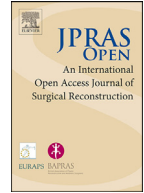




Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

JPRAS Open

journal homepage: www.elsevier.com/locate/jpra



Original Article

Lip symmetry following rotation advancement cleft lip repair in 5-year-old children treated by Ralph Millard and Ron Pigott

F. Maggiulli^a, C. Hinton^b, L. Simpson^b, S. Gujral^c,
J. Hardwicke^d, R. Slator^b, R.W. Pigott^e, T.L. Su^f, B. Richard^{b,*}

^a Department of Pediatric Plastic Surgery, Competence Centre for Cleft Lip and Palate CHU University Hospital Lapeyronie 371 Av. du Doyen Gaston Giraud, 34090 Montpellier, France

^b West Midlands Cleft Lip and Palate Service, Birmingham Children's Hospital NHS Foundation Trust., Steelhouse Lane, Birmingham, B4 6NH, UK

^c Department of Plastic Surgery, Royal Devon & Exeter NHS Foundation Trust, Barrack Road, Exeter, EX2 5DW, UK

^d Department of Plastic Surgery, University Hospital Coventry, Clifford Bridge road, Coventry CV2 2DX, UK

^e Deceased, 17th February 2020, former cleft surgeon, Department of Plastic Surgery, Frenchay Hospital, Bristol, BS16 1LE, UK.

^f Division of Dentistry, School of Medical Sciences, Faculty of Biology, Medicine and Health, University of Manchester, UK.

ARTICLE INFO

Article history:

Received 2 March 2022

Accepted 17 May 2022

Available online 17 June 2022

Keywords:

Cleft lip and palate

Millard

Pigott

Symnose

facial aesthetic outcomes

ABSTRACT

Objective: To compare the symmetry of the lip following Rotation-Advancement cleft lip repair by Millard and Pigott and to investigate the effect on the symmetry of cleft side and gender by using different surgical protocols. Symmetry following cleft surgery was compared to that of non-cleft children.

Design: Retrospective study of photographs of children aged 5 years.

Setting: Three decades of post-operative photographs of children treated by Millard and Pigott.

Patients: Eighty-nine children treated by Millard, 87 by Pigott and 91 non-cleft children.

* Corresponding author: Bruce Richard, Department of Plastic Surgery, Birmingham Children's Hospital, Steelhouse Lane, Birmingham B4 6NH, UK. Telephone ++44 7754501063

E-mail address: bruce.richard@nhs.net (B. Richard).

Interventions: Photographs were assessed using the Symnose Computer program, a rapid semi-objective quantitative assessment of lip symmetry.

Main Outcome Measure(s): Asymmetry score for each surgeon, and non-cleft children.

Results: There was no significant difference in the median lip % mismatch score of Millard, 36.65% and Pigott, 38.52%. Right-sided clefts showed better symmetry than left-sided clefts for Millard ($p < .001$). This was reversed for Pigott ($P = .0121$). There was a difference ($P < .001$) between the symmetry of the two cleft cohorts and the non-cleft children (asymmetry 19.9%), and between Millard's outcomes following different lip surgical protocols ($P < .0001$), but no difference between Pigott's outcomes using different palate surgical protocols ($P = 0.59$).

Conclusions: Cleft lip repair by Millard and Pigott resulted in similar lip asymmetry (37% and 39% symmetry mismatch, respectively). Lip surgical protocol and cleft side may affect lip asymmetry. Palate surgery did not affect lip asymmetry. Following cleft surgery, children were more asymmetric than non-cleft children.

© 2022 The Authors. Published by Elsevier Ltd on behalf of British Association of Plastic, Reconstructive and Aesthetic Surgeons. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

Introduction

In 1955, Millard (Figure 1a) described the rotation advancement (RA) method of repairing the unilateral cleft lip,^{1,2} and this technique rapidly became one of the most used methods of cleft lip repair throughout the world.

Since 1970, Millard modified his cleft lip repair and used a preliminary lip adhesion followed by formal RA repair a few months later,³ and since 1979, he has been using pre-surgical orthopaedics, lip adhesion and gingivoperiosteoplasty, and a few months later RA.⁴ Millard did not report the effects of these changes in technique on the appearance of the lip. Throughout his career, he did a soft palate repair with the three-month lip procedure, and the hard palate was repaired at about 18 months of age.⁴

Pigott (Figure 1b) studied under Prof. Millard in 1967 and established a large cleft practice in the United Kingdom. He used the Millard RA technique for his lip repair throughout his career. Over three decades, Pigott changed his palate repair technique in an attempt to improve facial growth. He initially used the Cuthbert modification of Veau Wardill Kilner.⁵ He then utilised lateral Von Langenbeck releasing incisions⁶, and finally he described the so-called Medial Langenbeck releasing incision.⁷ He published improved facial growth outcomes with this medial releasing technique.⁸

Facial appearance as an outcome of treatment for cleft lip±palate (CL±P) is of the utmost importance to the family and the child. However, despite numerous modifications of lip repair techniques, there is little good-quality evidence that any one of the techniques described results in more acceptable outcomes than any others. This is at least in part because there is no reliable and valid facial aesthetic outcome tool.⁹ To date facial aesthetic outcome measures largely rely on subjective judgement and methodological complexity,^{9,10} and there have been minimal improvements in the reliability of reporting facial aesthetic outcomes.¹¹

Pigott and Pigott developed the semi-objective symmetry measurement system known as Symnose.^{12,13} Symnose removes much of the subjectivity of human scoring. It also includes the whole range of possible outcomes in contrast to about 30% of human raters who never score a result as either Excellent (Likert 1) or Very Poor (Likert 5). Furthermore, a few human raters are almost random in their ability to rate an image.¹⁴ Symnose has been proven to be a more objective assessment

The Pigott cohort of 87 children consisted of 59 (68%) with a left-sided cUCLP and 28 (32%) with a right-sided cleft. All the children were Caucasian. From the original 139 children selected for Pigott, 96 (69%) were males and 43 (31%) females, but we were not able to confirm that the ratio was the same for the 87 children examined in this study as that data were not available.

The proportions of gender and cleft side for the cohorts from the two surgeons were statistically similar (Univariate analysis: Gender; $P = .76$, Cleft Side; $P = .50$) and consistent with published gender and cleft side frequency in cUCLP.^{11,16}

Non-cleft cohort

The normal cohort consisted of 91 five-year-old children without CL±P. They were all Caucasian. Forty-eight were males and 43 females. The details of the methodology and results using Symnose for this cohort have been previously published as a reference scale for non-cleft lip symmetry.¹⁵

Surgery

As described above, Millard had three phases of cleft lip repair technique:

- 1st - classic lip rotation advancement repair (RA);
- 2nd - preliminary lip adhesion, followed by a later definitive lip repair (LARA);
- 3rd - presurgical orthopaedics, followed by lip adhesion with gingivoperiosteoplasty, and then lip repair (POPLA).

The Millard cohort had a primary lip repair between 3 and 4 months, or a lip adhesion at 3–4 months and a definitive lip repair between 8–10 months. They all had a soft palate repair with the 3-month lip procedure, and the hard palate was repaired at about 18 months of age.⁴

Pigott used the Millard RA cleft lip repair with no presurgical orthopaedics for his whole career. He performed the primary definitive lip repair with gingivoperiosteoplasty between 3–6 months of age. Cleft palate repair was performed using one of the three techniques described below at the age of 6 months.

- 1st - Veau Wardill Kilner palate repair (VWK)
- 2nd - Von Langenbeck palate repair (VL)
- 3rd - Medial Langenbeck palate repair (ML)

The exact age at primary surgery for each child was not available to the authors.

Pigott reported that several of his children had lip revision surgery before the photograph at the age of 5 years, and this was also the practice of Millard (personal communication, Pigott). Pigott's description of the patients in his three different palate repair techniques paper, states that 9 of the 70 children (13%) had a lip revision before the age of 5 years photo. There is no published record of Millard's lip revision rates, and we were not able to glean it from his records.

Symnose

All photographs were digitized for analysis. The Symnose program (version 6.22; © Brian Pigott 2007–2015) measures asymmetry using a tracing of the lower border of the nose and an outline of the upper lip (Figure 2.) Details of the Symnose outcome measure are described in their original paper.¹² Perfect symmetry results in 0% mismatch.

Five independent investigators traced the lower border of the nose and the upper lip (Figure 2). Not less than one week later, all investigators retraced the images for a second time. These raters included a cleft surgeon, two cleft surgical trainees, and two medical students. They all had previous experience in using Symnose.

There were two raters for Millard's cohort and three different raters for Pigott's cohort. There was no statistically significant difference in lip perimeter mismatch (asymmetry percentage) between the first and second tracings. The Intraclass Correlation coefficient (ICC) of the five raters ranged from

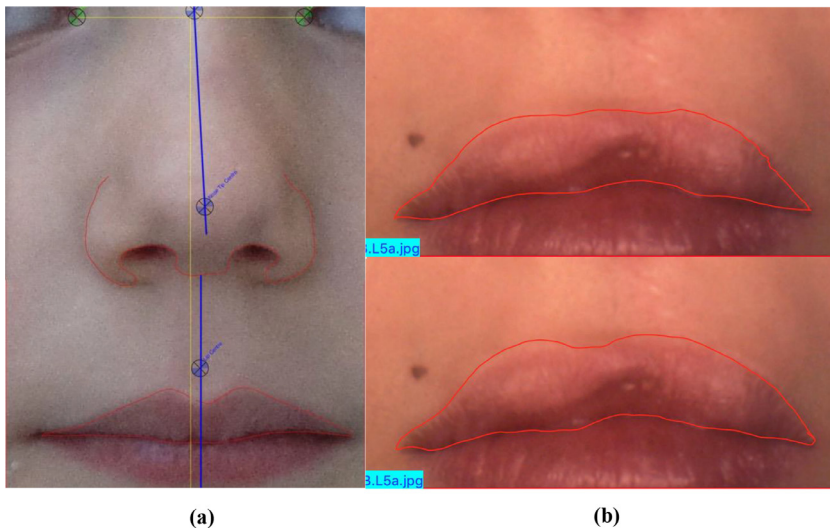


Fig. 2. (a) The Symnose program (version 6.22) measures asymmetry after tracing the lower border of the nose and an outline of the upper lip. A vertical axis bisects a line joining the medial canthi. For the lip the axis of reflection is drawn through the widest points of the lip. (b) The same upper lip image traced by two different raters. The visual differences between the two lines demonstrates the semi-objective nature of the assessment. Each rater traces all the images and repeats the process after 2–6 weeks. Thus, an intra-rater and inter-rater validity can be assessed.

0.76 to 0.87, and the inter-raters ICC was 0.69 (Millard: two raters) and 0.70 (Pigott: three raters). The inter- and intra-observer agreement was found to be Good to Excellent between the five tracers for the lip tracings.¹⁷

The images were archived and then imported into Symnose, one at a time, correlated by superimposing the canthal roundels, and a percentage mismatch calculated.

Statistical analysis

Descriptive statistics were applied to the summarized data. Specifically, the median with first and third quartiles together with minimum and maximum values were used for percentage of lip mismatch, and numbers and percentages were used for categorical data. Between and within observer agreement were quantified by the ICC. The Mann Whitney U test was used to compare median lip symmetry scores from the two surgeons' differing surgical techniques, cleft side and gender. To consider the impact of covariates (surgical technique and cleft side) on lip mismatches, linear mixed effect model¹⁸ was applied in order to take into account that there were several raters tracing the same patients' pictures multiple times. A likelihood-ratio test was used to compare various nested models to determine key covariates that influence the outcomes. Mean and standard error were used to report the effect size of the covariates. P-values were quoted when possible, and the threshold considered for statistical significance was $P < 0.05$. All analyses were conducted using R (version 3.6.0; <https://www.r-project.org/>). R Packages *lme4* (<https://cran.r-project.org/web/packages/lme4/index.html>) were used for mixed effect modeling.

Results

Table 1 shows the un-adjusted (raw) percentage lip mismatch score by the two surgeons, stratified by surgical technique, the side of the cleft, and gender. There was no significant difference in the overall median (Q1, Q3) lip percentage mismatch for Millard [36.6% (26.2%, 53.2%)] and for Pigott [38.5% (27.3%, 54.5%)] ($P = .149$).

Table 1

Symnose results presented as a percentage lip mismatch by surgeon, technique, and side of cleft.

Surgeon,Technique, Cleft side	Time period the technique was practised	Cohort size	Lip asymmetry percentage Median (1 st , 3 rd quartile)	(Min, Max)
Millard		N=89	36.6 (26.2, 53.2)	
Technique				
RA	1956-1971 (n=15) 1973 (n=2) 1977 (n=1) 1996 (n=1)	19	29.9 (24.7, 42.0)	(14.9, 79.9)
LARA	1970-1990 (n=32) 1993 (n=1)	33	37.7 (26.4, 52.8)	(13.3, 80.9)
POPLA	1979-1997	37	39.5 (27.1, 60.8)	(13.6, 132.9)
Side				
Left		55	40.5 (28.9, 56.5)	(13.6, 132.9)
Right		34	30.3 (24.7, 44.3)	(13.3, 84.6)
Gender				
Male		64	36.3 (25.3, 51.1)	(13.3, 102.2)
Female		25	40.6 (28.1, 58.2)	(13.6, 132.9)
Pigott		N=87	38.5 (27.3, 54.5)	
Technique				
VWK	1972-1980	41	37.3 (27.5, 53.5)	(15.1, 151.6)
VL	1981-1989	34	38.4 (26.9, 53.1)	(9.1, 164.8)
ML	1990-1992	12	45.8 (29.7, 71.8)	(12.0, 103.5)
Side				
Left		59	35.4 (26.9, 49.9)	(9.1, 151.6)
Right		28	45.4 (31.3, 66.1)	(12.1, 164.8)

Millard lip techniques were: RA = Rotation Advancement, LARA = Lip adhesion and later definitive repair, POPLA = Pre surgical orthopaedics then lip adhesion and gingivoperiosteoplasty, and a few months later rotation advancement. Pigott palate techniques were: VWK = Veau Wardill Kilner V-Y retroposition, VL = Lateral von Langenbeck, ML = Medial von Langenbeck, releasing incisions.

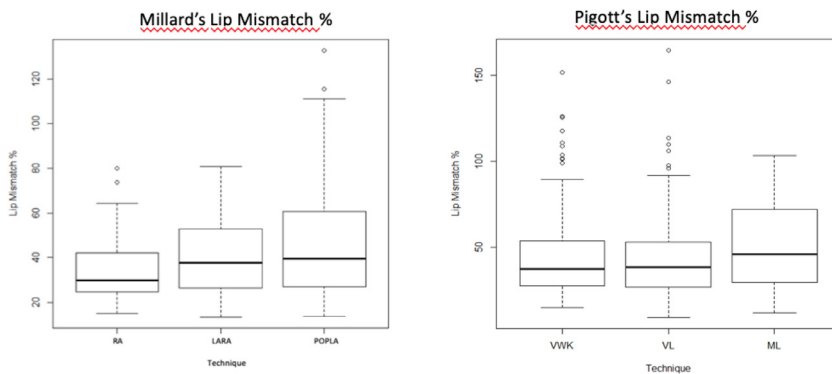


Fig. 3. The box plot data for lip asymmetry for Millard's three different surgical protocols and Pigott's three different palate repair techniques that each used respectively through their careers.

Of Millard's 89 patients, 21%, 37%, and 41% had RA, LARA, and POPLA cleft lip repair protocols, respectively. The RA group had a median mismatch of 29.9% (IQR: 24.7, 42.0) compared to 39.5% (IQR: 27.1, 60.8) median mismatch in the POPLA group. There was a statistically significant difference ($P < .0001$) between these surgical protocols (Figure 3).

All of Pigott's 87 patients had a RA lip repair, and 47%, 39%, and 14% of the children had VWK, VL, and ML palate repair protocols, respectively. There was no significant difference in lip symmetry between these three palate repair protocols ($P 0.59$) (Figure 3).

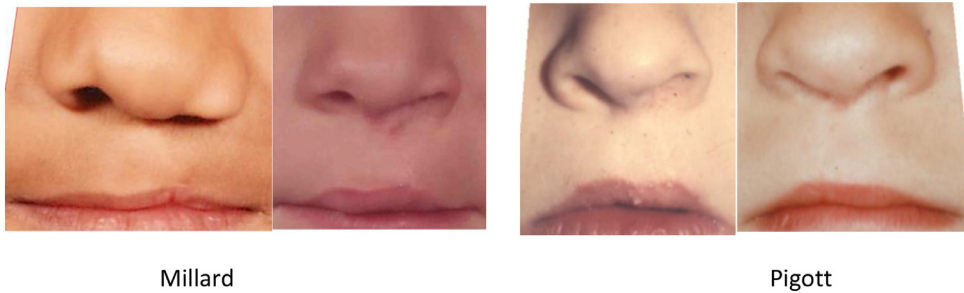


Fig. 4. Cropped images of two examples of the most symmetric lip outcomes for Millard and Pigott.

In the Millard cohort, right-sided clefts resulted in a better median mismatch score (30%, IQR: 24.7, 44.3) than left-sided clefts (41%, IQR: 28.9, 56.5) ($P < .0001$). In the Pigott cohort median mismatch scores were better for left-sided clefts (35%, IQR: 26.9–49.9) than for right-sided clefts (45%, IQR: 31.3, 66.1) ($P = .0121$).

Compared separately to the normal children, who had 19.9% median asymmetry (Kornmann et al., 2019), both cleft cohorts were significantly less symmetrical, $P < .001$.

In the Millard cohort, males (36.26%, IQR 25.30, 51.15) had better symmetry than females (40.59%, IQR 28.05, 58.21) ($P < 0.0001$). There was no gender data for children in the Pigott cohort. Clinical photographs showing two examples of the included patients of Millard and Pigott are shown in Figure 4.

Discussion

The aim of this study was to measure lip asymmetry following cleft lip repair by Millard and Pigott using the Symnose outcome measure. Overall, the post-operative lip asymmetry of these two surgeons did not differ significantly, and for both surgeons was significantly greater than the asymmetry of children who had no facial surgery. The difference between the symmetry found in non-cleft children and those who had a cleft lip repair was the largest difference in symmetry in this study.

Recently, 240 A/P photos of 5-year-old cUCLP children collected as part of the Cleft Care UK (CCUK) study (See refs.^{20,21}) were assessed using the Symnose measure. These children were treated using varying surgical protocols. The median asymmetry of this group was 37.2%, which is comparable to the results of Millard (36.6%) and Pigott (38.5%) in this paper and suggests that there is little evidence that lip symmetry, as assessed objectively by Symnose, has improved in recent decades.

Investigation of the association between lip repair protocol and lip asymmetry showed that Millard's most symmetric results were achieved earliest in his career using the least surgical intervention, namely, a lip repair involving RA alone. The least good results occurred later in his career when he used presurgical orthopaedics and a lip adhesion before definitive lip repair. It is possible that additional scarring in the alveolus following the lip adhesion could have contributed to a less good outcome. This is consistent with the findings of the Dutch cleft randomized controlled trial which showed no positive or negative effect of presurgical orthopaedics on facial appearance.¹⁹

In contrast, palate repair technique would not particularly be expected to affect frontal facial aesthetics and, in this study, no association was found between palate repair technique and lip symmetry in the Pigott cohort, who all underwent the same lip repair technique but had three different palate repair techniques. This is consistent with Lee²⁰ who found no relationship between frontal and worms eye view facial aesthetics (using the Asher McDade method)²¹ and maxillary retrusion (measured using the five-year index) in children with cUCLP. Both Symnose and Asher McDade methods use a frontal 2D photograph which will not clearly show the effects of maxillary retrusion.

The children in this study were grouped according to their surgical protocol over time. If increased experience leads to better outcomes, it might be expected that the most recent surgical protocols would result in least asymmetry. This was not the case. In the Millard cohort, the most recent lip

surgery technique group had the least symmetry. In the Pigott cohort, who all had the same lip surgery technique, lip asymmetry remained similar over time. This may be because both surgeons were experienced cleft surgeons prior to treating the children in this study, and both could be considered relatively 'high volume' operators.²⁵ The increased lip asymmetry in the younger Millard children in this study was most likely due to changes in lip repair protocol.

This study showed that asymmetry following cleft lip repair differed according to the side of the cleft. This was found in both the Millard and the Pigott cohorts, but in the Millard cohort right-sided clefts resulted in better symmetry and in the Pigott cohort left-sided clefts resulted in better symmetry. It may be of note that Millard was right-handed and Pigott was left-handed. There is, however, no obvious explanation for how the handedness of the surgeon might have an effect on outcome.

The authors have previously noted that human raters of cleft repair images attribute about 15% of increased severity of asymmetry to right-sided clefts.¹⁴ This is thought to be an unconscious bias on the part of the human observer as the finding can be eliminated by mirroring the right to appear as left-sided clefts.^{10,22} Advice for human raters of 2D photographs by an Asher McDade type assessment is to convert all the right-sided clefts to be viewed as left-sided before starting the assessment.¹⁰ Symnose itself does not see any difference in symmetry between right- and left-sided clefts, but it is possible that there is a human bias at the time of the tracing of the image on the digitiser.

This study has limited information on gender, but where there was information, males were found to have statistically significant better lip symmetry than females. In the Symnose study on 5-year-old non-cleft children, males were also found to have statistically significant better symmetry than females.¹⁵ The gender of the child is not easily apparent to the rater of a cropped naso-labial image nor to the human digitising a Symnose image. However, in studies, where the whole face was seen by raters of craniofacial malformations, female subjects received higher facial impairment scores than males. The raters' gender was found to be neutral to the outcome.^{23,24} The authors suggest that in future studies both gender and the side of the cleft are considered as additional confounding factors for facial aesthetic outcomes.

The measurement of lip asymmetry as an aesthetic outcome using Symnose helps to remove the subjective element of the outcome measure and also now allows us to compare against a non-cleft population. This study provides a benchmark of lip asymmetry outcomes. Further studies of younger cohorts of children representing different surgeons and/or techniques are needed before we can confidently say there is evidence of improvement in lip symmetry since Millard originally described his RA technique.

Limitations

Pigott selected the children in the two surgeon's cohorts which may have introduced bias. However, there was no significant difference between the overall lip asymmetry for the two operators so it is unlikely that selection bias has occurred.

As the data studied was historic, information was missing in one or both cohorts of children in a number of areas. The authors were not able to identify the exact age at the time of lip surgery for Millard's cases. This study is unable therefore to investigate whether the timing of lip surgery affected symmetry at the age of five years, as opposed to the technique used.

Inadequate information was available regarding the number of children who had lip revision surgery before the age of five for Millard, whilst for Pigott, it was approximately 13%.⁸ We understand that both practised lip revision and this would be important information to know before any one surgical technique, or protocol, or surgeon could be considered to result in better outcomes than another.

The ethnicity of the Millard group is not known; thus, it was not possible to investigate whether ethnicity had an impact on symmetry outcomes. Ethnicity is known to affect lateral view aesthetics,²⁶ but the Symnose technique assesses frontal view symmetry mismatch between the two halves of the lip. Ethnicity is unlikely to be a significant factor in this study.

In Millard's cohort, post-operative photographs were taken at age 5 plus or minus 2 years. In Pigott's cohort, the post-operative photos were all taken at age five plus or minus a few months. Information on the gender of the children studied was not available for the Pigott cohort.

Symnose has now added a Thin Lip Correction (TLC) feature and this appears to improve the reliability of the symmetry assessment.¹⁵ We were not able to use this feature as we no longer had access to the original Symnose files to be able to add this assessment via the new software package.

Symnose is an objective and unbiased tool which is easy to use but is not a surrogate for human raters as facial aesthetics is more than just asymmetry. Artificial intelligence and 3D assessments may yet provide a better outcome measure in the future.

Conclusion

This study established the degree of lip asymmetry at the age of 5 years (± 2 years) in a cohort of children with cUCLP treated by Millard, providing a benchmark for future studies, and showed that Pigott achieved similar lip asymmetry using a similar technique. Additional lip surgery and gingivoperiosteoplasty appeared to reduce lip symmetry for Millard. But modifications in palate surgery by Pigott made no difference to lip symmetry. Lip symmetry results may be affected by the gender of the child and the side of the cleft. The greatest asymmetry difference found was between the two cleft cohorts and the non-cleft cohort.

Funding

None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this manuscript.

Institutional ethical approval

The study used historical data, and all patient identifiers were removed and photographs cropped to a trapezoid mid-face such that they were pseudo-anonymised. Prof. S Anthony Wolfe who holds the historical Millard data, and Mr Ron Pigott who held the historical Bristol, UK, data both gave permission to use the data. A NIHR UK Ethical review board approved the use of cropped and pseudo-anonymised images, and that no further ethical or parental permission was required.

Conflict of interest

The authors state no conflict of interest.

Acknowledgements

The authors thank S Anthony Wolfe, Chief, Div Plastic Surgery, Nicklaus Children's Hospital, Florida, USA, and Nigel Mercer, Cleft Surgeon, Bristol, UK, for their help in verifying some of the historical aspects of this paper.

References

1. Millard Jr DR. A primary camouflage of the unilateral hare-look. In: Skoog T, ed. *Transactions of the first International Congress of Plastic Surgery, Stockholm, Sweden 1955*. Baltimore: Williams & Wilkins; 1957:160.
2. Millard DR. Rotation-advancement principle in cleft lip closure. *The Cleft Palate Journal*. 1964;12:246–252.
3. Millard DR. A Preliminary Adhesion. *Cleft Craft I*. 1976;437 **ch36**.
4. Millard DR, Latham R, Huifen X, Spiro S, Morovic C. Cleft lip and palate treated by presurgical orthopedics, gingivoperiosteoplasty, and lip adhesion (POPLA) compared with previous lip adhesion method: a preliminary study of serial dental casts. *Plast Reconstr Surg*. 1999;103:1630–1644.
5. Cuthbert J. Transposed flaps in cleft palate repair. *Br J Plast Surg*. 1951;4:185–187.
6. Von Langenbeck B. Professor Langenbeck on uranoplastics. *Medical Times and Gazette*. 1861;20:69 1861; July.
7. Murison MS, Pigott RW. Medial Langenbeck: experiences of a modified von Langenbeck repair of the Cleft palate. A preliminary report. *Br J Plast Surg*. 1992;45:454–459.

8. Pigott RW, Albery EH, Hawthorn IS, Atack NE, Williams A, Harland K, Orlando A, Falder S, Coghlan B. A Comparison of Three Methods of Repairing the Hard Palate. *Cleft Palate Craniofac J.* 2002;39(4):383–391.
9. Sharma VP, Bella H, Cadier MM, Pigott RW, Goodacre TE, Richard BM. Outcomes in facial aesthetics in cleft lip and palate surgery: a systematic review. *J Plast Reconstr Aesthet Surg.* 2012;65(9):1233–1245.
10. Deall CE, Kornmann NS, Bella H, Wallis KL, Hardwicke JT, Su TL, Richard BM. Facial Aesthetic Outcomes of Cleft Surgery: Assessment of Discrete Lip and Nose Images Compared with Digital Symmetry Analysis. *Plast Reconstr Surg.* 2016;138(4):855–862.
11. Mercado A, Russell K, Hathaway R, Daskalogiannakis J, Sadek H, Long RE, Cohen M, B A, Semb G, Shaw W. The Americleft study: an inter-center study of treatment outcomes for patients with unilateral cleft lip and palate part 4. Nasolabial aesthetics. *Cleft Palate Craniofac J.* 2011;48(3):259–264.
12. Pigott RW, Pigott BB. Quantitative measurement of symmetry from photographs following surgery for unilateral cleft lip and palate. *Cleft Palate Craniofac J.* 2010;47:363–367.
13. McKearney RM, Williams JV, Mercer NS. Quantitative computer-based assessment of lip symmetry following cleft lip repair. *Cleft Palate Craniofac J.* 2013;50:138–143.
14. Bella H, Kornmann NS, Hardwicke JT, Wallis KL, Wearn C, Su TL, Richard BM. Facial aesthetic outcome analysis in unilateral cleft lip and palate surgery using web-based extended panel assessment. *J Plast Reconstr Aesthet Surg.* 2016;69(11):1537–1543.
15. Kornmann NSS, Tan RA, Mulder FJ, Hardwicke JT, Richard BM, Pigott BB, Pigott RW. Defining the aesthetic range of normal symmetry for lip and nose features in 5 year old children using the computer based program SymNose. *Cleft Palate Craniofac J.* 2019;56(6):799–805.
16. CRANE Database Organisation, UK. The Cleft Registry and Audit Network, a database of children with cleft lip and or palate. 2022 Available at: www.crane-database.org.uk
17. Cicchetti, Domenic V. Guidelines, criteria, and rules of thumb for evaluating normed and standardized assessment instruments in psychology. *Psychological Assessment.* 1994;6(4):284–290.
18. McCulloch CH, Shayle R, Searle, John M. Neuhaus Generalized, Linear, and Mixed Models, 2nd Edition. ISBN: 978-0-470-07371-1 July 2008.
19. Prah C, Prah-Andersen B, Mv Hoft. Kuijpers-Jagtman AM. Infant orthopedics and facial appearance: A randomized clinical trial (Dutchcleft). *Cleft Palate Craniofac J.* 2006;43(6):659–664.
20. Lee TVN, Ireland AJ, Atack NE, Deacon SA, Jones TEM, Matharu J, Wills A, Al-Ghatam R, Richard BM, Ness AR, Sandy JR. Is there a correlation between nasolabial appearance and dentoalveolar relationships in patients with repaired unilateral cleft lip and palate? *Cleft Palate Craniofac J.* 2020;57(1):21–28 Hinton C, Simpson L, Timmins I, Su T, Richard B. Comparing CCUK aesthetic outcomes with non-cleft children using Symnose. *European Cleft Palate Craniofacial Association Congress Abstracts.* OS 44.8, 282, 2019.
21. Asher-McDade C, Roberts C, Shaw WC, Gallager C. Development of a method for rating nasolabial appearance in patients with clefts of the lip and palate. *Cleft Palate Craniofac J.* 1991 Oct;28(4):385–390 discussion 390-1.
22. Feragen KJ, Semb G, Magnussen S. Asymmetry of left versus right unilateral cleft impairments: An experimental study of face perception. *Cleft Palate Craniofac J.* 1999;36:527–532.
23. Okkerse JM, Beemer FA, Cordia-de Haan M, Heineman-de Boer JA, Mellenbergh GJ, Wolters WH. Facial attractiveness and facial impairment ratings in children with craniofacial malformations. *Cleft Palate Craniofac J.* 2001;38(4):386–392.
24. Demellweek C, Humphris GM, Hare M, Brown J. Children's perception of, and attitude towards, unfamiliar peers with facial port-wine stains. *J Pediatr Psychol.* 1997;22:471–485.
25. Williams AC, Shaw WC, Sandy JR, Devlin HB. The surgical care of cleft lip and palate patients in England and Wales. *British Journal of Plastic Surgery.* 1996;49(3):150–155.
26. Richard B, Russell J, McMahon S, Pigott R. Results of randomized controlled trial of soft palate first versus hard palate first repair in unilateral complete cleft lip and palate. *Cleft Palate Craniofac J.* 2006;43(3):329–338.