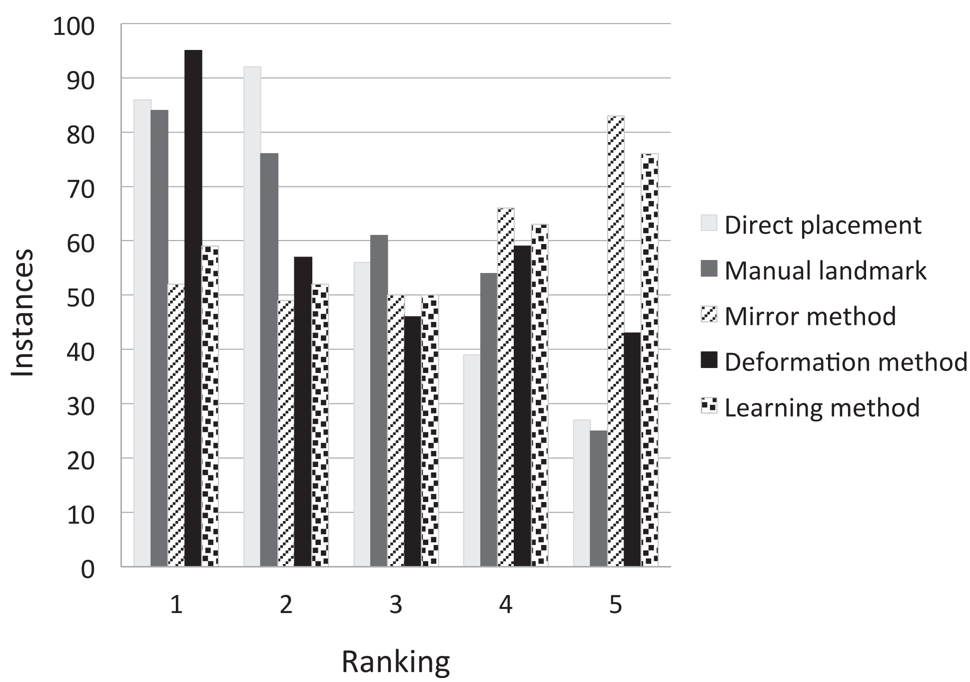

FIGURE 5 Distribution of rankings for each method of defining a reference plane. Six raters ranked how close the displayed planes approximated the mid-facial plane. The five methods of producing reference planes were applied to 3D images of 50 subjects (35 UCL, 10 BCL, and five controls). Each method was assigned 300 rankings.

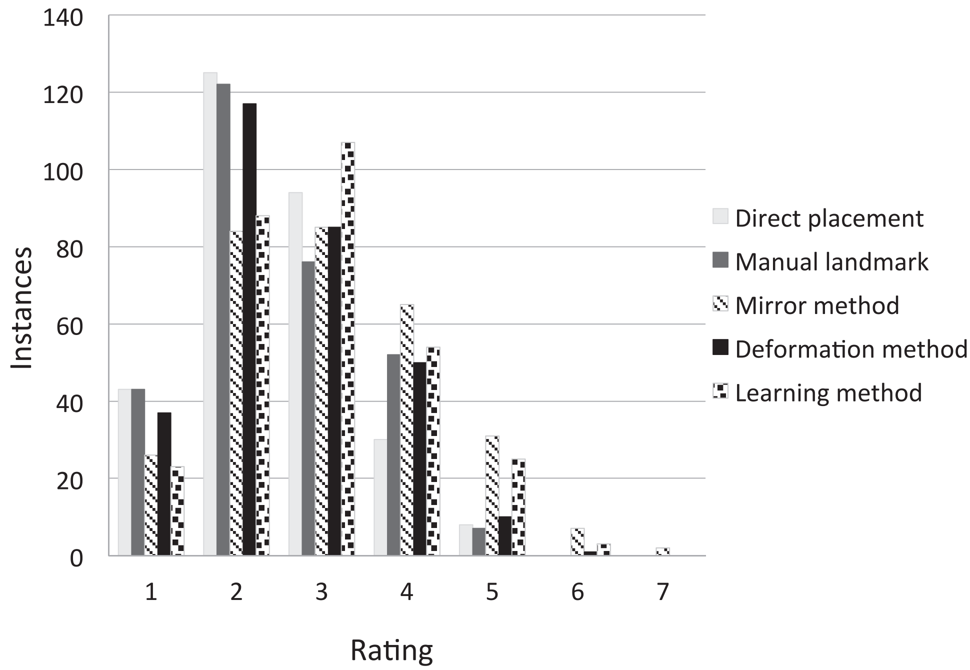

FIGURE 6 Distribution of ratings for each method of defining a reference plane. Six raters ranked how close the displayed planes approximated the mid-facial plane using the visual guide and rating scale in Figure 2 and Table 1. The five methods of producing reference planes were applied to 3D images of 50 subjects (35 UCL, 10 BCL, and five controls). Each method was assigned 300 ratings.

plane of symmetry with the mid-facial plane (that ignores the nasolabial region) would imply symmetry, and divergence would imply asymmetry. The mid-facial plane could then be used to quantify severity and treatment success.

The Mirror method repeatedly mirrors an object until the calculated plane of greatest symmetry is found (Nkenke et al., 2006). As expected, this method performed well for normal controls (grossly symmetric) and less well for children with unrepaired cleft lip (grossly asymmetric). to better define the mid-facial plane for children with unrepaired cleft lip, we modified computer-based methods of facial analysis that we had previously developed. The Learning method involved a two-step process of landmark-related region detection using "artificial intelligence" and mid-facial reference plane computation using the defined regions to calculate the midline of the face (Wu et al., 2011). We modified this method to ignore the nasolabial region so that the geometric midline of the rest of the face could be calculated. The second method we modified was one that was developed to automatically identify facial anthropometric landmarks (Liang et al., 2013). The Deformation method uses a template mesh with predefined landmarks and involves a computer-based method to deform the template to fit the subject mesh. We removed the nasolabial landmarks from the algorithm so that the geometric midline of the face could be determined in children with unrepaired cleft lip. In preliminary tests, the modifications seemed to produce a more accurate midline in the case of unrepaired cleft lip. None of these methods, including the Mirror method, have been validated for assessment of the unrepaired cleft lip. We found that all performed well in this study but that the Deformation method most closely achieved the plane placed by humans. Although both manual methods received the best scores, defining these planes was tedious and time-consuming, and there was no significant difference in scores for the manual methods compared with the Deformation method. As such, the Deformation method can be considered as an option for defining the mid-facial plane to quantify symmetry in infants with unrepaired cleft lip when either objective measures warrant their use or when the volume of ratings being sought is prohibitive. Both manual methods were tedious and time-consuming.

TABLE 4 Pearson correlation Coefficients for Interrater Reliability of Ratings

Rater	*2*	*3*	*4*	*5*	*6*
1	.48	.41	.46	.5	.48
2		.53	.35	.5	.51
3			.18	.37	.46
4				.38	.35
5					.5

Although we did not specifically assess these methods and the generated reference planes on children following cleft lip repair, we did include several control subjects in the sample set (Table 3). In this subgroup, the manual methods performed best, but among the automated methods, the Deformation method performed better or similar to the other methods. Given that facial symmetry of children with

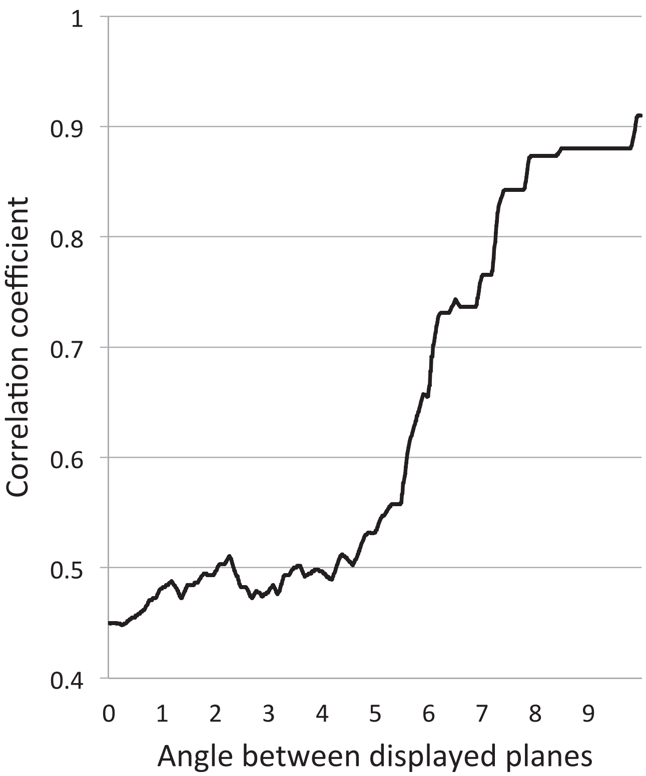

FIGURE 7 The average Pearson correlation coefficient for rating scores was higher when the angle between planes was greater. Differences were more readily perceived when differences were greater than 6° as reflected by the higher reliability coefficients.

cleft lip following repair likely approaches that of control subjects, we would assume that the Deformation method could be used for longitudinal assessment of subjects through their course of treatment. In further preliminary studies, we have used the Deformation method to define the mid-facial plane to quantify symmetry before and after CL repair (Wu, 2014). We have also developed computer-based tools using these measures that are capable of predicting cleft severity, as defined by an expert cleft surgeon (Wu et al., 2014).

The subject characteristics in this study were consistent with typical cleft patterns observed in patients treated at our center. We included control subjects without CL to ensure validity and because their degree of symmetry would represent the treatment goal. Given that there is no gold standard to measure facial symmetry and the ultimate objective following cleft treatment is the human perception of symmetry, we used a panel of six raters to determine the best mid-facial plane. Human visual perception outperforms any available technology (Lu and Bartlett, 2014), and it was not surprising to find that manual methods of defining the mid-facial plane performed better than automated methods.

In this study, we used 3D stereophotogrammetry to represent 3D form. Given that images are viewed on a 2D screen, we required raters to rotate each 3D image so that 3D stereoscopic form could be perceived. The movement creates motion parallax (Lu and Bartlett, 2014) that provides the rater with cues for depth perception. The movement also ensured that the face was positioned in the best frontal view for each individual rater.

Perceptions of differences in the mid-facial planes were difficult for the raters to determine. This may have been because all of the methods performed well. When we restricted analyses to those images in which planes differed by more than 6° of rotation, the differences were more readily perceived as reflected by the higher reliability coefficients.

The current climate of health care demands objective measures of outcome. Given that symmetry is one of the major goals of treatment for cleft lip, quantification of changes over time would be useful to measure; this would help researchers identify which factors affect treatment success. Given the gross asymmetry of unrepaired cleft lip, a mid-facial plane of reference needs to be defined; of those evaluated here, the Deformation method performed best and appears to be a reasonable replacement for manual assignment of this reference plane.

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References

Al-Omari I, Millett DT, Ayoub AF. Methods of assessment of cleft-related facial deformity: a review. *Cleft Palate Craniofac J*. 2005;42:145–156.

Alqattan M, Djordjevic J, Zhurov AI, Richmond S. Comparison between landmark and surface-based three-dimensional analyses of facial asymmetry in adults. *Eur J Orthod*. 2015;37:1–12.

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 Craniomaxillofac Surg*. 2006;34:253–262.

Bugaighis I, Mattick CR, Tiddeman B, Hobson R. 3D asymmetry of operated children with oral clefts. *Orthod Craniofac Res*. 2013;17:27–37.

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*. 2007;44:391–395.

Djordjevic J, Pirttiniemi P, Harila V, Heikkinen T, Toma AM, Zhurov AI, Richmond S. Three-dimensional longitudinal assessment of facial symmetry in adolescents. *Eur J Orthod*. 2013;35:143–151.

Djordjevic J, Toma AM, Zhurov AI, Richmond S. Three-dimensional quantification of facial symmetry in adolescents using laser surface scanning. *Eur J Orthod*. 2014;36:125–132.

Dusková M, Kristen M, Smahel Z. The anthropometric verification of corrective surgery outcome in cleft secondary deformities. *J Craniofac Surg*. 2006;17:447–453.

Farkas LG, Hajnis K, Posnick JC. Anthropometric and anthroposcopic findings of the nasal and facial region in cleft patients before and after primary lip and palate repair. *Cleft Palate Craniofac J*. 1993;30:1–12.

Ferrario VF, Mian F, Peretta R, Rosati R, Sforza C. Three-dimensional computerized anthropometry of the nose: landmark representation compared to surface analysis. *Cleft Palate Craniofac J*. 2007;44:278–285.

Fisher DM, Tse R, Marcus JR. Objective measurements for grading the primary unilateral cleft lip nasal deformity. *Plast Reconstr Surg*. 2008;122:874–880.

Gorney M, Harries T. The preoperative and postoperative consideration of natural facial asymmetry. *Plast Reconstr Surg*. 1974;54:187–191.

Hajnis K. Cephalometric features in patients with facial clefts prior to primary surgical repair. *Acta Universitatis Carolinae–Biologica*. 1978;XII:69–103.

Hartmann J, Meyer-Marcotty P, Benz M, Häusler G, Stellzig-Eisenhauer A. Reliabilität einer Methode zur Berechnung der Gesichtssymmetrieebene und des Asymmetriegrades basierend auf 3-D-Daten. *J Orofac Orthop*. 2007;68:477–490.

Heike CL, Upson K, Stuhaug E, Weinberg SM. 3D digital stereophotogrammetry: a practical guide to facial image acquisition. *Head Face Med*. 2010;6:18–36.

Hoefert CS, Bacher M, Herberts T, Krimmel M, Reinert S, Hoefert S, Goz 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*. 2010;71:221–234.

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

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*. 2004;41:27–35.

Jones BC, DeBruine LM, Little AC. The role of symmetry in attraction to average faces. *Percept Psychophys*. 2007;69:1273–1277.

Kane AA, DeLeon VB, Valeri C, Becker DB, Richtsmeier JT, Lo L-J. Preoperative osseous dysmorphology in unilateral complete cleft lip and palate: a quantitative analysis of computed tomography data. *Plast Reconstr Surg*. 2007;119:1295–1301.

Komori M, Kawamura S, Ishihara S. Averageness or symmetry: which is more important for facial attractiveness? *Acta Psychologica*. 2009;131:136–142.

Kriens OE. LAHSHAL: a concise documentation system for cleft lip, alveolus and palate diagnosis. In: Kriens OE, ed. *What Is a Cleft Lip and Palate? A Multidisciplinary Update*. New York: Thieme Medical Publishers; 1989:30–34.

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*. 2006;43:350–355.

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 Aesthet Surg*. 2013;66:1109–1116.

Liang S, Wu J, Weinberg SM, Shapiro LG. Improved detection of landmarks on 3D human face data. *Conf Proc IEEE Eng Med Biol Soc*. 2013;2013:1–4.

Little AC, Jones BC. Evidence against perceptual bias views for symmetry preferences in human faces. *Proc Biol Sci*. 2003;270:1759–1763.

Little AC, Jones BC, DeBruine LM. Facial attractiveness: evolutionary based research. *Philos Trans R Soc Lond B Biol Sci*. 2011;366:1638–1659.

Lu SM, Bartlett SP. On facial asymmetry and self-perception. *Plast Reconstr Surg*. 2014;133:873e–881e.

Mori A, Nakajima T, Kaneko T, Sakuma H, Aoki Y. Analysis of 109 Japanese children's lip and nose shapes using 3-dimensional digitizer. *Br J Plast Surg*. 2005;58:318–329.

Mosmuller DGM, Griot JPWD, Bijnen CL, Niessen FB. Scoring systems of cleft-related facial deformities: a review of literature. *Cleft Palate Craniofac J*. 2013;50:286–296.

Nakamura N, Okawachi T, Nishihara K, Hirahara N, Nozoe E. Surgical technique for secondary correction of unilateral cleft lip-nose deformity: clinical and 3-dimensional observations of preoperative and postoperative nasal forms. *J Oral Maxillofac Surg*. 2010;68:2248–2257.

Nkenke E, Lehner B, Kramer M, et al. 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*. 2006;43:129–137.

Oh TS, Choi JW, Koh KS. Upper lip asymmetry perception using three-dimensional anthropometry in patients with unilateral cleft lip deformity. *J Craniofac Surg*. 2011;22:2080–2083.

Schwenzer-Zimmerer K, Chaitidis D, Berg-Boerner I, Krol Z, Kovacs L, Schwenzer NF, Zimmerer S, Holberg C, Zeilhofer H. 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-Maxillofac Surg*. 2008;36:431–438.

Schwenzer-Zimmerer K, Chaitidis D, Boerner I, Kovacs L, Schwenzer NF, Holberg C, Zeilhofer H. Systematic contact-free 3D topometry of the soft tissue profile in cleft lips. *Cleft Palate Craniofac J*. 2008;45:607–613.

Semb G, Shaw WC. Simonart's band and facial growth in unilateral clefts of the lip and palate. *Cleft Palate Craniofac J*. 1991;28:40–46.

Simanca E, Morris D, Zhao L, Reisberg D, Viana G. Measuring progressive soft tissue change with nasoalveolar molding using a three-dimensional system. *J Craniofac Surg*. 2011;22:1622–1625.

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*. 2007;10:161–166.

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*. 2008;69:268–282.

Tse R, Booth L, Keys K, et al. Reliability of nasolabial anthropometric measures using three-dimensional stereophotogrammetry in infants with unrepaired unilateral cleft lip. *Plast Reconstr Surg*. 2014;133:530e–542e.

van Loon B, Maal TJ, Plooij JM, et al. 3D stereophotogrammetric assessment of pre- and postoperative volumetric changes in the cleft lip and palate nose. *Int J Oral Maxillofac Surg*. 2010;39:534–540.

Wu J. *Analysis of Human Face Shape Abnormalities Using Machine Learning*. Seattle: University of Washington; 2014. Dissertation.

Wu J, Tse R, Heike CL, Shapiro LG. Learning to compute the plane of symmetry. In: *BCB 2011 Proceedings of the 2nd ACM Conference on Bioinformatics, Computational Biology, and Biomedicine*. 2011:471–474.

Wu J, Tse R, Shapiro LG. Learning to rank the severity of unrepaired cleft lip nasal deformity on 3D mesh data. *Proc IAPR Int Conf Pattern Recogn*. 2014;2014:460–464.

Yamada T. Nasolabial and alveolar morphology following presurgical orthopaedic treatment in complete unilateral clefts of lip, alveolus and palate. *J Craniomaxillofac Surg*. 2003;31:343–347.

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