Changes in Nasolabial Dimensions Following Repairs of Unilateral Cleft Lip: A Follow-Up Anthropometric Study in Late Childhood

Glossary of abbreviations[11]

sn (subnasale): angle between base of columella and upper lip
al (alare): most lateral point of the nasal ala
sbal (subalare): most caudal point of nasal ala
cphi (crista philtri inferior): the most caudal point of the philtral column
ch (cheilion): the labial commissure, or most lateral point of the lip

sn-al: heminasal width
sbal-cphi: lateral oblique component of vertical lip height
sn-cphi: medial oblique component of vertical lip height
cphi-ch: transverse labial length

Section 1: Introduction

Repair of unilateral cleft lip and nasal deformity is executed in three dimensions with the goal being nasolabial symmetry. The final result is a function of a dynamic process due to children's growth and movement, collectively defining the fourth-dimension. Differences in growth rates between the cleft and non-cleft sides may lead to asymmetry that is obvious at rest or is altered with animation. The former can be measured by direct anthropometry using calipers; the latter would require real-time digital imaging.

Mulliken and LaBrie[1] assessed the post-operative changes in anthropometry over six years in 99 children with repaired unilateral cleft lip.[1] Their study showed different growth rates in heminasal width, labial height and transverse labial width between the cleft and non-cleft sides. Specifically, they found at six year follow up that the heminasal width initially less on the cleft side had drifted laterally at a greater rate than on the normal side. Sn-cphi (one measure of vertical labial height) was initially slightly longer on the cleft side but was the same length at six-year follow-up, while sbal-cphi (another measure of vertical labial height) was initially shorter on the cleft side and remained so because of similar growth rates between the cleft and non-cleft side. They also documented that the transverse labial width was initially shorter on the cleft side, but this discrepancy decreased over six years.

Farkas et al[2] studied the natural history of anthropometric changes in Caucasian North American children and found that by six years of age, the vermilion upper labial height and total upper labial height reached nearly mature dimensions in females and the cutaneous upper labial height reached nearly mature dimensions for both males and females. In contrast, they found that the other nasolabial dimensions ie. nasal height, width and tip protrusion did not reach adult measurements until adolescence or beyond. Based on this study, it was expected that anthropometric stabilization would occur later in follow-up of the unilateral cleft lip repair patients.

The investigators of this study aim to assess the extended anthropometric trends in unilateral cleft lip repair patients. This study involves 50 patients from the cohort included in Mulliken and LaBrie's original study and assesses changes in the same four dimensions, now approximately 11 years after cleft repair. These dimensions were originally selected

for measurement because of expected change with growth and the possibility for modification during the initial repair.[1]

Background

Internationally, cleft lip with or without cleft palate occur in 9.92 per 10,000 births.[4] Based on maternal ethnicity in the United States, cleft lip with or without palate affects approximately 15.4 in 10000 Caucasians, 13.2 in 10000 Asian-Americans, and 10.2 in 10000 African-Americans. Cleft lip may be complete or incomplete, and cleft lip/palate is unilateral in 80 of cases and bilateral in the remainder.[23] The development of cleft lip/palate is multifactorial and occurs to due to embryologic failure of fusion of nasal, labial, and palatine components between weeks 4 and 7. [11] Cleft lip/palate usually occurs sporadically but may also be a part of a number of syndromes, most commonly van der Woulde and diGeorge.[11]

In an unrepaired cleft lip, anthropometry has shown that dimensions of the cleft side lip labial and the transverse width are deficient when compared to the non-cleft side.[5,14] The nasal deformity is characterized by lateral, inferior, and posterior placement of the alar base, slumped lower lateral cartilage, lengthened heminasal width and flattening of the involved nose.[6,7] Unilateral cleft lip can be broadly separated into microform, incomplete, and complete, in ascending order of severity, as shown in Figure 1.[8]

Treatment of unilateral cleft lip is a staged process that may involve preoperative orthopedics, nasolabial adhesion, and primary nasolabial correction.[9] The most common techniques are variants of Millard's rotation-advancement method, first published in 1958. This method has withstood the test of time because it accepts modifications without changing the underlying principles.[10] According to a recent survey of cleft surgeons, 84% use Millard's rotation-advancement technique for complete cleft lip repair and 45% incorporate various modifications. Statistics for incomplete repair were similar.[9]

Nasal correction performed at the time of cleft repair has been controversial.[9] The same survey found that only 22% and 28% of responding surgeons never performed primary nasal correction in complete and incomplete clefts, respectively.[9] Many studies have shown that manipulation of the nasal cartilages does not negatively affect growth.[7,15,

[17] Furthermore, early nasal correction has been found to give better symmetry and less frequent need for corrections.[16,19]

Anthropometry is a useful tool to objectively document the outcomes of cleft labial repair. Baseline direct anthropometry is done at time of primary repair and repeated as the child grows. Indirect anthropometry using 2D or 3D photography can also be used.[11] Standard nasolabial measurements applied to unilateral cleft lip repair include: heminasal width (sn-al), labial height (sn-cphi, sbal-cphi), and transverse labial width (cphi-ch). Figure 2 illustrates these points in an unrepaired complete cleft lip.[11]

Question and Significance

Nasolabial symmetry is the grail in repair of unilateral cleft lip. Case-control and longitudinal cross-sectional studies have assessed outcomes in symmetry, but we are aware of no other studies looking at unilateral cleft lip repair in a prospective cohort to 11.5 years post-operatively.[12,13] This project is the second phase of a long-term prospective assessment of anthropometric outcomes in unilateral repair. Better understanding for how nasolabial features change over time will result in technical alterations at primary correction that will improve long-term outcomes.

We hypothesized the following anthropometric changes after repair of unilateral cleft lip and nasal deformity:

1. Heminasal width (sn-al) will increase more on the cleft side than on the non-cleft side in the second follow up period. The divergence between the growth in sn_al on the non-cleft and cleft sides will decrease in the second follow-up period compared to the first follow-up period.

2. Labial height (sn–cphi and sbal–cphi) will grow less on the cleft side than on the non-cleft side in the second follow up period. The divergence between the growth in labial height (sn-cphi and sbal-cphi) on non-cleft and cleft sides will decrease in the second follow-up period compared to the first follow-up period.

3. Cupid's bow peak to commissure (cphi–ch) on the cleft and non-cleft sides will equilibrate in the second follow-up period. The divergence between the growth of cphi-ch on non-cleft and cleft sides will decrease in the second follow-up period compared to the first follow-up period.

Section 2: Methods

Patients and Anthropometric Methods

This prospective study encompasses two follow-up periods: the first period included infancy to early childhood and the second period included early to late childhood. Mulliken and LaBrie's first phase study, published in 2012, comprised 99 children with unilateral cleft lip (complete or incomplete) with or without cleft palate, repaired by rotation-advancement and primary nasal correction between 1999 and 2004 by senior surgeon JBM at Boston Children's Hospital. The 50 patients included in this second phase study are a subset of those included in the first phase study. First period anthropometric measurements were conducted from 1999 to 2009 and second period measurements in 2010 to 2014. Study patients with complete cleft lip were first treated with active orthopedics, nasolabial adhesion, and alveolar gingivoperiosteoplasty.[1]

135 total patients underwent repair by the senior author (JBM) between 1999 and 2004. From these 135 patients, a subset best representing the cohort in the first phase's 2006 study was culled using two filters described in the original paper: year of operation in 1999-2004 with immediate post-operative measurements and follow-up measurement in 2004-2009. This produced a 98 patient dataset, used in place of the 99 included in the original study to give a follow up cohort and to test for ascertainment bias, as described below. The original study's methodology was repeated using these 98 patients and the results are available in Appendix 1.

To generate a cohort for the follow-up study, patients from the subset of 98 described above were excluded if they did not have two follow-up sets of measurements or if they had undergone revisions expected to affect the anthropometric measurements of interest: unilimb Z-plasty of the vermilion border and/or V-Y advancement of the alar base. The 50 remaining patients ("survivors") were included in this second-phase follow-up study.

All repairs and measurements were by the senior author (JBM) at Boston Children's Hospital. As previously described, initial nasolabial measurements were made intraoperatively at completion of primary repair. Measurements of sn-al (*subnasale-alare*), sn-cphi (*subnasale-crista philtri inferior*), and sbal-cphi (*subalare-crista philtri inferior*)

were made using a Castroviejo caliper. Measurements of cphi-ch were made with a ruler graduated in 1.0-mm intervals. Postoperative measurements were performed in the clinic with the child lying supine.

Ascertainment Bias

Of the cohort of 98, 48 patients were excluded either because of revisions or loss to follow-up. To assess for ascertainment bias, the cohort of 50 survivors was compared to the cohort of 48 "nonsurvivors" using age at operation, sex, and measurements obtained intraoperatively. The difference between cleft and non-cleft sides for each measurement was expressed as a percentage of the cleft side. The age at operation and the four measurement percentage differences were compared using t-tests for independent samples. Sex difference was tested using z-score test for sample proportions.[22] No difference was found to be significant among any measurement tested. Tables showing these results are available in Appendix 2. An alternative assessment for ascertainment bias was performed using the extent of cleft lip/palate deformity as a measure of severity. The difference in severity between groups was not found to be significant using t-test for independent measures. Thus, the cohort of 50 was considered appropriately representative of the original cohort of 98.

Statistical Methods

Changes in patient anthropometry over time were tested against the null hypothesis of no difference using t-tests for correlated measures. Changes over time were converted to percentages in order to standardize measurements among patients of different sized facial features. The disparity between cleft and non-cleft rates of growth over time was tested against the null hypothesis of no difference, again using t-tests for correlated measures. Differences between left and right side cleft deformities were not tested given the absence of findings in the first phase study. Gender differences were also not tested in this study.

Additional Subsets

Two additional inclusive subsets from the original cohort of 98 were created. The first included patients with two follow-up measurements but excluding patients who had undergone unilimb Z-plasty of the vermilion border. The second included patients with two follow-up measurements but excluding patients having undergone a V-Y advancement of the alar base. Unilimb Z-plasty of the vermilion border would be expected to affect the labial height (sn-cphi and sbal-cphi) but not heminasal width. V-Y advancement of the alar base would be expected to affect the heminasal width (sn-al) as well as sbal-cphi, but would be expected not to alter sn-cphi and cphi-ch. T-tests for correlated measures were repeated for each measurement using the appropriate inclusive supplemental subset. Results of these calculations are available in Appendix 3.

Section 3: Results

Operative measurements were taken during 1999 to 2004 and follow-up measurements from 2006 to 2014. Of the cohort of 50 used in this study, average age at operation was 172 days (*n* = 50, SD = 46.8); average age at first follow-up evaluation was 6.64 years (n = 50, SD = 1.62); average interval between operation and follow-up anthropometry was 6.16 years (*n* = 50, SD =1.62); average age at second follow-up evaluation was 11.43 years (n = 50, SD = 1.62); and average interval between operation and second follow-up was 10.96 years (n = 50, SD = 1.64). The average interval between the first follow-up and second follow-up period was 4.79 years (n = 50, SD = 1.41). 34% of patients (n = 17) were female, 56% of patients had complete cleft lip/palate (n = 28), and 60% of patients (n = 30) had left sided cleft deformities.

Hypothesis 1. Heminasal width (sn-al) will increase more on the cleft side than on the non-cleft side in the second follow up period. The divergence between the growth in sn_al on the non-cleft and cleft sides will decrease in the second follow-up period compared to the first follow-up period.

Intraoperatively, at both 6.6-year and 11.5-year follow up, heminasal width was narrower on the cleft side than on the normal side. The first phase study showed that the cleft side was 0.7mm narrower than the non-cleft side at the six-year follow up study. This same difference was found at 6.6-year follow-up in the cohort of 50 patients used in this study. At the 11.5-year follow-up, this difference had decreased to 0.5 mm with a mean 2.35% higher rate of change on the cleft side than on the non-cleft side.

Nevertheless, when the difference between rates of change on the cleft side and non-cleft side in the first period was compared to the difference in rates of change between the cleft side and non-cleft side in the second period, there was no statistical significance between these two metrics of disparate growth. Thus, we could not show that the difference in rates of growth between cleft and non-cleft side changed over time.

This analysis was also done using the supplemental inclusive cohort of 63 patients from the original cohort of 98 excluding patients who required V-Y advancement of the alar

base but not those who required a unilimb Z-plasty. This also showed a difference of 0.5 mm between mean non-cleft heminasal width and mean cleft heminasal width at the end the second follow-up period. The mean difference in rates of growth was 1.84% higher on the cleft side in the second period. These data are available in Appendix 3.

Hypothesis 2. Labial height (sn–cphi and sbal–cphi) will grow less on the cleft side than on the non- cleft side in the second follow up period. The divergence between the growth in labial height (sn-cphi and sbal-cphi) on non-cleft and cleft sides will decrease in the second follow-up period compared to the first follow-up period.

sn-cphi

At the time of operation, sn-cphi on the cleft side was longer (mean difference 0.7 mm in this cohort and in the original study[1]) than the normal side and remained longer on the cleft side at 11.5-year follow-up; the mean difference was 0.3 mm.

In the first period, the non-cleft side grew by a mean rate of growth of 17.76%, compared to a cleft side mean rate of growth of 12.59% (a difference of 5.2%). The rate of growth for non-cleft sn-cphi in the second period was 3.02% and was 3.53% for the cleft side; however, the difference was not statistically significant. The decrease in differential rates of growth between cleft and non-cleft side over the two periods was statistically significant.

sbal-cphi

Immediately post-operatively, sbal-cphi was shorter on the cleft side by a mean difference of 0.4 mm, which corresponded to the difference of 0.4mm found in the first phase study.[1] Sbal-cphi remained shorter on the cleft side at 6.6-year follow-up and 11.5-year follow-up by mean differences of 0.4mm and 0.3mm, respectively. These differences were all statistically significant. This follow-up study failed to find a statistically significant difference in rates of growth between cleft and non-cleft sides in the second phase assessment.

Hypothesis 3. Cupid's bow peak to commissure (cphi–ch) on the cleft and non-cleft sides will equilibrate in the second follow-up period. The divergence between the growth of cphi-ch on non-cleft and cleft sides will decrease in the second follow-up period compared to the first follow-up period.

At time of operation, cleft side cphi-ch was 2.1 mm shorter than non-cleft cphi-ch with a large Cohen d's effect size of 1.25. A discrepancy persisted in the second phase analysis, with a mean difference between non-cleft and cleft sides of 0.7mm at 11.5-year follow up.

The mean difference was 1 mm at 6.6-year follow up with the cleft side growing 5.5% more than the non-cleft side in that period. In the second phase, the cleft side grew by a mean difference of 1.6% ($p = 0.0579$) more than the non-cleft side. This decrease in differential rates of growth was statistically significant.

Section 4: Discussion, Limitations, Conclusions, and Suggestions for Future Work

Alar Base Position

The cleft side heminasal width was persistently narrower than the non-cleft side through the second phase assessment period by a mean difference of 0.5 mm, decreased from 0.7mm at 6.6-year follow-up, i.e. the average cleft side rate of growth was larger than the non-cleft side. According to Farkas' growth curves, nasal width reaches maturity in 98.4% of females by 12 years and in 95.4% of males by 14 years.[2] Nevertheless, when the analysis was performed controlling for sex, differences in rates of growth were not statistically significant in either group.

The first phase study showed that the cleft side heminasal width grew by an average of 6.33% more than the non-cleft side in the first follow up period, although it was still narrower than the non-cleft side. However, using the cohort of 50 patients, the cleft side rate of growth was only 2.53% higher than the non-cleft side in the first period. In the second period, the cleft side continued to demonstrate a higher rate of lateral drift (by 2.35%) compared to the non-cleft side. Although at 11.5 years follow up it is still narrower on the cleft side, Farkas's growth curves showed maturation in later adolescence; it is possible that the cleft side heminasal width will equilibrate with non-cleft side heminasal width.

There was no statistical difference between rates of growth on the cleft and non-cleft sides when compared between the first and second follow up periods. We were therefore not able to demonstrate that the growth rate differential was smaller in this period, i.e. the cleft side continued to outstrip the non-cleft side at the same differential grate of growth.

At primary repair, the cleft alar base was set on average 1.0 mm more medial than the normal side to allow for expected lateral drift of the cleft side alar base.[1] Given the persistent finding of a medial cleft side alar base over 11.5 years, one might argue that the initial repair should not aim for the cleft alar base to be a full 1.0 mm more medial than the normal side. However, given that the cleft side rate of change was greater than the non-cleft side in the second period there is no clear evidence to place the cleft side alar base more

lateral at the time of primary repair. Furthermore, a laterally displaced alar base is a well-recognized stigma of repaired unilateral cleft lip and more noticeable than a medially displaced alar base. [JBM]

Underscore that 14.1% of the original 135 patient cohort and 18.4% of the 98 patient cohort required revision of the alar base, specifically advancement and endonasal rotation to correct for lateralization. Therefore, this dimension in patients included in this second study would be expected to be closer to symmetry than the original cohort of all patients with repaired unilateral cleft lip. As shown in the initial study, complete cleft lips evidenced greater differences in rates of growth than non-cleft patients in sbal-cphi and ch-cphi.[1] Therefore, it was suggested that patients with more severe cleft lip may require more medial placement of the cleft side alar base at primary repair.[1]

Of the cohort of 50, 56% were complete cleft lip/palates; of the cohort of 98 that ultimately underwent alar revision, 82% complete (z-score -1.94 with one-tailed $p<0.05$). Of those requiring alar base revision, a greater percentage had complete cleft lip/palate suggesting that the more severe cleft lip/palates may be more likely to need revision of the alar base. Among the patients requiring alar base revision, mean cleft side heminasal width was placed 0.9 mm less than mean non-cleft heminasal (similar to the 1 mm for the entire cohort). More medial placement may have avoided the need for alar base revision. However, this isn't recommended.

Of note, 26.7% of original cohort of 135 and 28% of 51 patients included in this study required resuspension of alar cartilage. This was not expected to affect the heminasal width and so patients were not excluded for these procedures.

As described in the initial study, the alar base was secured to the maxillary periosteum in a subset of the patients with the expectation that this maneuver would decrease heminasal width lateralization. Although the first study did not identify any statistically significant difference in the first period, it is possible that this technique became significant in the second period.

<u>Labial Height</u>

The measurement of labial height as a function of sn-cphi and sbal-cphi depends on the placement of Cupid's bow peak (cphi) during primary repair of the cleft. Similarly, the location of cphi affects the transverse labial dimension (cphi-ch), which is discussed below.

The identification of lateral cphi point has been discussed.[1] Noordhoff recommended a method of identifying cphi at the point at which the vermilion is widest, just as the red line and white skin roll begin to converge ("Noordhoff's point").[18] In the patients in this study, lateral cphi was located where vermilion height is greatest, such that sbal-cphi on the cleft side is within 1mm of sbal-cphi on the normal side while the lip is relaxed.[1] As seen from the immediate post-operative measurements, this method results in an initially shorter sbal-cphi and longer sn-cphi on the cleft side than on the non-cleft side.

The sn-cphi distance on the cleft side continued to lengthen through the second year follow up period such that there was a small effect size between cleft and non-cleft sides. Mulliken and LaBrie[1] proposed that the movement of cphi was a combination of a lateral and caudal shift. Their figure, reproduced below in Figure 4, illustrates this nicely, It is most likely continuation along that trajectory that leads to the increases in sn-cphi and sbal-cphi in the present study.

The sbal-cphi length on the non-cleft side was persistently longer than on the cleft side although the effect size is small at the time of second follow up assessment. Furthermore, there was no statistical difference in rates of growth between the cleft and non-cleft sides in the sn-cphi or sbal-cphi metrics in the second period. According to Farkas' growth curves, cutaneous lip height in females reaches maturity at age three but also undergoes two growth spurts at ages 12-13 and then again 15-17.[2] Although the cleft and non-cleft growth rates were no longer significantly different in the second follow up period (and therefore continued growth at those rates would not be expected to yield asymmetry), the cleft side may respond differently to pubertal growth spurts.

Of note, twenty percent of the original 135 patients (27.5% of the cohort of 98) required revision of an elevated vermilion by unilimb Z-plasty. The necessary exclusion of these patients from the second study leaves a cohort with better symmetry of the Cupid's bow peaks. In the first study, a significant difference in percentage growth was found between incomplete and complete clefts (completes having increased growth of cleft side sbal-cphi).[1] This differential growth rate would likely have continued in the second period.

Transverse Labial Width

The lateral lip in cleft lip/palate patients is hypoplastic and constrains the initial transverse lip width.[20] As discussed in the first study, the cleft side at operation is set shorter than the non-cleft side by the placement of cleft cphi.[1] JBM set the cphi such that there is a mean difference of 2.1 mm shorter cleft side at the time immediately post operatively (the original paper found a difference of 1.9 mm). By the end of the second follow up period, the cleft side cphi-ch caught up, reaching a mean difference of 0.7mm.

In comparing the first and second periods, there was a statistically significant difference in the growth rate disparities between cleft and non-cleft sides. This suggests that in effect the disproportionate lengthening of the cleft side is equilibrating over time.

Limitations

The follow-up measurements in this study were performed on children lying supine in the clinic. Measurements often needed to be repeated if the lip moved. Obtaining measurements under general anesthesia would be impractical.

The conclusions in this study are founded on one surgical technique employed by one surgeon. They may therefore have limited utility in application to the other techniques. Although 84% of surgeons currently employ a version of the rotation advancement technique there are several modifications that may affect the applicability of the study's data.

Future Work

Adjustments for multiple comparisons using the false discovery rate will be calculated. Further changes in data analysis may be made as we prepare this project's manuscript for submission.

This study assessed a cohort through pre-adolescence but would not be complete without follow-up through later adolescence after completion of facial growth.

As discussed above, the first study assessed the function of periosteal attachment in repair and found no statistical difference in alar base measurements in the first period. However, given the possibility that a difference may occur in the second phase, we may analyze the comparison in the second phase.

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Tables

Table 1 - Cohort 50		sn_al				
		Mean	SD	t	p	Effect Size
Operation	Non-cleft	14.95	1.28			
	Cleft	13.94	1.22	8.24	<0.05	0.81
Early Follow-Up	Non-cleft	16.65	2.30			
	Cleft	15.87	2.44	4.03	<0.05	0.33
Late Follow-Up	Non-cleft	17.84	1.86			
	Cleft	17.31	1.79	5.18	<0.05	0.29
Early To Late % Change	Non-cleft	8.16%	0.12			
	Cleft	10.51%	0.14	1.78	<0.05	0.18

Table 2a - Cohort 50		sn_cphi				
		Mean	SD	t	p	Effect Size
Operation	Non-cleft	10.22	1.48			
	Cleft	10.95	1.48	6.84	<0.05	0.49
Early Follow-Up	Non-cleft	12.01	2.27			
	Cleft	12.26	2.32	1.71	<0.05	0.11
Late Follow-Up	Non-cleft	12.26	2.12			
	Cleft	12.58	2.16	4.22	<0.05	0.15
Early To Late % Change	Non-cleft	3.02%	0.11			
	Cleft	3.53%	0.12	0.54	0.2954	0.04

Table 2b - Cohort 50		sbal_cphi				
		Mean	SD	t	p	Effect Size
Operation	Non-cleft	10.47	1.17			
	Cleft	10.10	1.03	3.75	<0.05	0.34
Early Follow-Up	Non-cleft	13.22	1.66			
	Cleft	12.82	1.70	4.76	<0.05	0.24
Late Follow-Up	Non-cleft	13.69	1.86			
	Cleft	13.36	1.76	3.85	<0.05	0.18
Early To Late % Change	Non-cleft	3.88%	0.11			
	Cleft	4.68%	0.10	1.05	0.1488	0.08

Table 3 - Cohort 50	cphi_ch

		Mean	SD	t	p	Effect Size
Operation	Non-cleft	22.94	1.76			
	Cleft	20.84	1.59	9.22	<0.05	1.25
Early Follow-Up	Non-cleft	23.47	2.58			
	Cleft	22.44	2.08	4.87	<0.05	0.44
Late Follow-Up	Non-cleft	25.07	2.76			
	Cleft	24.38	2.93	4.36	<0.05	0.24
Early To Late % Change	Non-cleft	7.33%	0.11			
	Cleft	8.96%	0.12	1.60	0.0579	0.15

Table 4 - Cohort 50
Difference in growth rates between cleft and non-cleft sides

		Mean	SD	t	p	Effect Size
Sn-al	Period 1	2.5370%	0.10			
	Period 2	2.3507%	0.09	0.07	0.4712	0.02
Sn-cphi	Period 1	-5.1776%	0.10			
	Period 2	0.5126%	0.07	2.67	<0.05	0.68
Sn-bal	Period 1	0.4057%	0.09			
	Period 2	0.7994%	0.05	0.22	0.4148	0.05
Cphi-ch	Period 1	5.4573%	0.10			
	Period 2	1.6355%	0.07	1.96	<0.05	0.45

Figures

Figure 1. Illustrating top to bottom: microform cleft, incomplete cleft lip and bilateral asymmetrical complete cleft lip.[8]

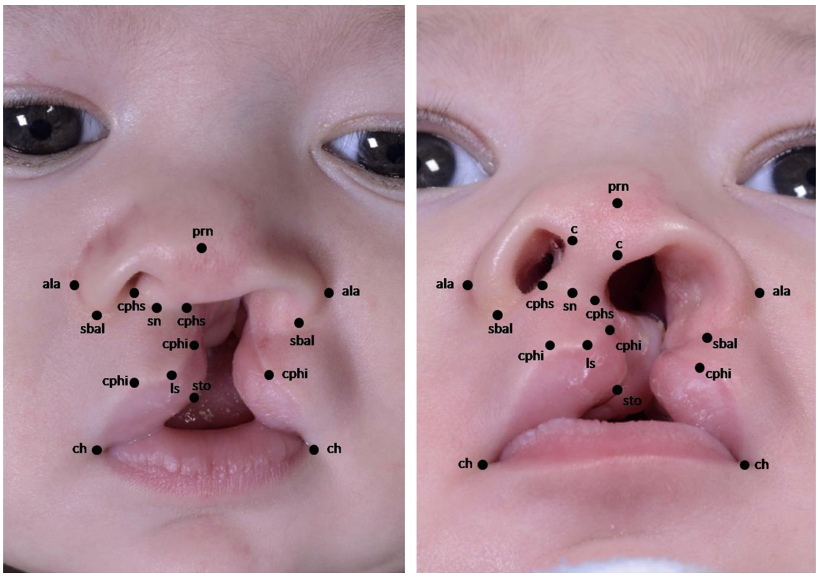

Figure 2. Anthropometric landmarks in an unrepaired complete cleft lip.[11]

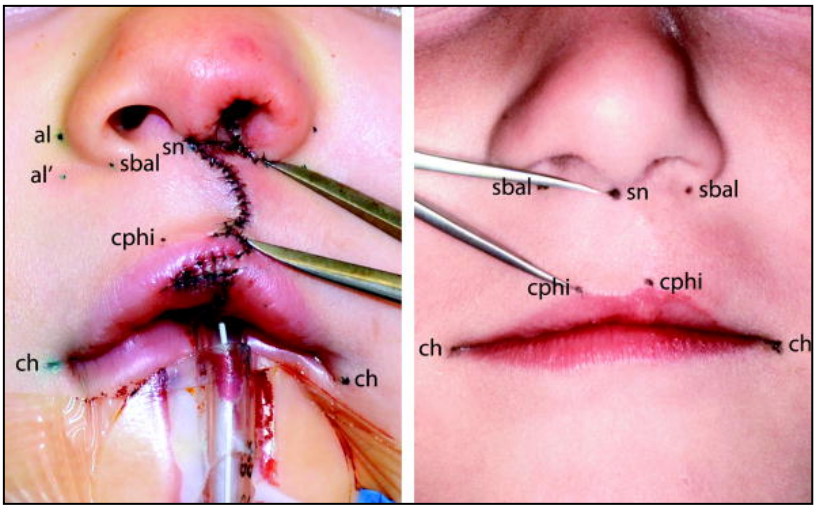

Figure 3. Illustrating anthropometric measurement in repaired cleft lip at time of operation and at later follow-up.[1]

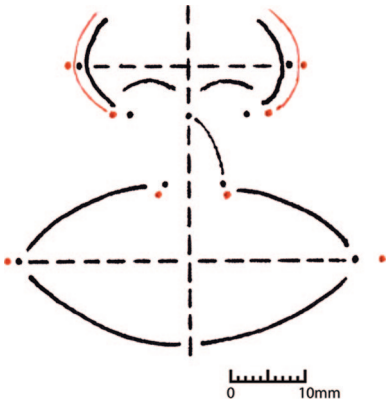

Figure 4. Illustration to scale demonstrating changes in nasolabial dimensions in the first 6 years post-operatively[1]

Appendix 1

Table 1 – Cohort 98		**sn_al**			
		Mean	**SD**	**t**	**p**
Operation	*Non-cleft*	*14.89*	*1.27*		
	Cleft	*13.91*	*1.14*	*11.45*	*<0.001*
Follow-up	*Non-cleft*	*16.56*	*2.14*		
	Cleft	*15.88*	*2.18*	*5.27*	*<0.001*
%Change	*Non-cleft*	*11.71*	*15.53*		
	Cleft	*14.69*	*16.25*	*3.28*	*<0.001*

Table 2 – Cohort 98		**sn_cphi**				***sbal_cphi***			
		Mean	**SD**	**t**	**p**	***Mean***	***SD***	***t***	***p***
Operation	*Non-cleft*	*10.39*	*1.41*			*10.59*	*1.12*		
	Cleft	*11.09*	*1.36*	*10.47*	*<0.001*	*10.21*	*1.08*	*5.92*	*<0.001*
Follow-up	*Non-cleft*	*12.20*	*2.08*			*13.32*	*1.55*		
	Cleft	*12.21*	*2.17*	*0.14*	*0.4437*	*12.88*	*1.63*	*6.70*	*<0.001*
%Change	*Non-cleft*	*17.94*	*16.01*			*26.19*	*11.46*		
	Cleft	*10.65*	*17.36*	*7.05*	*<0.001*	*26.41*	*11.76*	*0.25*	*0.4019*

Table 3 – Cohort 98		**cphi-ch**			
		Mean	**SD**	**t**	**p**
Operation	*Non-cleft*	*22.84*	*2.04*		
	Cleft	*20.92*	*1.89*	*13.42*	*<0.001*
Follow-up	*Non-cleft*	*23.53*	*2.60*		
	Cleft	*22.89*	*2.48*	*3.93*	*<0.001*
%Change	*Non-cleft*	*3.34*	*10.96*		
	Cleft	*9.87*	*12.05*	*6.92*	*<0.001*

Appendix 2

	Survivor Mean (StdDev)	Nonsurvivor Mean (Std Dev)	Effect Size	t	p
Age at Operation (days)	171.92 (46.82)	206.69 (160.62)	0.29	1.47	0.1456
% difference sn_cphi	8.19 (7.19)	6.97 (5.40)	0.19	1.32	0.3473
% difference sbal_cphi	5.02 (5.01)	5.16 (3.90)	0.03	2.20	0.8806
% difference sn_al	6.94 (5.13)	7.00 (4.33)	0.01	2.63	0.9517
% difference cphi_ch	9.12 (6.20)	7.64 (4.85)	0.27	1.11	0.1912

	Survivor Mean	Nonsurvivor Mean	z	p
%Female	34	38	0.36	0.7188
%Complete	28	34	1.52	0.1235

The survivor group includes the 50 patients of the 98 representing the first study who did not undergo a major revision and for whom three sets of anthropometric measurements were available. The nonsurvivor group includes from the 98 patients who were excluded from the cohort of 50.

Appendix 3

Table 2b - Unilimb Revisions Excluded		sbal_cphi				
		Mean	SD	t	p	Effect Size
Operation	*Non-cleft*	10.55	1.18			
	Cleft	10.22	1.08	3.35	<0.05	0.29
Early Follow-Up	*Non-cleft*	13.31	1.65			
	Cleft	12.92	1.69	5.00	<0.05	0.23
Late Follow-Up	*Non-cleft*	13.77	1.86			
	Cleft	13.49	1.77	3.94	<0.05	0.15
Early To Late % Change	*Non-cleft*	0.04	0.10			
	Cleft	0.05	0.09	1.56	0.0620	0.11

Table 3 - Unlimb Revisions Excluded		cphi_ch				
		Mean	SD	t	p	Effect Size
Operation	*Non-cleft*	22.94	1.72			
	Cleft	20.86	1.56	9.72	<0.05	1.26
Early Follow-Up	*Non-cleft*	23.51	2.45			
	Cleft	22.46	1.98	5.38	<0.05	0.47
Late Follow-Up	*Non-cleft*	25.15	2.59			
	Cleft	24.50	2.81	4.14	<0.05	0.24
Early To Late % Change	*Non-cleft*	0.07	0.10			
	Cleft	0.09	0.12	2.00	<0.05	0.18

Table 1 - Alar Base Revision Excluded		sn_al				
		Mean	SD	t	p	Effect Size
Operation	*Non-cleft*	14.99	1.29			
	Cleft	13.93	1.19	9.42	<0.05	0.85
Early Follow-Up	*Non-cleft*	16.74	2.27			
	Cleft	16.04	2.34	4.16	<0.05	0.30
Late Follow-Up	*Non-cleft*	18.05	1.99			
	Cleft	17.54	1.90	5.51	<0.05	0.26
Early To Late % Change	*Non-cleft*	0.09	0.11			
	Cleft	0.11	0.13	1.58	0.0592	0.15