Three-Dimensional Assessment of Facial Morphology in infants with Cleft Lip and Palate

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Summary

In our modern society, physical appearance is an important determinant of social acceptability. Cleft lip and /or palate is the most common abnormality in the cranio-facial region and occurs in 0.77:1000 live births in Scotland. Dissatisfaction with facial appearance or the unfortunate consequences of being perceived as 'different', prompt children and their families to seek surgical revisions to improve how they look. In this context, an integral part of cleft rehabilitation is the need to provide children with a facial appearance more like their peers, as early in their development as possible.

The goals of primary surgical repair are the restoration of normal morphology and function, without disruption of growth potential. Qualitative and quantitative differences in the soft tissues surrounding the cleft account for the multitude of varieties of presentation of cleft facial morphology. The assessment and documentation of these differences prior to operation is of paramount importance, yet traditional methods cannot capture the three-dimensional nature of soft tissue abnormality. Moreover, the potential influence of initial cleft severity on facial shape has not previously been investigated. The impact of surgery on early facial growth is a subject of continued debate and comprehensive evaluation has been hindered by the lack of an objective, non-invasive, accurate and repeatable method of quantifying facial parameters in infancy. The aims of the development studies were to validate computerised stereophotogrammetry (C3D^{TM}) for three-dimensional assessment of facial morphology of infants with orofacial clefting. The aims of the main study were to characterise and quantify the magnitude of the cleft deformity in the soft tissues and the resultant improvement with surgery and growth in infants with unilateral cleft lip (UCL) and infants with unilateral cleft lip and palate (UCLP). A further aim was to assess the relationship between initial cleft severity and facial soft tissue morphology outcomes at age 2 years.

Methods

The errors of the C3D^{TM} digital colour stereophotogrammetry system in recording facial morphology were quantified using facial plaster casts of cleft infants. The C3D^{TM} system was also validated against a gold standard of 3D co-ordinates obtained by a highly accurate co-ordinate measuring machine (CMM). System error was demonstrated to be 0.83mm. Landmark reproducibility on cleft infant C3D^{TM} models was 0.6mm for a single digitisation, and 0.5mm for repeated landmark digitisation. The 3-dimensional facial

morphology of cleft infants was captured before and after surgical repair, and during the period of early growth up to the age of 2 years. Cross-sectional analysis of facial dimensions was performed for 32 infants prior to surgical repair, 28 infants after lip/nose surgery, 30 children at 1 year and 32 children at 2 years of age. Mixed longitudinal analysis of facial changes with surgery and with growth was also undertaken. Differences between cleft groups were quantified. A new measure was developed to quantify facial shape asymmetry (Asymmetry Score) and used to localise and quantify asymmetry in specific facial features and determine outcomes, following corrective surgery and with facial growth, with reference to non-cleft controls. Residual deformity in the shape of the facial features was quantified by Procrustes distance from a control mean shape (PDFN Score) at 2 years of age. These measures were used to correlate initial cleft severity with outcome at age 2 years.

Results

Differential growth was demonstrated between facial features and within some facial features. In particular, the columella, nostrils and philtrum did not grow significantly after surgery, although this would be considered normal in the age group studied. Facial growth in children with UCL and UCLP was independent of the head and body growth. The presence of a cleft of the secondary palate accentuated the amount of soft tissue disruption by the cleft in the lip and nose, but not the pattern of disruption. Primary lip / nose repair had no detrimental effect on the early growth and development of the facial features. Likewise, palate repair had no discernable effect on facial soft tissue growth at age 2 years. Primary lip / nose repair had a beneficial effect on facial morphology in terms of reducing asymmetry and was most successful in the improving philtrum and nasal base symmetry, less successful in improving the nasal rim asymmetry. A possible early beneficial effect of cleft repair remote from the surgery site was noted in the reduction of upper face asymmetry in the first year of life. Residual asymmetry in the facial features did not change by age 2 years, despite increases in size with growth. Facial morphology outcomes for UCL and UCLP children in this study were generally similar at 2 years of age, despite marked differences in pre-operative facial form. However, nasal base asymmetry, upper face asymmetry and residual nostril shape deformity were significantly greater in UCLP children at 2 years of age, than in UCL children. These shape differences were not detectable by measurement of facial dimensions alone. A more severe nasal deformity was not associated with poorer outcome at age 2 years. However, philtrum deformity and lip deformity at age 2 years may be related to initial deformity in terms of philtrum height discrepancy.

Conclusions

This is the largest and most comprehensive study of 3-dimensional facial soft tissue morphology in the infant cleft population. Objective 3D assessment of pre-operative morphology has enhanced understanding of the complexity of the disruption soft tissues of the face in infants with unilateral clefts. Early objective assessment of surgical results enabled identification of areas where surgery was most successful and areas where outcome was less successful, which may require modification of pre-surgical or surgical management.

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Hood, C.A., Bock, M., Hosey, M.T. & Ayoub, A.F. (2003) Facial Asymmetry - 3D assessment of infants with cleft lip and palate. *International Journal of Paediatric Dentistry.* Vol. **13** (6): 404-410

Hood, C.A., Hosey, M.T., Bock, M., White, J., Ray, A. & Ayoub, A.F. (2004) Facial characterisation of Infants with cleft lip and palate using a 3D capture technique. *Cleft Palate Craniofacial Journal* Vol. **40** (1): 41-48

Ayoub, A., Garrahy, A., Hood, C., White, J., Bock, M., Siebert, J. P., Spencer, R. & Ray, A. (2003) Validation of a vision-based, three-dimensional facial imaging system. *Cleft Palate-Craniofacial Journal.* Vol. **40** (5): 523-529.

1 Introduction

1.1 Background

Cleft lip and /or palate is the most common abnormality in the cranio-facial region. Approximately 15% of facial clefts are associated with a known syndrome, and of these, 25-30% involve the palate in isolation. The incidence of non-syndromic cleft lip and / or palate (CLP) and isolated cleft palate (CP) is approximately 1.35 in 1000 live births. CLP occurs more commonly in males; CP more commonly in females. Two thirds of all cases of unilateral cleft lip and palate have left-sided defects regardless of gender, race or severity (Fraser & Calnan 1961).

1.1.1 Prevalence

1.1.1.1 UK studies

In the United Kingdom, an average of 650 new cases of clefting occur each year, which accounts for 65% of all congenital craniofacial abnormalities (Williams, Shaw & Devlin 1994). Meaningful interpretation of birth prevalence figures is fraught with difficulty - true birth prevalence figures would have to take account of the rate of induced and spontaneous abortion and stillbirth. Figures from prevalence studies carried out in the UK suggest that there has been a decline in the number of cleft births in recent years. There is concern that some trends in cleft incidence are, in part, a reflection of the differences in completeness of recording of cases. Moreover, the national UK reporting system is voluntary and is therefore likely to be an underestimate of the number of orofacial clefts born (Shaw, Roberts & Semb 1996).

1.1.1.2 Scotland

In Scotland, the Scottish Congenital Anomalies Register at the Information and Statistics Division (ISD) of the Common Services Agency records cleft births. In addition, the Managed Clinical network for cleft services in Scotland (CLEFTSiS) registers all cleft lip and palate births, and acts as a central repository for serial photographic, radiographic and study model records for every child with a cleft in Scotland. The Scottish population has a particular predilection for congenital malformations generally and approximately 100 new cases of orofacial clefting occur each year. In particular, Glasgow also has the highest rate of congenital anomalies of all the EUROCAT (European Central Registry for Congenital

Malformations at Birth) centres (Stone & Dolk 1994). There is a remarkably high ratio (almost 1:1) of cleft lip and/or palate [CL(P)] to isolated cleft palate(CP) in Scottish and Northern Irish populations (FitzPatrick, Raine & Boorman 1994; Gregg, Boyd & Richardson 1994). This is not typical of the UK in general or other foreign centres, where the ratio more commonly is 2:1. A low rate of cleft lip, a high rate of cleft palate, and a high rate of associated defects, was reported in Glasgow in the period 1974-85 (Glasgow Congenital Malformations Register). It was postulated that this may be due to the interaction of an unidentified environmental teratogen with a susceptible population (Womersley & Stone 1987).

Comprehensive data on birth prevalence of orofacial clefting in Scotland was recently reported in 2003 (Clark, Mossey, Sharp et al. 2003). Eight hundred and thirty-four cases of orofacial clefting were recorded over a ten year period from 1989-1998. Birth prevalence was 1.46:1000 live births for all cleft types and 0.77:1000 for CL(P).

1.1.2 Aetiology

Non-syndromic clefts are generally described as having multifactorial inheritance. A genetic predisposition, with a variety of implicated genes, may be involved, as well as variable environmental factors which may combine at the right stage of embryological development to contribute to a cleft. Isolated cleft palate is an aetiologically distinct entity from clefts of the lip and/or palate.

1.1.3 Genetic predisposition

Family studies have provided the basis of estimations of risk of recurrence of clefting. Children of parents with cleft lip, for example, have a 1:20 chance of having a cleft condition. If other siblings or close relatives also have clefts, the frequency is 1:6 (Bixler, Fogh-Andersen & Conneally 1971). It is now thought that major genes predispose to non-syndromic clefting in certain individuals and families. An association of CL(P) with transforming growth factor alpha (TGF-alpha) locus has been identified and allele frequency distribution at this locus has been shown to differ in parents of children with CL(P) and CP (Mossey, Arngrimsson, McColl et al. 1998). In recent years, a number of significant breakthroughs in characterization of the underlying gene defects associated with several important clefting syndromes. For example, mutations in the interferon regulatory factor-6 (IRF6) gene have been identified as the cause of Vander Woude syndrome. Whilst no specific disease-causing gene mutations have been identified in non-syndromic clefting,

a number of candidate genes have been isolated through both linkage and association studies (Cobourne 2004).

1.1.4 Environmental factors and gene/environment interaction

In Scotland, there is an established link between socioeconomic status, measured by derivation category (DEPCAT), and prevalence of orofacial clefting. The risk of having a child with a cleft was reported as 2.33 times greater for those resident in the most deprived areas, compared to the least deprived areas. This pattern was stronger for CL(P) than for CP (Clark et al. 2003).

Maternal factors such as consumption of alcohol during pregnancy or smoking have been found to increase the relative risk of non-syndromic clefting in offspring (Little, Cardy, Arslan et al. 2004; Munger, Romitti, ack-Hirsch et al. 1996; Wyszynski, Duffy & Beaty 1997). Use of certain drugs during pregnancy such as corticosteroids and phenytoin use have been linked with increased risk of cleft and /or palate (Carmichael & Shaw 1999; Strickler, Dansky, Miller et al. 1985). Vitamin supplementation in the first 4 months of pregnancy has been demonstrated to have a protective effect against CP and CL(P) (Loffredo, Souza, Freitas et al. 2001). However, excessive intake of other vitamins (e.g. A, D, E) have been implicated as embryotoxic. Folic Acid supplementation has a proven protective effect in neural tube defects (MRC Vitamin Study Research Group. 1991) and there has been much interest in the hypothesis that it would also decrease the incidence of orofacial clefts, although the evidence has been equivocal (Tolarova & Harris 1995).

There is growing evidence to support a gene/environment interaction theory. Genetic susceptibility has been shown to influence the potential of environmental factors to cause orofacial clefts. This has been demonstrated in relation to interactions between genetic polymorphisms at the TGFα locus in infants and maternal smoking (Shaw, Wasserman, Lammer et al. 1996) and lack of maternal folic acid supplementation during pregnancy (Shaw, Wasserman, Murray et al. 1998).

1.1.5 Associated anomalies

There are over 300 known syndromes in which oro-facial clefting is a feature. Even in cases of non-syndromic clefts, other anomalies may be associated (Shprintzen, Siegel-Sadewitz, Amato et al. 1985). The presence of a cleft, therefore, may herald the presence of additional abnormalities (Pashayan 1983).

Occult clefts of the lip and soft palate may occur where intact skin or mucosa hides a submucous defect of bone or muscle. This may not be readily apparent at birth but can result in the same hearing, speech and feeding problems as more overt clefts (Gosain, Conley, Marks et al. 1996). Middle ear problems are common in children with cleft palate and the vast majority will suffer from glue-ear and otitis media at some stage. Approximately 25% of cleft children will have early feeding difficulties (Jones 1988). Speech and language difficuilties are common in patients who have repaired clefts of the palate. Problems encountered range from hyper/hypo-nasality, intelligibility, nasal emission and articulation errors to velopharyngeal insufficiency (Sell, Grunwell, Mildinhall et al. 2001).

An international, multicentre clinical audit of treatment outcome for complete UCLP concluded that approximately half of the cases of UCLP will have maxillary hypoplasia to such an extent that they will require an osteotomy as young adults (Shaw, Dahl, Asher-McDade et al. 1992).

1.1.6 Classification

A wide variety of deformities arise within the spectrum of the cleft lip/palate abnormality. Accordingly, a wide variety of systems for classification has developed that range from simple descriptions of broad groups, to complex attempts to incorporate every variety of cleft. Fogh-Andersen's landmark study of cleft incidence in Denmark showed that cleft lip and/or palate and isolated cleft palate should be regarded as separate entities because of the differences in respect of embryology, timing of fusion, and epidemiological characteristics they exhibit (Fogh-Andersen 1942). His classification method thus formed the basis for the numerous systems in contemporary use.

Kernahan & Stark (1958) introduced a descriptive classification scheme, which was simple but lacked detail, yet is probably still the most commonly used. Orofacial clefts were classified into three broad categories: Cleft lip (CL) referred to clefts of the lip and/or primary palate; Cleft lip and palate (CLP), described clefts of the lip, primary palate and secondary palate. Both anomalies could occur unilaterally or bilaterally (UCLP, BCLP). Cleft palate (CP) referred to an isolated cleft of the secondary palate. Two major drawbacks of this system were that it could not distinguish between clefts of the lip or alveolus, nor the hard and soft palate, and did not allow easy recording of displaced or deficient tissues. The nomenclature committee of the American Association for Cleft

Palate rehabilitation published a more comprehensive classification in 1962, which was later adopted by the Cleft Plate Association. However this was criticised as being too unwieldy and failed to gain universal acceptance. The most commonly used symbolic classification system is Kernahan's striped 'Y', which is capable of recording up to 63 cleft variants (Kernahan 1971). Millard added symbols to allow recording of the extent nasal floor and nose involvement (Millard 1976). A modified version was proposed, which included a separate coding sheet, but this offered little advantage over the American Association system and it too was deemed too complex for general use (Friedman, Sayetta, Coston et al. 1991). A 3-digit coding of all cleft variants was later added to allow computer data entry (Schwartz, Kapala, Rajchgot et al. 1993).

1.2 Cleft Severity

1.2.1 Assessment of Cleft Severity

When assessing outcomes, it is important to have a valid system of initial assessment in order to allocate individuals to groups receiving different interventions and to be able to measure them appropriately. Qualitative evaluations must be supplemented by objective assessments, which enhance the validity and accuracy of subjective judgements, both preoperatively and postoperatively (Farkas, Hajnis & Posnick 1993). Rating scales have been developed to quantify the severity of facial disfigurement and attractiveness in children and young adults with clefts after surgery (Asher-McDade, Roberts, Shaw et al. 1991; Tobiasen, Hiebert & Boraz 1991; Vegter, Mulder & Hage 1997). Until 10 years ago, there was no equivalent tool to rate initial facial impairment in newborns, prior to surgical repair. In 1995, a study by Slade et al established a link between social perceptions of facial attractiveness and initial cleft severity. (Slade, Bishop & Jowett 1995). Cleft severity was classified by a fairly simple anecdotal categorization system (Freedlander, Webster, Lewis et al. 1990), routinely used by plastic surgeons. A complete cleft was classified as more severe than an incomplete cleft, and a bilateral cleft more severe than a unilateral cleft. The study showed that infants with more severe clefts were considered less attractive (Slade et al. 1995). Studies such as this demonstrate that there is scope for developing objective measures of initial cleft severity which correlate with aesthetic judgements.

Initial cleft severity is often cited as a confounding factor in residual facial deformity after surgery. Attempts to separate the influence of the initial defect from the effects of treatment regimes have proved unsatisfactory. In part, this can be attributed to the design

of approach. Investigations of the multifactorial effects of cleft anatomy and interventions using retrospective analysis methods can suffer from lack of information due to incomplete or anecdotal documentation of initial cleft severity. This necessitates the development of measures of cleft severity using available records - commonly study casts. As a result, there are several methods of quantifying cleft severity according to measurements of cleft width in the palate or area of the cleft as a percentage of total palate area (Bacher, Göz, Pham et al. 1998; Johnson, Williams, Singer et al. 2000; Peltomaki, Vendittelli, Grayson et al. 2001; Suzuki, Mukai, Ohishi et al. 1993; Wada & Miyazaki 1976). A lack of landmarks in the edentulous infant palate has hampered this approach and quality of dental casts and operator experience cited as factors which reduce reproducibility (Seckel, Van der Tweel, Elema et al. 1995). These methods, when used to establish correlation between initial cleft size and outcome measures such as occlusion or midface skeletal development, have returned contradictory results (Johnson et al. 2000; Peltomaki et al. 2001; Suzuki et al. 1993).

Nonetheless, simply measuring the cleft in the palate cannot evaluate the extent of the soft tissue defect in the lip and nose, nor quantify the disruption of facial appearance. A recent study by (Yeow, Huang, Lee et al. 2002) explored the relationships between 3 key soft tissue measurements in the cleft lip and nose as possible indicators of facial cleft severity in 125 3 month old infants with UCL. The width of lip 'gap', difference in nasal floor widths and vertical height discrepancy in the philtrum were measured directly with callipers in infants with complete and incomplete cleft lip, at the time of operation. A strong correlation was found between the two horizontal measures of severity in both cleft groups, but a weak linear relationship between vertical and horizontal measures, could only be demonstrated in the complete cleft group. It was concluded that, in the incomplete cleft cases, a severely short philtrum could occur in the presence of a relatively mild transverse tissue deficiency. This study highlighted the need to consider the severity of different aspects of cleft lip and nose deformity separately.

1.2.2 Influence of cleft severity on outcome

Little is published about the potential influence of the initial severity of a cleft on the morphological development of soft tissues of the face. A lack of soft tissue landmarks and availability of practical, objective methods of quantification have contributed to this. The size of a cleft in the lip and nose will reflect differing contributions of tissue deficiency and displacements. In wider clefts, there may be more difficulties associated with repair due to a lack of tissue in the locale, or greater separation of the cleft segments warranting more extensive tissue mobilisation to affect closure.

Some authors have reported correlation between the grading of initial cleft severity and ratings of deformity after surgery. Two such related studies developed pictorial grading systems to rate different aspects of nasal and lip deformity and combine them as a composite score (Anastassov & Chipkov 2003; Mortier, Martinot, Anastassov et al. 1997). In the first study, two surgeons rated photographs of 43 subjects with partial UCL prior to their repair and at least 1 year post-operatively, although the interval between surgery and post-op rating varied. The authors reported that the pre-op severity scores were moderately correlated (0.41) with post-op ratings (Mortier et al. 1997). The second study concerned 13 UCLP and 16 BCLP subjects prior to lip repair, 12 subjects requiring lip revisions and 9 subjects requiring nose revisions (Anastassov & Chipkov 2003). This mixed study was descriptive in nature and no statistical analysis was presented. The grading system developed and applied in these studies was subjective and only allowed conclusions about the general nature of the severity of the initial cleft defect. The post-op rating system was weighted according to the authors' opinions of how difficult it would be to correct the initial defect and so the award of scores could not be considered to be without bias.

A tentative, weak link between objective measurements of severity of initial cleft lip/ nasal deformity and outcome, was only relatively recently demonstrated (Hurwitz, Ashby, Llull et al. 1999). This retrospective, computer-assisted indirect anthropometric study comprised of 19 children with UCLP, who were assessed prior to surgery, and then followed annually. Frontal & basal view photographs were measured using extended NIH public domain Image-analysis software. The congenital deformity was scored by combining measurements of lip and nose parameters, weighted according to aesthetic importance, then categorised as mild, moderate or severe, according to the cumulative score. Correlation between pre-op scores and post-op scores at age 5 years were weak ($R^2 = 0.22$). Moreover, this study was limited by the fact that photographs were the assessment media

i.e. a 2D assessment of a 3-dimensional entity and thus represented an over-simplification of the complex problem of cleft severity.

There has been no comprehensive 3D analysis of facial soft tissue morphology, which has sought to quantify the degree of the initial cleft deformity in infants and investigate the possible influence of different aspects of initial cleft severity on facial shape outcomes.

1.3 Morphology of the Unilateral Cleft Face, prior to surgical repair

Quantitative and qualitative description of cleft severity requires a full analysis of the deformity within the context of the entire face. An appreciation of the skeletal, nasal and peri-oral anatomy of the condition is prerequisite. Direct clinical observation and peri-operative documentation of the naso-labial deformity are the main sources of anatomical information in the cleft neonate. Accordingly, exploration of the anatomical aberrations of cleft deformity in vivo is limited to the area of surgery. Traditional descriptions of the functional anatomy of the facial muscle complex have been challenged as microsurgical dissection techniques have facilitated more detailed observation of anatomical structure and relationships in cadaver studies (Breitsprecher, Fanghanel, Metelmann et al. 1999; Breitsprecher, Fanghanel, Noe et al. 2002). Objective documentation of skeletal morphology in un-repaired cleft children is more complete, due to the wide availability of traditional cephalometric radiography. Advances in radiographic techniques have also seen the application of 3 projection cephalometry methods (Dahl, Kreiborg, Jensen et al. 1982; Hermann, Jensen, Dahl et al. 2000; Hermann, Jensen, Dahl et al. 1999b; Hermann, Jensen, Dahl et al. 1999a) and CT scanning (Breitsprecher et al. 1999; Fisher, Lo, Chen et al. 1999). However, the use of ionising radiation in the young patient is a controversial area (Mackay, Bottomley, Semb et al. 1994; Shaw et al. 1992).

1.3.1 Anatomy of the Unilateral Cleft lip/nose and palate

In UCL cases, there is considerable diversity in the extent of involvement of hard and soft tissues, from minimal notching of the vermillion border to a complete defect extending to floor of the nose and through the alveolus. Seventy percent of unilateral clefts of the lip are also associated with a cleft palate. Similarly, in UCLP cases, varying degrees of clefting in the lip and palate can exist, in a wide range of combinations. In complete clefts of the lip and palate there is direct communication between the oral and nasal cavities on the side of the cleft.

1.3.1.1 Cleft Lip anatomy

In the complete unilateral cleft lip, the fibres of the orbicularis oris muscle are disrupted. They proceed horizontally from the corner of the mouth towards the midline, then turn upwards along the margins of the cleft. The muscle fibres in the lateral segment terminate beneath the alar base, and in the medial segment, most attach to the periosteum of the maxilla beneath the columella (Malek 2001).

In incomplete unilateral clefts; where the cleft is less than two-thirds of the lip height, the muscle fibres above the level of the cleft remain intact. These narrow bridges of tissue are known as Simonart's bands. The prevalence of soft tissue bridges in Caucasian cleft populations has been reported to be between 20 - 31% (Semb & Shaw 1991; Silva Filho, Cristovao & Semb 1994). A protrusion of excess muscle may be seen and palpated on the lateral aspect of the cleft, due to heaping up of muscle fibres which have been prevented from developing to their full potential. On the medial side, however the muscle tends to be underdeveloped, manifesting as a marked thinning of the muscle layer in the half of the philtrum adjacent to the cleft. The exact configuration and contribution of the orbicularis oris muscles and the lip levator muscles to the anatomy of the philtrum is debated (Namnoum, Hisley, Graepel et al. 1997; Schendel, Pearl & De Armond 1989). The skin of the unilateral cleft lip is both retracted and displaced secondary to the initial hypoplasia and a lack of normal muscular function (Delaire 1978; Schendel, Pearl & De Armond 1991). Nasal skin is found in the upper portion of the lip medially and laterally and atypical cleft mucosa replaces normal vermilion mucosa on the borders of the cleft. The philtrum is shortened and its crest abnormal and a modified white roll is evident (Mulliken, Pensler & Kozakewich 1993; Schendel 2000).

1.3.1.2 Nasal anatomy in cleft lip/nose

A degree of nasal deformity accompanies both the complete and incomplete cleft lip. The nasal tip tends to be displaced towards the cleft side and the columella base to the non-cleft side. The vomer is deviated laterally at its line of attachment to the palatal process on the non-cleft side. This deviation can be almost horizontal in severe cases. There is often constriction and functional occlusion of the nostril on the non-cleft side due to nasal septum deviation and approximation of the alar base and columella. The alar ridge on the cleft side is usually stretched and flattened depending on the width of the cleft, and the alar base is laterally deviated and retropositioned (McComb 1990).

1.3.1.3 Cleft Palate anatomy

In complete UCLP, the anterior or primary palate segment is often tilted superiorly and medially into the cleft, on the cleft side. Clefts of the secondary palate may involve the hard and soft palates in combination, or the soft plate alone. Clefts may extend from a bifid uvula all the way through in a 'V' shape to the incisive foramen. Clefts of the secondary hard palate are characterised by deficiency of mucosa and underlying bone. The degree of separation of the palatal shelves varies substantially. In the soft palate, the mucosal deficiency is combined with shortening of the velar musculature, which in addition have abnormal sites of insertion (Sommerlad 2001).

1.3.1.4 Position of major and minor cleft segments

Dislocation of the maxillary segments to varying degrees, is a feature in pre-op UCLP infants (Bacher et al. 1998; Breitsprecher et al. 1999). Opinions differ as to whether the pull of disrupted facial muscles, tongue position in the cleft or a combination of these factors is responsible for the malpositioned cleft segments. Distortion may be sufficient to affect the ease of lip repair. There is debate about whether the lesser cleft segment is retropositioned, and rotated towards or away from the non-cleft side (Bacher et al. 1998; Kriens 1991; Wada & Miyazaki 1976). The extent of bony element displacement in cleft lip and alveolus tends to be less marked than in cleft lip and palate, but outcomes may not be necessarily better where a partial cleft is involved. Kreins' (1991) study of the pre-op maxilla in infants with complete UCLP and UCLP with a partial cleft lip concluded that differences in maxillary dimensions pointed to a more serious underlying skeletal deformity, masked by the presence of a partial lip cleft. The limitation of this study was the

range of ages within the sample and comparison with an unmatched control group. Nevertheless, there was strong evidence for tongue position being a factor in palate shape and the position of major and minor segments and this has been confirmed by others (Bacher et al. 1998). However in the long term, the presence of a partial cleft lip or Simonarts band in UCLP does not appear to have a detrimental effect and these individuals can have a slightly more favourable maxillary growth (Semb & Shaw 1991).

1.3.1.5 Facial Muscle Balance

An intact 3D system of facial muscle slings for is necessary for balanced facial development (Markus, Delaire & Smith 1992b). A cleft causes disruption of all muscle slings, symmetry, and power vectors, causing interruption of connections between the facial suture systems and the periosteal growth fields of the nasal bones, maxilla and mandible. Disturbance of the anatomy and function of this 3D facial muscle sling system is postulated as the trigger for the aesthetic, functional and developmental problems seen in UCLP (Breitsprecher et al. 2002).

1.3.2 Skeletal Morphology in Unilateral cleft infants, before surgery.

Knowledge of the intricacies of anomalous skeletal morphology in facial clefting, aids understanding of the reasons for the pattern of disruption of soft tissue morphology and differences associated with surgery, dysplastic or compensatory growth. Studies of un-operated individuals have confirmed that some craniofacial aberrations seen in older cleft individuals are unrelated to surgery and have an intrinsic relationship to the primary anomaly (Bishara 1973; Dahl 1970; Mars & Houston 1990). Generally speaking, individuals with complete clefts differ more from the norm than those with incomplete clefts (Dahl 1970). No differences in craniofacial morphology, have been reported in relation to side of cleft, in radiographic studies of either cleft lip or cleft lip and palate (Hermann et al. 1999b; Jain & Krogman 1983).

The differences in craniofacial morphology between infants with clefts involving the primary palate alone, and isolated secondary palate have been described by various authors (Dahl et al. 1982; Molsted, Palmberg, Dahl et al. 1987; Nakamura, Savara & Thomas 1972). Dahl et al.(1982) compared craniofacial characteristics of 30 children with cleft lip and 30 children with isolated cleft palate, aged 2-3 months. Cephalometric films in 3 views

of each infant were examined. It was suggested that in children with clefts of the primary palate, some width dimensions of the upper face (inter-orbital distances in particular) were influenced by the cleft, together with asymmetry of the anterior part of the maxilla, reflecting differences in embryological development (Dahl et al. 1982). There was no non-cleft control group in this particular study. An increased inter-orbital width has been reported in children and adults with clefts of the primary palate in relation to non-cleft individuals (Dahl 1970; Nakamura et al. 1972).

Increased inter-orbital dimensions were reported in a cephalometric study of 38 infants with unilateral clefts of the lip only, and 34 infants with unilateral cleft lip and varying degrees of alveolar cleft (Friede, Figueroa, Naegele et al. 1986). However, this mixed longitudinal study presented data from birth to age 6 years, and did not include a control group. Data were compared with published 'norms' for inter-orbital distance, although no statistical comparisons were made (Costaras & Pruzansky 1982).

In a more recent cephalometric study comparing craniofacial growth in different cleft types, data were reported for infants aged 4 months, prior to lip repair by (Han, Suzuki & Tashiro 1995). A small sample of 10 males with UCLA, was compared with 17 UCLP males and 14 isolated CP female infants were compared with 16 UCLP females. A non-cleft control group was not included for the younger ages. All facial widths, including inter-orbital dimensions, were reported as being wider in the UCLP group, compared to the UCLA group and similar to those with isolated CP, prior to lip repair.

It appears to be accepted that only mildly deviant facial skeleton morphology occurs in subjects with isolated cleft lip, with differences being limited to the cleft region. This has led to infants with incomplete or minor clefts of the lip only being used as a control group for radiographic studies, since they are regarded as having craniofacial morphology as close to normal as possible. This was illustrated in a large comprehensive cephalometry study of craniofacial morphology in 75 2-month-old infants with incomplete UCL and 82 infants with complete UCLP (Hermann et al. 1999b). The study was based on archived material collected between 1976 and 1981 (Jensen, Kreiborg, Dahl et al. 1988). Cephalometric radiographs in three projections were obtained for each infant. The authors reported that aberrations of the maxillary complex and overlying soft tissues were evident, but the calvaria, cranial base, orbital region and mandible also display abnormal morphology. The authors noted that all studies of un-operated infants with clefts of the secondary palate have demonstrated maxillary and mandibular retrognathia. Increased

maxillary width was found in UCLP infants and authors offered the hypothesis that this combined with bimaxillary retrognathia results in a total facial type, which could be considered a significant liability factor in increasing the probability of UCLP.

Older children and adults with UCLP have been described as having a cranial base which is shorter and flatter (Dahl 1970; Hayashi, Sakuda, Takimoto et al. 1976). In infants, an increased cranial base width, maxilla width, and increased bilateral angulation of the petrous temporal bone and the sphenoid bone were reported in 52 3-month-old children with complete UCLP, compared with 48 3-month-old children with incomplete UCL. (Molsted, Kjaer & Dahl 1995). Again, the UCL infants were considered to be a control group.

As noted in clefts restricted to the primary palate, an increased inter-orbital distance has also been reported in UCLP compared with CP and non-cleft individuals. A longitudinal study of PA cephalometric radiographs in 51 UCLP, 27 BCLP and 62 isolated CP infants, reported wider maxillary and inter-orbital dimensions and increased upper face height in the UCLP group compared to the CP group in the birth to 4 month age group. BCLP infants had the widest dimensions of all three groups (Ishiguro, Krogman, Mazaheri et al. 1976). A study of similar methodology to that of Ishiguro et al (1976) examined 64 UCLP, 32 BCLP and 78 CP infants, concluded that the larger upper face and maxillary widths seen in infancy in the UCLP children may reflect a preoperative maxillary segment translocation. (Jain & Krogman 1983).

More recently, three-dimensional evidence to support this theory was reported by Zemann and co-workers (2002). Variable dislocation of the orbital region, maxillary segments and nasal region were demonstrated by analysis of 21 3D skull models of 3 month old UCLP infants, prior to surgical intervention. The nasal aperture asymmetry was attributed to horizontal and vertical translocation of the lateral piriform margin. Increased inter-orbital distance was also confirmed and attributed to a predominantly caudal translocation of the infraorbital rim (Zemann, Santler & Karcher 2002).

1.3.3 Facial Soft tissue Studies of Unilateral cleft infants, before surgery

Qualitative and quantitative differences in the soft tissues surrounding the cleft account for the multitude of varieties of presentation of cleft facial morphology. The assessment and documentation of these differences prior to operation is of paramount importance, yet the available literature on morphological problems is surprisingly sparse. Studies are often descriptive or anecdotal and limited by the lack of a means to measure what they describe. Where quantitative assessment has been reported, this is often of questionable validity due to the limitations of the assessment methods chosen. Even with advances in assessment techniques and imaging technology, objective quantitative evaluations of the facial soft tissue morphology of children with unilateral cleft lip and palate prior to surgical intervention are limited and few. The findings of studies which have attempted to objectively evaluate soft tissue facial morphology, prior to surgery, in infants with unilateral clefts, are reviewed.

Only limited direct anthropometric documentation of facial characteristics in UCLP infants has been reported in the literature. Nasal length, width and face width in 54 UCLP Czech infants aged 3-12 months were compared to an existing norm for 3-6 month old infants of the same ethnic origin, collated by Figalova in the 1970's (Farkas et al. 1993). Nasal widths were mostly larger than normal, nose heights were within the normal range or slightly large, and face width was increased in half of the UCLP infants.

A comparison of soft tissue profile in 2 month old UCL and UCLP infants, prior to surgery, was reported as part of the 3 projection cephalometry study by Hermann and colleagues (1999). A flatter nose, which was retruded in relation to the facial plane and anterior cranial base, was reported in UCLP infants. In addition, the upper lip was described as shorter and more prominent and the lower lip was retruded in relation to the anterior cranial base. Upper and lower face heights were decreased and the anterior pole of the eye occupied a more sagittal and vertical position in relation to the cranial base in UCLP infants, compared with findings in UCL infants.

A full understanding of the complex deficiencies and 3-dimensional nature of the cleft deformity is a prerequisite for the measurement of change following surgical repair.

Data relating to one infant with cleft lip and palate prior to and immediately following surgical repair was reported in order to illustrate the potential of a liquid crystal scanner to measure 3D cleft morphology (Yamada, Sugahara, Mori et al. 1999). This group later published a mixed cross-sectional report of the soft tissue features of Japanese UCLP infants repaired by the triangular flap method (Yamada, Mori, Minami et al. 2002b). A pre-operative assessment was included for a cohort of 8 infants who were measured prior to surgery, and at 2 weeks and 3 months post-op, respectively. Individual changes in this period were not reported. Cross-sectional comparison with a group of 97 non-cleft control infants aged 4 months was reported for the pre-op and post-op measurements. Although 3D data were collected, analysis was limited to inter-landmark distances and no 3D shape analysis was attempted. Asymmetry was measured simply by comparing cleft with non-cleft sides. The novel semi-automatic landmark extraction programme developed by the authors, resulted in unfamiliar landmark labels and measurements which were difficult to interpret and equate with conventional anthropometric measurements. Despite this, quantitative morphological problems reported in UCLP infants prior to repair consisted of a wide intercanthal distance, increased cleft side alar width and mouth width; deviation and inclination of the columella towards the non-cleft side; a flattened nasal tip and asymmetry of the alar wings and Cupid's bow.

Pre-operative findings were reported in a study of the effects of lip adhesion on labial height in 37 UCLP and 6 UCLA infants, aged 2-3 months (Vander Woude & Mulliken 1997). Direct anthropometric measurements of the philtrum area were obtained at the time of surgery with callipers. Cleft and non-cleft side measurements were compared and although the error was not stated, measurements were acquired three times, by the same surgeon. The medial aspect of the philtrum was found to be consistently shorter than on the non-cleft side, together with a shortened distance from the alar base to the Cupid's bow on the cleft side, prior to surgical repair.

The increasing trend towards primary nasal tip repair has prompted an interest in evaluating childhood nasal form. (Fisher et al. 1999) reported the nasal morphology of 12 Chinese UCLP infants, before cleft repair. A computerised analysis and direct measurements were taken from reconstructed CT scans. The authors reported that the cleft lip nasal deformity was characterised by 4 main features. Deviation of the columella base to the non-cleft side; a more posteriorly placed cleft side piriform margin than on the non-cleft side; posterior displacement of the alar base on the cleft side; a laterally displaced non-cleft side alar base, which was also consistently further from midline than the cleft

side alar base, were noted. These findings were attributed to the muscular pull on the alar base and columella by an unopposed cleft orbicularis oris and nasolabial muscles.

Disrupted nostril form is one of the most obvious manifestations of the cleft defect. Descriptive studies can document differences in nostril shape and asymmetry in relation to the non-cleft side, but are unable to quantify these properties. Nostril form has been quantified by (Hurwitz et al. 1999) as part of an overall scoring system of cleft severity, using anisometry. This technique defines the properties of an ellipse which 'best fits' the nostril, not the nostril shape itself. However, only the non-cleft side nostril was included as part of the overall assessment using anisometry, as this method could not be applied to a non-elliptical cleft-side nostril. Few studies to date have explored nostril form in un-operated infants.

Yamada et al (2002a, 2002b) quantified nostril deformity by measuring differences between right and left 3D landmark points at the superior and inferior extent of the nostril between in relation to a projected plane or axis. No measurements were reported pre-operatively, however and this was probably due to the system's inability to identify and automatically extract landmarks from the pre-op cleft side nostril.

From a survey of the literature, it is apparent that there are few objective quantitative studies of facial soft tissue morphology in UCLP infants and even fewer involving UCL infants. There are obvious differences between UCL and UCLP prior to surgery, with respect to the extent of soft tissue disruption and underlying facial skeleton disruption by the cleft. A gap exists in the literature for comprehensive 3-dimensional soft tissue quantification of the facial form of cleft infants, prior to surgical management.

No comparable 3D data for the Caucasian non-cleft infant population in the UK, Europe or the United States was available until very recently. White conducted an investigation into the facial morphology and growth in infants from the age of 3 months to 2 years (White 2005). The methodology used in this study was similar to that of this investigation and the same research tools were applied. Normal facial and body dimension for Scottish 3 month old children have been published (White, Ayoub, Hosey et al. 2004).

1.3.4 Gender differences in facial form

MRI studies have shown that adult males and females have differences in intracranial and cerebral size that remain after controlling for height (size) differences (Nopoulos, Flaum, O'Leary et al. 2000). Gender differences in facial size but not shape, were demonstrated by Ferrario et al. in adult males and females (Ferrario, Sforza, Poggio et al. 1994a). A 3D study of facial form demonstrated that facial size *and* shape were related to gender differences (Hennessy, Kinsella & Waddington 2002). Gender dimorphism in 3D facial form was reported in adults, using an analysis of 3D landmark configurations, comparable to the present study.

Evidence for gender differences in the craniofacial morphology of cleft children is contradictory. Several authors reported gender differences in craniofacial form and growth pattern in young children (Jain & Krogman 1983; Krogman, Jain & Long, Jr. 1982) However, no gender differences were reported in 22 month old cleft infants, after surgical repair or with growth (Hermann et al. 1999a; Hermann et al. 2000). No evidence of gender dimorphism was reported in 3D studies of facial soft tissue morphology in 97 Japanese infants, either with or without clefts (Yamada et al. 2002b; Yamada, Mori, Minami et al. 2002c), despite male / female differences in body measurements.

Gender dimorphism was recently reported in some soft tissue facial dimensions in a group of 3-month-old Scottish infants. The sample consisted of 41 males and 43 females who had their facial morphology captured by a digital stereo-photogrammetry system (C3D). Differences between male and female facial dimensions were largely explained by differences in weight, but differences in the nasal base and nostrils remained after the effects of body size were taken into account (White et al. 2004).

1.4 Management of Cleft Lip and Palate

1.4.1 Surgical Management

The story of cleft repair is one of progressive improvement in cosmetic and functional results, as surgeons have come to appreciate the true nature of the cleft defect. The main advances in surgical repair of the unilateral cleft lip are the functional muscular reconstruction of lip, with or without orthopaedic moulding, resulting in improved morphology. Interest in early correction of nasal deformity is being revived.

1.4.1.1 History of Cleft Surgery

Cleft repair has evolved over a long time and the early pioneers of cleft surgery were concerned simply with closing the cleft. Millard described the history of cleft repair in his monograph entitled 'Cleft Craft – the evolution of its surgery'(Millard 1976). The first report of cleft lip repair is attributed to an unknown Chinese physician in the late 4th Century AD. The first 'surgical' closure was carried out by a Flemish surgeon called Yperman in the early 1300s, but reports of methods that proved later to be fore-runners of the various modern lip closure techniques did not start to appear until the mid to late 19th century. The concept of closure of the cleft lip using local flaps was proposed by Malgaigne in 1843, and modified by Mirault to include a lateral flap advanced across the cleft. This method formed the basis of all current lip closure techniques. Alternative designs started to appear towards the end of the 19th century and beginning of the 20th century - the Z-plasty and rectangular flap of Hagedorn, and straight-line closure technique of Rose and Thompson. Although straight-line closure enjoyed popularity for the first half of the 1900's, interest was revived in the original techniques of Mirault, which involved a triangular flap advanced into the lower portion of the lip. Others subsequently described their innovations and developed their own variations on the triangular flap theme (LeMesurier 1949; Randall 1959; Tennison 1952).

A lip that looks natural at rest will not move symmetrically unless the muscles within it are properly realigned. The 'classical' surgical lip closure methods failed to focus attention on precise reconstruction of the muscles of facial expression. As understanding of the complexity of the cleft defect grew, so did the appreciation that primary lip surgery should also involve subtle dissection and re-orientation of the 3D facial muscle slings to provide a functional repair (Delaire 1978). From the late sixties, techniques favouring muscle insertion detachment and re-alignment developed (Fara 1971). Many evolutions of these techniques, with varying degrees of dissection of misdirected, dislocated and pathological muscle insertions and numerous designs to reconstruct the facial muscles have since been introduced (Breitsprecher et al. 2002; Joos 1989; Kernahan & Bauer 1983; Park & Ha 1995). Irrespective of skin incision design, many agree that primary lip/nose surgery should contain selective subperiosteal detachment of abnormal nasal and peri-oral musculature from the anterior piriform margin and the maxillary bone near the cleft and the anterior nasal spine. Complete detachment of other osseous, cartilaginous and cutaneous muscle insertions are best avoided (Breitsprecher et al. 2002).

1.4.1.2 Rotation Advancement Technique (Millard Repair)

In 1955, Millard developed his rotation-advancement concept. In recognition of the importance of preserving the philtrum dimple and cupid's bow of the lip, he proposed advancement of a lateral flap into the upper part of the lip, combined with a downward rotation of the cleft medial segment. In 1976 Millard refined his own rotation-advancement technique to include re-alignment of the orbicularis oris muscle, crosswise incisions and transposition into a true horizontal position (Millard 1976). Many surgeons today prefer the Millard rotation-advancement method of lip repair and the numerous published modifications to Millard's original technique, are a testament to its continued popularity. Modifications have been introduced to increase the size of lateral advancement flap, improve nasal symmetry and lengthen the columella, although. some would argue, however, that this procedure is not necessary in UCLP cases as the columella is not in fact short, but just displaced (Broadbent & Woolf 1984; Fisher & Mann 1998).

The claimed advantages of the modern Millard include masking of the scar in the philtrum crest and the nostril floor and improved relationship of the alar base on the cleft side, producing better symmetry of the nostril and nostril sill (Millard 1982). A reduced alar flare and molding of the alveolar process are also claimed advantages. Although considered a flexible technique, it has been described as a "cut as you go" technique, suffering from a lack of accurate preoperative measurement guidelines. As with all surgical techniques, the Millard repair has its limitations and it may be too technically demanding to perform in wide clefts (Millard 1968). In complete clefts, where the lateral lip element is small, rotation of the medial flap can be hindered and may require a further small Z-plasty above the Cupid's bow, to increase its length. The need for extensive soft tissue undermining, tension created across the nostril sill and consequent tendency for a constricted nostril on the cleft-side, have been noted. These are mainly clinical observations and few have actually been backed up by sound quantitative evaluations.

Vermillion reconstruction is receiving more attention of recent years, and a renewed interest in the recommendation for a lateral vermillion flap to augment the deficiency that exists pre-operatively, on the cleft side (Noordhoff 1984).

1.4.1.3 Cleft lip/nasal repair

Although Huffman and Lierle first reported the anatomy of the cleft lip/nose in 1949, nasal surgery was avoided in children due to fears about growth impairment. Synchronous primary lip and nose repair did not become commonplace until the 1970s. However there is renewed interest in primary treatment of nasal deformity at the time of lip surgery as it is long lasting, results in a better nasal structure and does not affect growth (McComb 1985; Salyer 1986). Cleft lip repairs that involve minimal undermining fail to free the cleft side alar cartilage from abnormal fibrous and muscular tethering to the maxilla (McComb 1975; Mulliken & Martínez 1999). Likewise, failure to reposition the alar cartilage when lip repair is carried out results in drooping of nostril rim, the lower border of alar cartilage pushes up an oblique ridge within the vestibule and nostril flaring occurs, which can worsen with time (Broadbent & Woolf 1984). In contrast, a good nasal repair is maintained throughout growth. As with most aspects of cleft surgery, opinions differ as to the extent of tissue undermining that should be performed. Most of the primary nasal correction methods involve undermining of the skin over the cleft half of the nose, alar dome lifting and suturing and closure of the nostril floor (McComb 1975). Other technical variations are advocated to lift the alar base, or reposition the nasal septum (Anderl 1990). Nevertheless, the nasal deformity is a difficult aesthetic problem and children with repaired clefts are as likely to be concerned about the appearance of their nose as they are about their scarred lip.

1.4.1.4 Alveolar Cleft repair

Contradictions exist in the literature with regard to surgery to the alveolus at the time of lip repair and its influence on maxillary growth. Interference with the vomero-premaxillary suture has been cited in the aetiology of growth impairment and it is suggested that a vomer flap performed in infancy disrupts growth of maxilla (Friede 1978; Friede 1998). However, the Oslo cleft team believes that a single layer closure of the nasal floor using a vomer flap allows early closure of cleft alveolus, thus decreasing frequency of nasoalveolar fistulas, without significant maxillary growth attenuation (Semb 1991).

1.4.1.5 Hard Palate Closure Techniques

The approaches to hard palate closure in modern day use have their own advocates, but it is still not known which is best for a given individual (Witt & Marsh 1997). The Von Langenbeck (1861) method was the first reliable method of palate cleft closure and

modified forms are still widely practised today. The hard palate is closed by means of bipedicle mucoperiosteal flaps anteriorly, which are slid together and joined in the midline along with the soft palate halves posteriorly. This enables excellent separation of nasal and oral cavities but problems associated with a short palate and closure of the velopharyngeal sphincter can have speech consequences in a number of patients. Creation of the bipedicle flaps involves releasing incisions medial to the alveolar process, so that areas of exposed palatal bone are left once the flaps are opposed. This can result in extensive scarring, which has been implicated in disturbance of maxillary growth and dentoalveolar crossbites (Enemark, Friede, Paulin et al. 1993; Mars 2001).

Veau first noted the absence of a normal levator veli palatini sling & aberrant insertion of diastatic muscles on the edges of the hard palate (Veau 1931). The 'pushback' technique was developed in an attempt to gain palate length by optimal posterior palate tissue mobilisation. It was subsequently adapted by Wardill and then Kilner and involves raising bilateral peninsular flaps, skeletonising greater palatine neurovascular bundles and fracture of the hamuli (Kilner 1937; Wardill 1937). The procedure leaves greater areas of denuded bone and the subsequently greater potential for scarring. Techniques have been developed to try to overcome this problem, such as avoiding releasing incisions completely and allowing the mucoperiosteal flaps to fall away from the palatal bone (Sommerlad, 1997). Reducing the number or position of releasing incisions (Delaire & Precious 1985; Murison & Pigott 1992) or scoring the periosteum to allow stretching and a tension-free closure (Reid & Watson 1988), have also been suggested.

1.4.1.6 Soft Palate Closure

The soft palate cleft may exist as an isolated entity or form part of a more extensive cleft. The Intravelar Veloplasty method involves dissection of soft palate muscle insertions, repositioning and plication to recreate the absent levator sling. It is used both in primary surgery and as a secondary procedure for velopharyngeal insufficiency (Kriens 1969; Kriens 1970).

The Furlow double-opposing Z-plasty repair incorporates soft palate lengthening and levator retropositioning to create the levator muscle sling (Furlow 1986). This is a straightforward procedure in a narrow cleft but can be difficult in wide clefts, where a lack of spare tissue cannot allow achievement of proper palatal length (Mars 2001).

This investigation reports on facial morphology outcomes in infants who have undergone the Millard primary lip repair, with various combinations of McComb primary nasal repair, single or two layer nasal floor closure, primary perioplasty alveolus repair, vomer flap, Veau-Wardill-Kilner or Von Langenbeck hard palate repair (with or without releasing incisions), Furlow Z-plasty or an intravelar veloplasty for soft palate closure.

1.4.2 Timing of primary surgery

The timing of primary surgery is a controversial area and in particular, the arguments for early versus late primary repair. At its most extreme, the possibility of cleft repair before birth has been raised. Human intrauterine surgery even for life-threatening foetal malformations, although now a reality, still carries significant pre-term labour risk (Estes, Whitby, Lorenz et al. 1992). The rationale for foetal cleft repair stems from studies using large animal models. Researchers have shown that lip skin heals without scarring in surgically created clefts (Hedrick, Rice, Vander Wall et al. 1996). However, these defects are not equivalent to the complex deformity of bone, muscle and skin that occur in human oro-facial clefting. Moreover, simply repairing the lip in utero would not address the co-existing nasal deformity.

Postnatal surgery protocols vary with centre, surgeon and favoured surgical and non-surgical management regime. Primary lip and nose procedures have traditionally been undertaken after the age of 3 months for physiological reasons, since anaesthesia may be more exacting before this due to a persistence of foetal physiology. Earlier neonatal lip repair has been advocated on the grounds of psychological benefit for the parents in accepting their cleft child, however neonatal repair has not provided significantly better results, nor has parental psychological impact been shown to be an advantage over later repair (Slade, Emerson & Freedlander 1999). There are often trade-offs to be considered with respect to the timing of palate surgery and its compromising effect on favourable maxillary growth and normal speech production. Early palate closure means that there is less tissue available for repair, surgery is more difficult, wide clefts may break down and the potential for iatrogenic severe midface retrusion is greater. In contrast, early soft palate closure before the development of speech is preferable and results in better speech outcomes. Recent studies have shown, however, that closure of the hard and soft palate in a single stage before the age of one year can produce both good growth and good speech outcomes (Sandy, Williams, Mildinhall et al. 1998; Sommerlad 2003).

1.4.3 Orthopaedic interventions

In the UK, McNeil is credited with significant development of pre-surgical orthopaedic treatment. Early techniques concerned realignment of cleft alveolar processes, which was thought to favour normal facial and dental arch growth and enhance feeding. They were also seen as acting to stimulate the 'growth impulse', although this was never proven (Hathorn 2001).

Contemporary presurgical orthopaedic methods involve the use of lip-strapping and active or passive acrylic plates to reduce distortion and provide a more normal bony foundation for surgery, keep the tongue out of the cleft and thus encourage better palatal shelf angulation and lateral growth (Ball, DiBiase & Sommerlad 1995). The simple practice of lip-strapping with elastoplast or tape is used to guide the soft tissues of the cleft margins into better apposition pre-operatively. The theory is that it reduces tension across wide clefts, but protocols are often based on subjective impression, local experience and there is no real evidence-base to support the perceived benefits.

The effect of acrylic 'feeding plates' was investigated in a randomised controlled clinical trial and found that they did not help in establishing successful feeding patterns (Prahl, Kuijpers-Jagtman, Van't Hof et al. 2005). Another multi-centre randomised controlled trial (Dutchcleft) showed no persistence of effect of acrylic plates on maxillary cleft width beyond lip repair, and authors recommended discontinuation on the basis that the practice resulted in only short-term gain(Prahl, Kuijpers-Jagtman, Van't Hof et al. 2003). Moreover, pre-surgical orthopaedics has been shown to have little impact in reducing surgery time, whilst tripling medical costs (Severens, Prahl, Kuijpers-Jagtman et al. 1998). Despite the weight of evidence against the efficacy of pre-surgical orthopaedics, many centres routinely incorporate it as part of their management strategy e.g. Millard's POPLA method: pre-surgical orthopaedics, gingivoperioplasty and lip adhesion (Millard, Latham, Huifen et al. 1999). However, the most effective orthopaedic treatment is repair of the anatomical musculature of the lip.

Nasal stenting of various designs on the other hand, are gaining popularity. The nasal stent was originally designed as a post-surgical adjunct to maintain alar cartilage shape and prevent nostril stenosis (Chen & Noordhoff 1992). Observations that ear deformities could be corrected by molding immature auricular cartilages before the age of 6wks with long-lasting results, led to the development of nasal stents for use prior to correction of primary

nasal deformity in cleft neonates (Matsuo, Hirose, Otagiri et al. 1989). Since an intact nasal floor was needed to use this technique, an intra-oral plate with a nasal stent extension for use in complete clefts (Grayson, Cutting & Wood 1993; Grayson, Santiago, Brecht et al. 1999). There have been several published variations of this technique, but the principal remains the same (Bennun, Perandones, Sepliarsky et al. 1999; Liou, Subramanian, Chen et al. 2004).

Post-op dynamic nostril splints, which can be customised with silicon rubber retainers, have shown promising short-term results. The idea is to precisely mould the nasal cartilage and maintain the corrected nasal tip and alar contour, by opposing contraction caused by cartilage memory and scar healing (Yeow, Chen, Chen et al. 1999).

1.5 Facial morphology outcomes in childhood

Studies that report facial morphological outcomes after primary surgery in children are reviewed. Reports of immediate changes in soft tissue morphology with corrective primary surgery in infancy are uncommon. Studies of the effects of surgery on facial morphology describe the face as a whole or consider specific regions of the face e.g. soft tissue profile, nasal morphology, lip morphology, asymmetry. Studies tend to report facial appearance long after the primary surgical events, without reference to a pre-op baseline. There is a diversity of assessment methods employed, age groups studied and variable selection of control group. There are few studies of facial soft tissue structures away from the midline in surgically-managed cleft children.

1.5.1 Facial morphology & residual deformity in children

Farkas reported that among the residual deformities in 119 UCLP subjects aged 6 years to 29 years, the commonest was nostril floor width asymmetry , followed by columella height asymmetry, a flat nasal bridge, wide soft nose and a flat , poorly protrusive nasal tip (Farkas et al. 1993). Some, but not all of the residual deformities that are described in adulthood are present in childhood. Analysis of soft tissue profile from lateral cephalometric radiographs or profile photographs are common themes in studies cleft-repaired facial morphology, in early childhood.

1.5.1.1 Soft tissue profile from radiographic studies in children

Soft tissues profile measurements were evaluated from cephalometric radiographs of 53 22-month-old UCL and 55 UCLP infants (Hermann et al. 2000). A Tennison lip repair was performed in both groups of infants and an additional vomer flap procedure carried out in the UCLP group to close the anterior hard palate. UCLP infants had not yet had their hard palate repair. Upper face height in UCLP was similar to UCL children after lip surgery. Midline upper lip length in UCLP infants was reported as similar to UCL children and less protruding in relation to the facial plane and nose-chin line. The nose in infants with UCLP was found to be retruded and flatter and the chin was retrusive, which was claimed to reflect retrognathia. Nasolabial angle was not significantly different in UCL and UCLP children. The distance from the anterior pole of the eye to the orbital opening was increased in UCLP and this was attributed to a more retrusive lower orbital margin. After lip and anterior palate repair, the premaxilla was no longer protrusive, and asymmetry and deviation to the non-cleft side was reduced. Likewise, the nasal septum was also less deviated after surgery.

A study by Smahel & Mullerova (1986) is often cited in studies of craniofacial morphology in UCLP children and investigated the effects of Tennison lip repair on facial morphology, prior to palate repair at age 5 years in 30 UCLP males subjects, compared with 27 controls. Lateral and PA cephalometric radiographs were examined and found many of the deviations described by the authors in adults with UCLP were present prior to palatal repair in their 5 year old sample. Upper face height was reduced, the maxillary dentoalveolar process was retroclined, but the length of the maxilla was not reduced. The widths of the maxillary complex and nasal cavity were increased, however increased inter-orbital distance demonstrated by others, was not evident. In terms of soft tissue findings, the height of the upper lip was shorter than in controls, but was of normal thickness and prominence.

In the case of complete UCLP, maxillary growth attenuation is the cumulative effect of lip and palate surgery, and the interval between the two procedures is small. In Western societies, it has not been possible to study the effects of lip repair in this group in isolation, as palate surgery is undertaken only a few months later. Moreover, there has been no non-invasive imaging modality that could be utilised multiple times during the early years. In Czechoslovakia however, a study of facial morphology associated with lip repair performed at 6 months was conducted in twelve 5 year old male UCLP children, prior to

palatoplasty. Using the finite element shape analysis method to compare facial skeleton shape and size characteristics from lateral cephalograms between clefts and aged matched controls, findings were reported for the effects of lip repair in isolation. Overall, the size of the facial skeleton in UCLP prior to palatoplasty was normal, but significant shape differences could be localised to the maxillary complex and mandible. The nose, lips and dentoalveolar process were altered in both size and shape after lip repair, but before palate repair. The authors concluded that the effects of lip repair were characterised by retroclination of the maxillary incisors and increased lip thickness (Hammond, Smahel & Moss 1993).

A comparative study of the soft tissue profile on lateral cephalometric radiographs reported differences between a sample of 20 5 year old UCLP children from Manchester, compared to a sample of 257 UCLP children from Oslo (Mackay et al. 1994). Children had undergone closure of the lip and palate by age 5 years, in contrast to Smahel's study. Midface height (n-sn) was smaller and the upper lip more retrusive in the Manchester group. Lower face height was similar in both groups. The difficulties of evaluating the antero-posterior position of the maxilla before the eruption of the permanent incisors were highlighted, together with methodological differences in landmark definitions and soft tissue profile was concluded to be a better indicator of facial development in the younger child.

A comparison of soft tissue thickness and upper, middle and lower face heights in 75 UCLP aged 4-18 years, with age-matched controls demonstrated discrepancies between skeletal morphology and soft tissue morphology, as assessed by lateral radiograph (Sadowsky, Aduss & Pruzansky 1973). The soft tissue overlying pogonion tended to be significantly thicker than that overlying nasion at all ages after 5 years of age. A more protrusive soft tissue chin was evident, when compared to the underlying skeletal chin. Other findings included an increased upper lip length and decreased lower lip length in UCLP children, compared to non-cleft controls. The authors also reported that cleft children grew very much like their non-cleft peers, and there was no reported mid-face deficiency. However a mixture of treatment regimes had been carried out in the cleft sample and the conclusion that surgery did not affect midface growth was not supported by the data.

1.5.1.2 Lip and mouth outcomes

Some lip repairs are reputed to produce a better lip form than others in terms of scar, lip length, philtrum asymmetry or so-called 'whistling deformity'. Measurements of vertical lip length in anthropometry originate from nasal floor and extend to points on the lip and are thus influenced by both lip and lower nasal form (Farkas et al. 1993).

Vertical height of the medial and lateral lip were reported after lip adhesion in 37 UCLP and 6 UCLA infants aged 5 months (Vander Woude & Mulliken 1997). The effect of lip adhesion was measured with callipers at the time of lip repair, and compared to pre-lip adhesion evaluation. The authors claimed that the discrepancies between the cleft and non-cleft sides of the philtrum and lip decreased with lip adhesion, but these were so small (0.3-0.6mm) that they were unlikely to be of clinical significance. The errors associated with direct anthropometry alone would cast considerable doubt on the validity of these findings.

Cutting & Dayan (2003) examined symmetry in lip height and width after extended Mohler lip repair, in an indirect anthropometry study, in 49 UCL±P children. Measurements were derived from photographs with callipers and cleft and non-cleft side measurements compared. The sample were of different ages and follow-up was variable (1-13 months after surgery and at least 2 years after surgery) and no pre-op measurements were recorded. Photographs were of mixed media (traditional black & white and digital). Intercanthal line was used to determine reference lines for lip measurements and to standardise photographs. No differences were reported in cleft-repaired side and non-cleft sides and changes over time in lip height, but a difference of 8.6% was noted at 1-13 months between cleft-repaired side and non-cleft lip widths (philtral point to commisure), and a difference of 5.8% at 2 years or more post-op. In addition, lip width increased with time (mean increase 0.91mm), but this was unlikely to be of clinical significance. This study was limited by the mixed age nature of the study group and variable follow-up period making interpretation of these findings difficult. In relation to lip width measurements, the philtral peaks and lip commisures are not in the same plane on frontal photographs and so foreshortening of these dimensions may occur. Furthermore, any rotation from true AP position would affect the validity of measurements derived by anthropometry from a 2D photograph.

In a group of 5-year-old UCLP children, lip and mouth widths, post-Millard repair, were compared with controls. Profile and frontal photographic views were used to assess upper

and lower lip protrusion, relative to a nasion-pogonion baseline. Prior to maxillary collapse, the cleft children were found to have less protrusive lower lips and narrower mouth widths (Zhu, Senewiratne & Pigott 1994). This usefulness of this methodology in longitudinal studies was limited by the choice of measurement baseline, as variations in the soft tissues overlying the chin (pogonion) have been shown to be thicker relative to those overlying the root of the nose (nasion) after 5 years of age (Sadowsky et al. 1973).

The ratio of nose width to mouth width is regarded as important in the assessment of the cleft-affected face. If this ratio is significantly greater than normal, an individual may be considered potentially unattractive (Vegter et al. 1997). In primary lip repair, it is postulated that a combination of the presence of scar tissue from the repair and an underlying deficiency of tissue could contribute to increased lip pressure (Bardach, Bakowska, Dermott-Murray et al. 1984; Susami, Kamiyama, Uji et al. 1993). This could also produce a narrow mouth which would become more marked with age. Opinions differ as to whether mouth width on its own or in combination with lip protrusion are out of the ordinary in cleft subjects. Susami et al (1993) found a shorter upper lip length and normal mouth widths in 41 cleft lip children, compared to 54 controls aged 9-12 yrs in their examination of mouth shape and elasticity. A lack of lip tissue, leading to less elasticity and subsequent increased upper lip pressure was postulated as one of the factors causing maxillary retrusion in cleft lip and palate individuals in the longer.

1.5.1.3 Nasal Outcomes

It is the residual deformity of the nose that stigmatizes affected children, not that associated with the lip (Witt & Marsh 1997). The argument for early correction of nasal deformity centres around improved aesthetics, function and the avoidance of subsequent nasal revisions. There is evidence to suggest that improvements in nasal form obtained by primary nasal surgery persist into adulthood, however, residual nostril asymmetry resulting from uncorrected septal deviation is unlikely to improve with growth (McComb & Coghlan 1996).

Short-term morbidity is associated with nasal airway obstruction caused by oedema following primary surgery, and nostril stenosis can be problematic. Usually, infants quickly adapt to mouth breathing without incident. A more insidious problem is narrowing of the airway due to dysmorphology of the floor of the nose and a deviated nasal septum that accompanies all unilateral clefts. Up to 25% of cleft individuals have been shown to

have a diminished nasal airway in pressure flow studies (Warren, Hairfield, Dalston et al. 1988).

Each surgical approach that is developed is claimed to produce improvement in an aspect of nasal morphology. A comparative study of two UCLP groups repaired with either a triangular flap or the rotation advancement (Millard) technique found similar nasal deformities to be associated with both methods. A vertical asymmetry of the nasal skin envelope, depression of the cleft-side alar dome, a short columella on the cleft side, and hooding of the nostril apex were described in both groups. The main difference between the two surgical approaches was in the position of the alar base, which was laterally displaced in cases repaired by triangular flap methods, in contrast to a more normal position achieved in those repaired by Millard's method (Cutting, Bardach & Pang 1989).

Long term results of a controlled clinical trial comparing a group of 44 UCL(P) who had non-surgical naso-alveolar moulding (NAM) with a surgically-managed group of 47 UCL(P) were reported. Caliper measurements and facial casts were obtained for cleft infants at age 2 days, 15 days, 30 days, 3 months, 1 year and 6 years and 48 noncleft controls were added at age 6 years. Casts scanned with a laser-scanner and measured. Surgical management involved a Millard repair with Delaire muscle reconstruction. The study claimed a significant increase of columellar length with the use of the nasal stent. Growth and cosmetic results of the nose at 6-year follow-up revealed better nostril symmetry, with no alar cartilage collapse, in the patients who had used the pre-surgical nasal stent (Bennun et al. 1999).

Nostril shape parameters were investigated as possible predictors of nasal aesthetics for individuals with and without clefts, using a nasal cast and video-imaging method (Russell, Waldman, Tompson et al. 2001). Only nostril perimeter and bulkiness correlated with high ratings of aesthetics. Nostrils with symmetrical perimeters reflected better aesthetics, whilst nostril size, degree of elongation and nostril location did not show a correlation with aesthetic ratings. Authors reported that the characteristics of symmetrical nostril morphology had limited influence on nasal aesthetic judgements due to the lack of correlation between nostril shape parameters and subjective aesthetic ratings. It was suggested that the 3D morphology of the entire nasal structure had greater influence on impressions of desirable nasal appearance.

A 3D method to quantify pre-operative nasal architecture and evaluate immediate improvement, as well as growth effects, is essential. Early objective evaluation will help develop even better surgical and non-surgical management practices to ensure excellent results in the longer term.

1.6 Facial Asymmetry

A degree of mild asymmetry is common to all faces (Farkas & Cheung 1981). Even aesthetically pleasing faces have a significant degree of skeletal asymmetry (Ferrario, Sforza, Poggio et al. 1994b). Facial soft tissues can have a masking effect on underlying bony asymmetry (Peck, Peck & Kataja 1991; Shah & Joshi 1978). Asymmetry varies according to the region of the face in which it occurs - the upper face and orbital region have the lowest mean frequency of clinically apparent asymmetries and the lower facial third, the highest (Ferrario, Sforza, Ciusa et al. 2001). Local asymmetry tends to be reduced by the interaction of the different components of the craniofacial complex. A study of six sets of 9-15 year old North American triplets showed that over time, the pattern of asymmetry remained constant within individuals, and did not worsen with increase in facial dimensions (Mulick 1965). Burke & Healy also demonstrated this in a 9-year longitudinal stereophotogrammetry study of six sets of twins. Fluctuating asymmetry was not a function of age within individuals and was not related to twin zygosity or the adolescent growth spurt (Burke 1992).

1.6.1 Studies of Facial Asymmetry in children with clefts.

Asymmetry is important outcome measure in cleft lip and palate assessment. There is great interest in developing surgical and non-surgical methods, which produce better symmetry results, both immediately and in the longer term. 2-Dimensional and 3Dimensional methods have been applied to study local and generalised facial asymmetries in children and young adults. In the infant age group, direct anthropometric studies or indirect anthropometric studies of 2D photographs are more common. In terms of 3D studies, Ferrario and Ras lead the field, but even these prolific researchers have not examined young cleft children or infants.

Three-dimensional asymmetry was reported in a cross-sectional study of 49 UCLP subjects with a mean age of 7.4 years and 80 controls with a mean age of 9.2 years (Ras, Habets, van Ginkel et al. 1994b). Stereophotogrammetry was used to obtain 3D images and

asymmetry quantified relative to sagittal, transverse and vertical reference planes. UCLP individuals displayed more facial asymmetry in the vertical direction and more asymmetry in the region of the cleft, compared to controls. Males also had more asymmetry in the nose than females.

Longitudinal changes in facial asymmetry in cleft children were also reported by Ras, Habets, van Ginkel et al. (1995b). A mixed longitudinal 3D study of 33 children with UCLP aged from 4 - 12 years examined how asymmetry changed with growth and facial development, compared to 63 non-cleft individuals using stereophotogrammetry. Individuals were measured on two occasions. This study suggested that the only discernible increase in facial asymmetry with time was in the alar base in both cleft and non-cleft children. In the area related to the cleft, there were no changes in the degree of asymmetry over time. However, the control group was not age-matched for 50% of the children in the UCLP group.

In cleft children, nasal symmetry has been studied as a primary outcome measure of surgery. Nasal symmetry has also been the subject of comparative studies of different primary surgical regimes.

Nasal symmetry after Millard and Delaire repairs were retrospectively compared in 4-5 year old children, using direct anthropometric measurements with callipers and measurements from 3 photographic views (Horswell & Pospisil 1995). Symmetry was determined as the difference between anthropometric measurements on the cleft and non-cleft sides of the face. No reproducibility values or errors were reported. Millard group noses were slightly more asymmetric, had greater nasal tip deviation, were shorter, wider and had less anterior projection than noses in the Delaire group. The authors concluded that the Delaire nasolabial muscle reconstruction had a beneficial effect on nasolabial development.

Nasal symmetry was examined in 19 9-year-old UCLP children who had received a conventional Millard lip repair and nine who had undergone a modified Millard repair with columella lift and alar mobilisation were compared to 20 7-11 year old controls (Brusse, Van der Werff, Stevens et al. 1999). Coghlan's computer-assisted methods (Coghlan, Laitung & Pigott 1993) were used to assess nasal and nostril outlines from photographs. Areas of overlap and nostril axis angles were used to assess asymmetry. Significant differences could not be determined between the primary nasal correction group and the

non-nasal correction group, although the sample was small and nostril dimensions were very variable. Primary nasal correction was favoured in terms of better morbidity, because no revisions were performed in this group.

Nasal cartilage moulding by way of nasal stenting is reputed to produce a more symmetrical nasal shape, with the added benefit of correcting septal deviation (Maull, Grayson, Cutting et al. 1999). A retrospective 3D study of the effects of nasoalveolar moulding (NAM) on nasal form, compared10 cleft children who had undergone NAM with a group of 10 cleft infants who had undergone pre-surgical alveoular moulding without nasal stenting. The authors acknowledged that the two groups were not matched for age (mean age 4 years and 9 years, respectively). Mean asymmetry index for nasal shape was better in the group that had received NAM, however, nasal growth was not at a comparable stage with the 'control' group. The greatest asymmetries were identified in the nasal domes, followed by the alar base and columella in the control nose. Asymmetries in these regions were milder in the NAM group and improved nasal tip position and septal deviation were claimed additional benefits.

The relationships between chronological age, skeletal maturity and upper lip and nose asymmetry were the subject of a retrospective mixed cross-sectional investigation in 23 UCLP children and 34 controls between the ages of 6-16 years (Kyrkanides, Bellohusen & Subtelny 1996). Frontal photographs were the assessment media and asymmetry was determined relative to a defined midline axis. Results suggested nasal asymmetry decreased with time and maturity. Nasal tip asymmetry peaked with the pubertal growth spurt in both UCLP and controls, however, asymmetry improved with time. The deviation of the midpoint of the vermillion border was not significantly different from controls at any age, and did not alter with time or maturity.

Better maxillary symmetry has been associated with primary bone grafting - a procedure which was previously avoided because of reported effects on facial growth (Molsted, Dahl, Brattstrom et al. 1993). A multicentre study of 72 children with UCLP examined PA cephalometric radiographic variables and maxillary arch width using study casts. Asymmetry was assessed with reference to a constructed perpendicular midline which bisected a horizontal line connecting the lateral walls of the orbit. Results showed that in contrast to procedures involving primary vomerplasty and no alveolar involvement, primary bone grafting was associated with better anterior maxillary symmetry and a more symmetric dentoalveolar development at age 9 years.

1.6.2 Facial Asymmetry in infants

There are few studies which seek to evaluate asymmetry in the very youngest children with clefts, and which incorporate a pre-surgical assessment. Direct anthropometry & 2D photographs were used to compare two surgical methods:- the Millard repair and the le Mesurier repair (Amaratunga 1988). The authors devised the Cleft Lip Component Symmetry Index, which was calculated from 6 pairs of measurements in the lip and nose on the cleft and non-cleft sides, although the statistics were poorly described. A mixed cross-section of 100 infants with UCLP were examined prior to lip repair, 1 month and 1 year after surgery. In terms of in asymmetry outcome at 1 year post-op, the author could not rate one surgical method above another. The Millard repair produced better nostril height and Cupid's bow symmetry, whilst the LeMesurier repair produced a better vermillion and philtral edge symmetry. This study did not use standard anthropometric landmarks and no other published studies that have adopted this method.

The facial morphology of 10 infants with UCLP, who had a rotation advancement lip repair and 10 UCLP infants who had a triangular flap lip repair, was reported in Japan by Yamada, Mori, Minami et al. (2002a). A group of 151 control children were included at 4 months and at 1.5 years. Three-dimensional facial information was obtained using an optical scanner and an automatic landmark co-ordinate extraction technique. Cross-sectional results for pre-op, 2 weeks post op, 3 months post-op and 1.5 years post-op were presented. Despite the availability of 3D data, there was no analysis of 'shape' in the 3D sense and conclusions drawn about 'asymmetry' of nostril form and 'shape' of facial features were descriptive or based simply on linear differences between cleft and non-cleft sides in the vertical (z) direction only. Only limited findings were discussed. Asymmetry of the nostril was evident in both group after repair. Some differences were highlighted in the position of the philtral peaks and in the rotation advancement group it was suggested that the cleft side was higher after surgery, but asymmetry improved by 1.5 years. In the triangular repair group, the cleft side was lower than the non-cleft side at age 1.5 years.

Longitudinal studies of how asymmetry changes or develops in young children with clefts are lacking. This is especially of interest, as the anomaly itself, growth and the surgical intervention, will influence facial morphology. It is therefore necessary not only to document asymmetry in all ages of children with clefts over time, but also to compare developmental changes in facial asymmetry, to an appropriate reference norm. It is

apparent that there is a gap in the literature for a comprehensive study of 3D facial asymmetry in infancy.

1.7 Growth in Cleft Children

1.7.1 Body growth in Cleft Children

There are several reference sources for growth norms in children and this has resulted in a certain amount of confusion over which should be used. Of these, only the Gairdner-Pearson (Gairdner & Pearson 1971) and the UK90 references (Freeman, Cole, Chinn et al. 1995; Preece, Freeman & Cole 1996) cover the infancy period, namely, birth to 2 years. The Gairdner-Pearson references were based on measurements of bottle-fed babies in the 1970's and their validity in relation to contemporary infants was the subject of scrutiny in the mid-1990's. They were found to be unreliable and had major discrepancies with respect to growth curves and gender discrepancies when applied to contemporary infants (Wright, Corbett & Drewett 1996). The UK90 growth reference charts are based on more recent and larger samples at all ages and are considered a better fit with infants today (Savage, Reilly, Edwards et al. 1999). A consensus group of the Royal College of Paediatrics and Child Health now recommends them as the only usable reference charts for clinical purposes (Wright, Booth, Buckler et al. 2002). These are routinely used to monitor weight, height and head circumference in Child Health clinic and Paediatric departments throughout the UK. Children who fall below the 0.4^{th} percentile, or above the 97^{th} percentile, would be considered outside the normal range for age.

In cleft infants, there appear to be differences in the somatic characteristics between cleft types, which are evident from birth. (Becker, Svensson & Kallen 1998) reported the birth weight, body length, body mass index and head circumference characteristics for a large sample of infants with orofacial clefts, born between 1973 and 1992 in Sweden. The sample was divided into different cleft types and consisted of 865 CL, 1139 CLP, 811 CP and 121 Pierre Robin infants, which were compared with a control group of 2,031,140 non-cleft infants born in the same period. At birth, individuals with cleft lip and palate and those with isolated cleft palate were generally shorter and lighter than non-cleft individuals. Infants with cleft lip, on the other hand, had normal body dimensions at birth.

In addition to differences in birth weight and height in some cleft sub-groups, cleft children do not always conform to growth norms in unaffected children. A large growth study

conducted in Denmark involved 602 cleft infants born over a five-year period from 1976-1981. Infants had plaster casts of the upper jaw, 3 projection cephalometric radiographs, somatic measurements recorded and information concerning cleft type and severity taken from hospital charts (Jensen et al. 1988). The radiographic material collected in this study later formed the sample for (Hermann et al. 1999b; Hermann et al. 1999a; Hermann et al. 2000). Data were collected at age 2 months and at age 22 months and authors compared their data cross-sectionally with that from a PhD study of Danish infants and to North American anthropometric charts. The detail of how they defined the 'normal range' was not described. Differences were identified between cleft subgroups and between males and females. At age 2 months, male and female UCLP infants and UCL males were lighter than controls. Head circumference was similar to the control mean in UCL and UCLP infants of both genders. Cleft females in all subgroups were of normal height at age 2 months when compared to controls, whilst males with CLP were shorter than the average norm.

A much smaller study from the Netherlands compared the somatic growth, from birth to age 2.5 years, of 12 UCL, 20 UCLP and 13 isolated CP infants, with 50 controls (Felix-Schollaart, Hoeksma & Prahl-Andersen 1992). Body growth was shown to be similar to that of controls, except in the parameter of height. In contrast with findings in non-cleft children, UCLP infant girls tended to be taller than boys. Factors such as feeding difficulties and GIT upset between the ages of 12 and 18 months and airway infections between birth and 3 months were cited as having a negative impact on growth in weight and height. However, these were not sufficient to distinguish between cleft types in their sample, as their growth curves did not differ in a meaningful way from those of controls. Sample sizes in the sub-groups were small and this may have affected statistical power. Head circumference, on the other hand, a measure of brain growth, was considered more stable and less influenced by general health or nutritional factors. This study also showed that at all ages from birth to 2.5 years, boys had a larger head circumference than girls, but both males and females grew at the same rate.

A number of studies have reported poor weight gain in children with clefts. One such study in the UK examined 83 children with cleft lip and/or palate aged birth to 4 years (Lee, Nunn & Wright 1997). As a whole, the sample grew poorly initially, but later achieved expected weight and height by their last follow-up. With respect to differences between cleft types, children with isolated clefts of the secondary palate showed the most abnormal growth and those followed by those with combined cleft lip and palate clefts, although type

and severity of cleft were not significantly related to follow up height. Children with cleft lip appeared to be less affected. Authors concluded that although a cleft palate was associated with significant growth faltering in early infancy, these children experienced 'catch-up' growth following surgical repair, such that there was no residual growth deficit.

A large retrospective South African study considered the weight of 640 cleft children at the time of primary surgery, compared with data from 872 controls, obtained from a previous nutritional survey in Cape Town (Lazarus, Hudson, Fleming et al. 1999). The sample consisted of 143 CL, 203 CLP and 294 CP children. Cleft type and age at surgery were considered important factors that influenced the percentage of infants who were underweight. Underweight was defined as being less than 80% of expected weight for age, or below the 3rd percentile on standard North American (NCH) growth charts. Children with cleft palate, with or without additional cleft lip, were significantly more underweight than those with cleft lip alone.

Although early body growth may be impaired in cleft infants, there is no information on how this might relate to the development of the face. When evaluating facial dimensions in particular, the potential influence of body size differences is unknown.

1.7.2 Facial Growth

1.7.2.1 Normal facial growth during childhood

It desirable that surgery to correct cleft deformities should proceed in such a way as to cause minimal disruption of growth centres, and is undertaken preferably at times when growth is not occurring (Farkas, Posnick & Hreczko 1992).

Much of the literature relating to normal facial growth regulation is theoretical and the mechanisms and sites of growth centres in the face, best avoided in surgery, are as yet unknown. Changes in the shape and size of the facial skeleton occur in 3 ways:- cartilage conversion to bone, sutural growth and remodelling. The functional matrix theory has taken over from early theories that these changes were governed by skeletal and septal cartilage growth primarily. It is now widely held that facial shape changes occur in response to the sum of the functional demands imposed by local muscles, brain growth and airway requirements (Moss 1968; Ranly 1980).

A review of facial growth described the concept of balance between the skeletal elements of the face, cranial base and vault and cervical spine, and concomitant equilibrium between these elements and the facial soft tissues (Markus, Delaire & Smith 1992a; Markus et al. 1992b). Early facial growth is under different influences than that which occurs after 4 years, or with puberty. In the newborn and infant, the frontal bone advances rapidly, as does the maxilla beneath; under the influence of the actively growing brain, the cartilaginous nasal capsule and nasal septum. After about age 4 years, forward translation of the maxilla is variable and related to the degree of growth activity of the cartilaginous nasal capsule, nasal septum, and developing frontal sinus.

Growth of the eyes parallels brain growth and up to age 3-4 years and has an important influence in maxillary elongation, exerting an active vertical 'push'. There is also a 'pulling' effect from the muscle connections with the mandible, tongue and soft palate. The nasal septal cartilage is regarded as an important growth site for the nasomaxillary complex (Delaire & Precious 1986; Friede 1998; Friede 1978). The nasal septum is thought to contribute to the lowering of the anterior nasal spine and is one of the few sites of cartilage replacement that remain at the end of the first year of life. From birth to about 2 years of age, the maxilla also undergoes a 5-degree anterior rotation, which is accompanied by an upward movement of the nasal bones and the nose. Some authors believe that it is this rotation which is key in establishing normal or pathological facial balance (Markus & Delaire 1993; Markus et al. 1992b).

A recent contribution to the debate about the mechanisms of craniofacial growth was made by Takeshita, Sasaki, Publico et al. (2001). A finite element growth strain analysis of serial cephalometric radiographs of the face from 40 subjects aged 4 years to 18 years demonstrated greatest mean changes in shape and size in the anterior maxillary complex. This is at odds with the generally held belief that greatest change in the craniofacial growth occurs in the mandible. The authors suggested that their results identified a centre for craniofacial growth, sited in the anterior maxillary complex. This would appear to fit with other's findings in respect of nasal septal cartilage mediated growth (Delaire & Precious 1986).

The first longitudinal studies of 3D facial soft tissue development in early childhood were published as two case reports. These studies used stereophotogrammetry to record facial parameters. In this technique, posing error for linear dimensions was negligible as a

difference in position was recorded by a different form of the contour lines and so compensated automatically (Burke 1972).

One case report documented serial stereophotogrammetric changes in the facial soft tissues in a subject with mild facial asymmetry from age 3 weeks to 10 years (Burke 1983). The other described changes in the lips and mouth shape (Burke 1980). In the first 2 years mouth width increased, whereas mouth height decreased, altering mouth shape from 'rosebud-like' to a more adult form. Both studies concluded that growth of facial parameters was very rapid in the first year, less rapid in the second year. Subsequent changes were slow and irregular from the age of 3 to 9 years, accelerating at the age of 10. Although these studies were limited in terms of sample size, they represent the only application of stereophotogrammetry to record 3D facial dimensions in infancy.

1.7.2.2 Craniofacial growth in cleft individuals

Differences in facial growth in cleft individuals are variously attributed to congenital dysmorphology of the midface; intrinsic variations associated with the cleft; functional adaptation and surgical iatrogenesis. There is no doubt that in individuals with certain types of cleft, impaired growth of the mid-face is related to the effects of primary surgery in infancy (Mars & Houston 1990). Nevertheless, the extent to which contemporary surgical procedures affect maxillary growth is still a matter of dispute. There are controversies over which proportion of impairment can be attributed to lip surgery and which to palate closure. Moreover the contribution of surgical procedure, timing and surgical expertise to the picture is widely debated. Studies in unoperated Sri Lankan subjects over the age of 13 years have provided evidence for normal potential for growth in cleft individuals. Facial growth in clefts of the primary palate appears to be minimally affected by lip surgery in infancy, except in relation to dento-alveolar development and maxillary incisor retroclination (Mars & Houston 1990). However in stark contrast, the cumulative effects of surgery to repair a complete defect involving the lip *and* palate may become more manifest as an individual reaches maturity and disrupted maxillary translocation, possibly from the presence of scar tissue created around the circum-maxillary sutures, may result in a more concave profile (Mars 2001; Mars & Houston 1990; Ross 1987).

There are few longitudinal studies of craniofacial growth in infants encompassing the birth to age 2 years period. An early radiographic study of 51 UCLP, 27 BCLP and 62 CP

infants was conducted in the United States. PA cephalometric films were obtained for subjects at 1-3 months, 6 months and then yearly from age 1 year to age 6 years (Ishiguro et al. 1976). Lip repair was carried out at 3.5 months and palate repair at 14 months. Facial breadth and height measurements were reported cross-sectionally and growth curves were constructed for incremental change over time. Total amount of change from 3 months to 3 years and 3 years to 6 years were also reported. Data were compared to Bolton Standards at age 3 years and 6 years. Relevant findings included a tendency to hypertelorism in UCLP and CP infants which was not present after the age of 3 years, whilst this persisted to age 6 years in BCLP children. Nasal and maxillary breadths were wider in BCLP and UCLP than in CP in the first year, and only a slight growth change occurred up to age 6 years. Differences between cleft types occurred only in the midface, although direction of growth and asymmetry in the upper face was similar. The nasal aperture grew in an asymmetric fashion in UCLP children; the cleft side grew vertically, whilst the non-cleft side grew down and laterally. Maxillary width followed this pattern. As the nasal floor dimensions were wider to begin with on the cleft side, the authors concluded that this would be a favourable growth pattern, as nasal breadth would come to approximate normal. CP children had a more symmetrical pattern of nasal growth. Upper face height was increased in the cleft groups compared to normal, but was close to normal by age 6 years.

A craniofacial growth study in the early 1980's concerned 1 month old to 10 year old children with clefts (Jain & Krogman 1983). Serial Lateral and PA cephalometric films were evaluated using a similar methodology to that of Ishiguro et al. 64 UCLP, 32 BCLP and 78 CP subjects were examined, although no control group was included. Changes in growth stages were reported for infancy (birth to 1 year), early childhood (1-6 years) and mid-childhood (6-10 years), although data appear to have been compared in cross-section at each age. This study hypothesised that in UCLP children larger face widths, including maxillary and inter-orbital width in infancy may reflect pre-operative segmental translocation of the maxilla on the cleft side.

A study from the 1990's examined serial lateral and PA cephalometric films for a sample of 10 UCLA, 33 UCLP and 14 CP children (Han et al. 1995). Cross-sectional craniofacial measurements were reported at 4months (pre-op), 2 years, 4 years and 8 months. A group of 33 non-cleft controls was included at age 8 years only. Incremental growth changes were also reported from 4 months – 4 years, 4-8 years and total growth over the 8 year period. The authors found a wider upper facial width in UCLP infants which diminished

slightly following surgery, but was still evident at 8 years of age. In subjects who had palate repair, less forward growth of the maxilla was noted. Other findings in UCLP subjects included a larger vertical growth increment in the anterior maxilla, short posterior maxillary height, large intercondylar width, a large gonial angle and a slightly retruded mandible, which the authors suggested was compensation to a wider and more retroclined nasomaxillary complex.

The most comprehensive study of craniofacial growth in infants with UCL and UCLP is that of (Hermann et al. 1999a). This study was one of the series of studies which examined lateral, PA and axial view cephalometric radiographs in 2 month old and 22 month old Danish infants. This particular paper reported the growth changes for 49 UCLP and 45 UCL as controls. Growth was quantified as the displacement vectors of landmarks from initial examination to follow-up at 22 months. In general the amount and direction of craniofacial growth were similar in UCL and UCLP children, but the UCLP group displayed a more vertical growth pattern in the maxilla and mandible. Results showed that infants with UCLP had a 'normal' growth potential in all craniofacial regions except where surgical intervention had had a direct influence, and the authors concluded that UCLP was not, therefore, a craniofacial anomaly. A hypothesis was offered that the facial type in UCLP was special and may be a liability factor that could increase the likelyhood of developing a cleft lip and palate.

Soft tissues can mask underlying skeletal pathology, and information about facial soft tissue growth in young cleft infants is conspicuous by its absence from the literature.

1.7.2.3 Facial soft tissue growth in cleft infants and changes after surgery

Very little is published about growth of the facial soft tissue features in cleft children in the period from birth to about 3 years, and the early development of individual facial features. Delay of assessment til age 5 years, as is common when assessing facial skeletal development, may be too late to assess the aesthetic success of a particular lip or nasal repair procedure, since by then, a child will already have entered wider society and started school. A few studies have examined early effects of primary lip/nasal surgery or naso-alveolar moulding on growth of the nose and lip.

Growth of the upper lip after triangular flap (Skoog) repair was reported in a longitudinal study in the mid 1980's (Saunders, Malek & Karandy 1986). Fifty UCL children had serial measurements taken from frontal photographs and a clinical evaluation, although the raw data were not presented in the paper. Lip length was measured from the columella base to the philtral peak and recorded at the time of operation, at 3 months post-p, age 1 year and every 2 years for 4 years. Measurements error was not reported and information on the method of standardisation of photographs was omitted. Two groups were compared – one where the lip was designed short to accommodate lip growth and one where the lip was designed the same length as the non-cleft side. Results demonstrated that there was no change in lip configuration with growth, irrespective of whether the lip was of normal length too long, or too short on the repaired cleft side to begin with. This study also included a table of data for with 27 Millard repair lips, the majority of which were judged too short on the repaired side. This was more an observational finding, rather than one backed up by valid objective measurement.

Growth of the upper lip following modified rotation advancement repair in 56 complete and incomplete UCL subjects was recorded by direct anthropometry using callipers, in a Korean study (Lee 1999). No nasal correction was performed. Eleven subjects were lost to follow-up and no measurement errors were reported. Growth ratios of the cleft and non-cleft sides were calculated immediately after repair and at follow-up, which varied from 8 to 84 months. Philtrum height, lip length from philtral peak to commisure and nostril sill width (nostril floor width) were measured and it was reported that there were no differences in growth ratios of philtrum and lip dimensions on the cleft-repaired and non-cleft sides, but the nostril sill became wider on the repaired side. The authors concluded that lip vertical and horizontal dimensions determined at the time of rotation advancement repair were retained at follow-up.

Changes in nasal growth and symmetry after the use of naso-alveolar moulding (NAM) were reported in a 3-year study of 25 consecutive UCL+P cases in Taiwan (Liou et al. 2004). Cleft and non-cleft side measurements were derived from 1:1 basal view photographs with sliding callipers (0.1mm precision) and a high correlation was reported between observers and repeated measurements. Measurements were recorded before and after NAM, 1 week after lip repair, and yearly up to age 3 years. Lip repair was carried out by the rotation advancement method and no nasal dissection was performed. Anthropometric measurements included nostril height, nasal dome height, columella length, nostril width and nasal base width on the cleft and non-cleft sides. Growth was

evaluated by comparing measurements between each post-op interval. Asymmetry was evaluated by comparing cleft and non-cleft sides and change in asymmetry as the difference between post-op intervals. The authors noted improvement in nasal asymmetry with the use of NAM, and further improvement after surgery. A slight relapse in asymmetry at age 1 year was attributed to differential growth in the nostril and nasal dome height, columella length, nostril width and nasal base width. However no differences in growth of the cleft and non-cleft sides were noted from age 1 year to age 3 years.

A longitudinal study of the effects of primary nasal correction on nasal dimensions in Korea reported direct and indirect anthropometric findings for a randomized sample of 30 subjects who had conventional lip repair and 30 subjects who had primary nasal repair (Modified Tajima method), aged 3 months (Kim, Cha, Lee et al. 2004). Average follow-up was 78 months. Subjects were examined and nasal measurements recorded prior to surgical repair, at age 6 months and at 3 years, and cross-sectional comparisons were made with controls. The errors of the study method were not reported, but one operator recorded the measurements three times and the average was taken. Anthropometric measurements considered were soft nose width (al-al), columella length and nasal tip projection, although columella length was not recorded pre-operatively. The authors alluded to 'problems' in obtaining measurements from the younger children, but reported no interference with growth in nasal width, projection or columella length in the primary nasal surgery group, compared with controls. Nasal tip projection continued to grow up to age 3 years but the amount of columella growth was small.

All of these studies were limited by the 2D nature of the assessment media (photographs) and/or the drawbacks associated with direct and indirect anthropometry. These are discussed further in the next section.

The beneficial effects of surgery are detectable immediately after surgical repair and if there were any direct early deleterious effects from soft tissue primary surgery on nasolabial growth, we might be able to detect these during the first rapid growth phase of infancy. A first step towards broadening our understanding is to examine the facial morphology of infants with lip and palate clefts and determine how facial features improve with surgery and how they continue to develop as a child moves from infancy to early childhood.

1.8 Assessment of Facial Morphology

1.8.1 Rating Scales and Panel Assessments

Serial frontal and profile photographic views are collected as part of a cleft child's routine records. The photograph is a 2D representation of an individual and only a moderate correlation between the dentofacial appearance in photographs and live subjects has been demonstrated (Howells & Shaw 1985). Nonetheless, they have formed the basis for assessment of facial appearance in children and adults with oro-facial anomalies and have enabled the development of reliable scales for lay and professional panel rating of facial attractiveness and residual deformity (Asher-McDade et al. 1991; Assuncao 1992; Howells & Shaw 1985; Roberts-Harry, Hathorn & Stephens 1992; Tobiasen & Hiebert 1988; Tobiasen et al. 1991). The literature suggests that methods such as pooled panel assessment are a more reliable means of rating *overall* nasolabial deformity, rather than grading specific facial features (Morrant & Shaw 1996). In this respect, panel assessments are useful for comparison of outcomes in intra and inter-centre studies, but where outcomes differ, there is a need to identify precisely where the discrepancies lie. This in itself is a complex issue. Morrant & Shaw's study suggested that overall nasal appearance was strongly influenced by nostril shape, symmetry and the centrality of the nose in the face. However, shape, asymmetry and relative spatial position cannot be specifically measured by panel assessment methods. The situation is further complicated by a lack of correlation between those methods which can measure (2D photogrammetry) specific facial features and ratings of appearance (Russell et al. 2001; Vegter & Hage 2001). Only photogrammetric analysis of overall soft tissue profile has been shown to be reliable and associated with panel ratings of attractiveness (Bearn, Sandy & Shaw 2002).

If improved facial appearance in the cleft population is the aim, then it is appropriate to measure how much and where exactly improvement is required. Objective quantification of the shape, symmetry and relative spatial orientation of entire and component parts of the face offers the most informative means of assessing initial severity and efficacy of primary correction techniques in children with clefts (eg asymmetry, shape of nasal base, columella, philtrum shape). Acquiring suitable facial data from infants presents its own challenges.

1.8.2 Quantitative methods of acquiring facial information

A multitude of 2-Dimensional and 3-Dimensional techniques has been applied in the study of facial appearance and deformity in cleft individuals, but of the conventional techniques and newer 3D methods, few have been successfully applied in the study of infants. When designing a morphometric study, the mode of data acquisition must be determined first since it can have as great an effect on the results as the method of analysis.

1.8.3 Anthropometry in cleft assessment

Anthropometry, derived from the Greek '*anthropos*' meaning 'human' and *'metron*' meaning 'measure', is the biological science of measuring size, weight and proportions of the human body (Farkas 1994). Traditional anthropometry is the study of anatomical locations and dimensions. Craniofacial anthropometry evolved for use in the medical and surgical field, to aid assessment of deviation from normal, surgical planning and post-op evaluation. In the 1950s, a group from Charles University in Prague developed craniofacial anthropometry techniques. Perhaps the best known member of this group, LG Farkas, has made a substantial contribution to knowledge of craniofacial morphology in normal populations, as well as in numerous syndromes and congenital deformities in the head and neck, as evidenced by over 115 publications. A vast part of this work has been the creation of an extensive database of cross-sectional normative data for over 1500 white North Americans ranging from 1 year to 18 years of age. These studies formed a series of publications in which data for infants younger than 1 year were omitted, due to small sample sizes and a lack of co-operation (Farkas et al. 1992). Craniofacial anthropometry is considered the 'Gold standard' of morphometry and although available for over 35 years, it has been adopted by few researchers in the cleft field due to the time-consuming nature of data collection and the number of impracticalities involved. Farkas developed very detailed anthropometric measurements for pre-operative assessment of children with cleft lip (Farkas 1990). However, anthropometric measurements have proved a challenge to record directly in the infant, without the aid of sedation or general anaesthesia. This is evidenced by the fact that there is only one published study from the Farkas group involving a pre-operative assessment of facial morphology in 54 3-12 month old Czech UCLP and 27 BCLP infants (Farkas et al. 1993). Authors recorded only 3 out of the 21 measurements recommended by Farkas to fully document the nasal and lip deformity prior to repair. Descriptive terms were applied to characteristics of the cleft lip/ nose that were 'not measurable', such as shape of the nose, symmetry and nostril size and symmetry. Data for

the preoperative group were compared to the only norms available, developed by Figalova and Smahel for 3-6 month old Czech children (Figalova 1972), but the actual data used were not presented in the Farkas' paper. 'Post-operative' data were also presented, but for an entirely different combined group of subjects aged 6-29 years, of North American origin, and so conclusions relating to before and after surgery appearance must be regarded with caution.

The general criticisms levelled at anthropometry, relate to potential sources of error and shortcomings of the technique. Mistakes cannot be rectified after the measurement session and information cannot be extended, repeated or new landmarks added after data registration. Subjects must be of capable of tolerating lengthy measurement sessions as 57 anthroscopic (qualitative) signs and 132 separate linear and angular measurements have been derived to fully document the craniofacial complex. Some dimensions require repetition of measurements or maintenance of head position for several minutes and collection of data from young children has required several return visits and considerable effort on the part of the operator (Farkas 1990). Often described as a 'simple' technique, data are collected directly from subjects using tapes, callipers and various custom-designed anthropometric devices. This presents several potential sources of error that can result from inadequate training or improper instrument usage, distortion of soft tissues by instrument pressure. The magnitude of the measurement and the ease of landmark identification can also substantially affect the reliability of the measurements obtained (Ward & Jamison 1991). Ward's study showed that less than half of the common facial anthropometric direct measurements could be considered precise and reliable. Small measurements involving hard to define landmarks in the upper lip and nasal areas were least reliable. It follows that in young subjects i.e. babies, whose physical dimensions are small, this might call into question the integrity of other measurements remote from the cleft area. The lip and nasal regions are of particular importance in the assessment of cleft infants, yet it would appear that they are not amenable to reliable measurement by direct means. Even if it were a practical assessment method in cleft infants, anthropometry is essentially a 2-dimensional technique which does not permit 3D assessment of surface topology. Further more, facial shape cannot be quantified and to capture abnormality there is considerable measurement redundancy (Hurwitz et al. 1999).

1.8.4 Indirect Anthropometry

Indirect methods were devised to attempt to overcome the limitations of direct subject measurement, but still few have been adequately applied in the study of cleft infants. The fundamental problem is finding a suitable, non-invasive, non-hazardous way of creating a life-like representation the facial surface of a pre-cooperative subject.

1.8.4.1 Facial Casts

In some cleft units, recording of the pre-op deformity of the cleft lip and nose by alginate facial impression was a routine practice. In the field of research, plaster casts of the face and maxillary arch, or nose have been used as a proxy for live subjects. In neonates the facial impression technique is not without it's hazards and although it's advocates vigorously defend the safety of the technique, they detail the requirement for an experienced neonatologist to be in attendance and an emergency intubation tray set up (Bacher et al. 1998). This technique is used to assess the spatial relationship of the maxillary arch to the midface and is not intended for facial morphology assessment. Nasal casts have been assessed by 2D techniques such as video and computerised anthropometry (Russell, Waldman & Lee 2000; Russell et al. 2001), 3D morphometric techniques such as Moire fringe (Bacher et al. 1998) and other structured light scanning methods (Maull et al. 1999). Nasal morphology recorded by impression will be subject to compressive distortion, especially in the cleft infant preoperatively. A acceptable level of difference between clinical and casts measurements of 10% has been suggested (Russell et al. 2000), but where dimensions are small and 3D shape preservation is the aim, any level of physical distortion would be unacceptable.

1.8.4.2 Monoscopic photographic techniques

Photographs have been used to evaluate of several aspects of facial outcome in cleft research including soft tissue profile, lip protrusion and symmetry (Asher-McDade, Brattstrom, Dahl et al. 1992; Bearn et al. 2002; Brattstrom, McWilliam, Larson et al. 1992; Coghlan, Matthews & Pigott 1987; Kyrkanides et al. 1996; Laitung, Coghlan & Pigott 1993; Roberts-Harry, Evans & Hathorn 1991; Zhu et al. 1994). Photogrammetry is the derivation of quantitative measurements from static photographs. Whilst the convenience and simplicity of photographs has made them an attractive proposition for cleft assessment, their accuracy is subject to alterations in subject position, facial expression, magnification, lens and film types, as well as processing distortion errors. When compared with direct

clinical measurements only 4 out of 23 photograph-based measurements of the nose were found to reliable (Farkas, Bryson & Klotz 1980). Standardisation of techniques and computer-assisted assessment methods have improved the reliability of measurements from photographs (Coghlan et al. 1987; Laitung et al. 1993). Standard analysis software exists (NIH), which renders the information obtained from frontal and submental photographs amenable to objective analysis (Hurwitz et al. 1999; Russell et al. 2000; Russell et al. 2001). Nevertheless, the overriding drawback of the photograph remains; it provides only a 2 dimensional impression of the subject and no appreciation of depth is possible.

1.8.4.3 Traditional Cephalometry

A vast amount of what we know about craniofacial development has involved the use of cephalometric radiograph. In traditional cephalometry, the morphology of the hard and soft tissues and is registered, providing a permanent record that can be digitised for analysis. Sources of errors associated with identification of landmarks on cephalograms are well documented (Houston 1983; Houston, Maher, McElroy et al. 1986). Digitisation may introduce additional errors associated with resolution, accuracy and linearity (Eriksen & Solow 1991). Serial cephalograms can be used to identify areas and rate of growth-related change, but they are still a snap-shot of a dynamic structure. The same drawbacks in obtaining mensurate data from a 2D photograph exist in cephalometry. Measurements derived from landmarks on cephalograms, are not in same transverse plane, and so will be an estimation of their 'true' values.

1.8.4.4 Use of cephalometry for soft tissue evaluation

Where the soft tissue outline is readily visible on the cephalometric radiographs, skeletal and soft tissue components of deformity can be analysed together. However in younger children, the maxilla is difficult to evaluate with any degree of accuracy prior to eruption of the maxillary central incisor. The presence of a cleft compounds the problem of evaluating the antero-position of the maxilla. Moreover, it was possible to detect differences in treatment outcome at age 5 years, using soft tissue profile alone (Mackay et al. 1994). The desirability of analysing soft tissue profile was highlighted in the Eurocleft studies, which compared outcomes for children with UCLP in 6 European centres (Molsted, Asher-McDade, Brattstrom et al. 1992). Although regarded as a valuable outcome measure, it is difficult to justify serial radiographs that have a poor diagnostic

yield in young children, for this purpose, when other methods of soft tissue realisation are readily available.

Three Projection Infant Cephalometry, combining information from lateral, PA and axial radiographs was applied to the study of facial morphology in infants with UCL, UCLP and CP in a series of Danish studies. The technique was originally described by Kreiborg and co-workers (Kreiborg, Dahl & Prydsoe 1977). The analysis of information obtained from the three radiographic views evolved into a highly detailed, labour intensive method that, whilst enhancing skeletal assessment in young cleft infants, offered no advantages over conventional techniques for the evaluation of soft tissue outline. Soft tissues were only visible in lateral projections, and here, landmarks were reported as among the least reliable (Hermann, Jensen, Dahl et al. 2001). Spatial distribution of landmark placement errors ranged from 0.5-3mm. Despite this, only 2 measurements based on soft tissue landmarks were excluded from subsequent studies reporting application of the method in infants with UCL and UCLP aged 2 months to 22 months (Hermann et al. 1999b; Hermann et al. 1999a; Hermann et al. 2000). The fundamental problems with this technique were the requirement to sedate infants in order to immobilise them for imaging, the limitations of a 2D assessment and the controversial issue of subjecting young infants to radiation. The ethical constraints in particular limit this technique's usefulness as a research tool, and it is unlikely that ethical approval would be granted for a similar contemporary study.

1.8.4.5 Roentgen stereophotography

Methods to construct 3-Dimensional information from cephalograms taken in different planes have evolved to overcome some of the limitations of a 2D assessment. The three-dimensional cephalogram was proposed as a method for stereo-locating landmarks on conventional PA and lateral radiographic views (Bookstein, Grayson, Cutting et al. 1991; Cutting, Bookstein, Grayson et al. 1986; Grayson, Cutting, Bookstein et al. 1988). However, homologous landmark identification on lateral and PA views is an issue and soft tissue points in particular are not identifiable on both.

1.8.4.6 Reconstructed Computed Tomography (3D-CT)

CT-scanning registers cross sections of the face or body using rotating x-ray beams and detectors. Slices are then piled up by computer software and used to reconstruct 3D structures (Alder, Deahl & Matteson 1995). With appropriate thresholding, hard or soft

tissues can be rendered and 3D and 4D visualisation is possible. 3D co-ordinates can be derived from the reconstructed scans. Equipment expense and high dosage ionising radiation limit the use of this technique to hospital settings. Concerns about cumulative radiation dose make it unsuitable for longitudinal studies of facial morphology in young children, where repeat scans cannot be justified on medical grounds. The depth of slice and the degree of separation limit the resolution of the image obtained. Optimal image sharpness requires slices of 1.5mm, and 35 scans are needed to capture the average adult head, even with 3mm slice separation. This delivers a skin dose of 30mSieverts (Moss, Linney, Grindrod et al. 1987), although contemporary systems now have low dose options. Distortion from metallic objects and blurring of hard tissue margins can also affect the integrity of the information acquired.

3D-CT was used to define the spatial relationships of nasal features in 12 preoperative 3 month old Chinese ULCP children (Fisher et al. 1999). CT-scanning times can be lengthy and in this study, infants required sedation with chloral hydrate. Although the accuracy of hard tissue CT scans for the craniofacial region have been previously well documented (Waitzman, Posnick, Armstrong et al. 1992), soft tissue CT accuracy was assumed and not tested. 3D-CT scans have also been combined with facial surface rendering techniques such as laser scanning, photographs and most recently digital stereophotogrammetry to advance understanding of the relationship between the soft tissues of the face and underlying facial skeleton (Khambay, Nebel, Bowman et al. 2002; Moss et al. 1987; Xia, Wang, Samman et al. 2000).

1.9 3D Image sensing of facial soft tissues

The face of a child is a complex, pliant surface and so measuring techniques must ideally be non-contact in nature. 3D Image sensing is now a reality and a variety of optically based imaging techniques have been developed and applied to the study of the human face. These techniques allow an appreciation of depth, similar to the way that the human brain interprets information from two eyes and works out how far away from an object we are. A variety of off-the-shelf 3D data acquisition systems are commercially available and utilise the principle of triangulation (Siebert & Marshall 2000).

The main differences between systems are in the choice of baseline employed:

- Laser Scanning Triangulation (laser-camera baseline)
- Moiré Fringe Contouring and other Structured Light Techniques (projector-camera baseline)
- Stereophotogrammetry (camera-camera / camera-projector-camera baselines)

The systems that have been applied in the study of children, with and without clefts are discussed.

1.9.1 Laser Scanning

The laser triangulation technique involves projecting a stripe of Helium-Neon laser light onto the object of interest and viewing it from an offset camera. The surface of the object reflects laser light back towards a receiver, which measures the time (or phase difference), between transmission and reception in order to calculate depth. Deformations in the image of the light stripe correspond to the topography of the object under the stripe. The stripe is then scanned across the object, or the subject is rotated to register the facial surface. Accuracy is better when inanimate objects, rather than live subjects are scanned (Foong, Sandham, Ong et al. 1999). When compared to direct caliper measurement, one study found that only a third of measurements from facial laser scans were within 1.5mm of the caliper values (Aung, Ngim & Lee 1995). Nevertheless there has been much interest in laser systems for medical imaging (Coombes, Moss, Linney et al. 1991; Cutting, McCarthy & Karron 1988; McCance, Moss, Fright et al. 1997).

Laser scanning techniques have been applied to the study of older children with clefts in limited studies (Duffy, Noar, Evans et al. 2000; Nute & Moss 2000). Analysis of laser scans mainly involves measurements derived from landmarks selected manually and sometimes directly applied to the face, in hard to define areas such as the forehead, prior to image registration (Coward, Watson & Scott 1997). However, registration of scans in a common coordinate system of anatomical landmarks also allows 'averaged' faces to be constructed, which can be superimposed for comparison. Differences in radial distances from the centre of rotation (ie the scanner chair) to the facial model surfaces can also be represented by changes of colour, similar to the contours of a map (Duffy et al. 2000). Landmark independent analysis methods of surface decomposition have also been described (Coombes et al. 1991). Scanning takes a relatively long time (up to 10 seconds in some systems) and is subject to gross and intrinsic facial movement, making it impractical for application in the pre-cooperative child.

1.9.2 Structured Light Scanners

There are numerous structured light systems which employ the same principal (Bhatia, Vannier, Smith et al. 1994; Maull et al. 1999; Yamada, Sugahara, Mori et al. 1998). Patterns of light (grids, stripes, or elliptical patterns) are projected onto an object. Surface shapes are deduced from the distortions of the patterns on object's surface. When the relevant camera and projector geometry is known, depth can be inferred by triangulation.

1.9.2.1 Liquid Crystal range Finder (LCRF)

An example of a pattern projection system, the LCRF is capable of measuring >30000 points from the entire facial surface in 1 sec, to an accuracy of 0.5mm (Yamada et al. 1998). A liquid crystal shutter generates 8 striped light patterns, and a CCD camera captures the scene. An original programme was developed with this system to automatically identify landmarks using linear distances, 3D curvatures and discriminant analysis of red-green-blue data. The technique was applied to the study of Japanese non-cleft infants and mixed cross-sectional analysis of the facial morphology in infants with cleft lip and palate (Yamada et al. 2002b; Yamada et al. 2002a). A photorealistic facial surface rendering is not a feature of this system, but colour images can be binarised to extract vermillion border shape. Image registration requires scanning from two different views to capture the facial morphology in young children, which would render the process sensitive to alterations in facial expression and lip pose.

1.9.2.2 Moire and contour photography

These methods involve the projection of grids of known dimensions onto the face and an image is formed in the plane of a reference grid. Differences in height and depth will interfere with the grid, transforming it into a series of contour lines (Moire fringe contour patterns) which appear as dark and light stripes on the face. Analysis of these patterns then gives accurate descriptions of changes in depth and hence shapes. Early work involved manually evaluating contours from 2D photographs (Leivesley 1983), but it is only since the 1980s, with advances in computing and video technology, that fully automatic Moire-based systems have become available. In conventional Moire methods, computer software interprets the contours and produce 3D co-ordinates for surface points (Chen & Iizuka 1995). Measurements were only reliable if landmarks lay precisely on contour lines and estimation of depth was obtained by interpolation. Phase-stepping techniques have been

introduced to improve depth resolution and image ambiguities and automated systems of this type (NEL Auto-MATE, OrthoForm systems) are capable of producing very accurate depth data. Compared to other methods of depth map acquisition they are computationally expensive and do not provide a photo-realistic rendering of the face. The potential application of this technique to map the face was demonstrated using one cleft lip infant, but there have been no further published studies in the cleft literature since (Kawai, Natsume, Shibata et al. 1991).

1.9.2.3 Automated Infra-red Photogrammetry (3DFM, ELITE)

This method involves 2 CCD cameras and an infrared sensor. The system does not generate a visual representation of the face, but senses the positions of 2mm diameter markers applied to the subject's face. The main advocate of this system claims that it is independent of head posture and projection errors (Ferrario, Sforza, Guazzi et al. 1996; Ferrario et al. 1994a; Ferrario, Sforza, Poggio et al. 1996). It has been applied to collate Italian population norms and study asymmetry, sexual dimorphism and growth in adults and older children. The need for direct application of markers and lack of anatomical detail precludes the use of this system in the study of cleft infants.

1.9.3 Stereophotogrammetry

Stereophotogrammetry involves the analysis of spatial information from 2 or more images of an object, taken from different viewpoints to produce depth by triangulation. Stereophotogrammetry has a number of advantages over other 3D data acquisition systems. The technique uses the entire field of view to provide 3D information and has the advantage over methods such as laser scanning in that the object does not require scanning. Rapid, simultaneous capture of both sides of the face is possible, as only one image is required per camera, which is an advantage over the other structured light techniques (Ayoub, Siebert, Moos et al. 1998; Siebert & Marshall 2000).

Early techniques involved the use of stereo-metric cameras and plotting machines to manually produce contour maps and x, y, z co-ordinates. The techniques were applied to map facial contours, measure asymmetry and describe congenital facial deformity (Burke & Beard 1967; Burke 1971; Berkowitz & Cuzzi 1977). Camera and equipment simplification allowed wider application and increased accuracy of measurements. By the early 1980's contour maps of 2mm interval were possible, which were capable of

measuring 60-70mm depth (Burke, Banks, Beard et al. 1983). Advances in computing and camera technology saw the introduction of CCD cameras and automation of stereo-imaging systems (Deacon, Anthony, Bhatia et al. 1991).

Computerised systems have been applied to the study of growth and asymmetry in cleft children and adults (Ras, Habets, van Ginkel et al. 1994a; Ras et al. 1994b; Ras et al. 1995b), however, these systems did not permit colour photorealistic rendering of the facial surface. The most recent and most important advance in stereophotogrammetry concerns the evolution of digital stereophotogrammetry and in particular, the C3D™ system.

1.9.3.1 Digital stereophotogrammetry

The C3D™ system has been developed over 10 years by the former Turing Institute and Department of Computing Sciences at the University of Glasgow and now forms the backbone of research applications of the 3D-MATIC laboratory. White light speckle-texture projection overcomes difficulties in gaining reliable stereo-matches when a bland surface such as the face is imaged (Siebert & Marshall 2000). Digital cameras allow high resolution image capture and so enhance the accuracy of the measurements possible. A colour overlay presents a life-like virtual 3D model of the face to the clinician, and facilitates anatomical landmark identification. In recent years, digital stereo-photogrammetry has been applied variously in studies of the face. The C3D system was used to assess facial changes after maxillofacial surgery (Ayoub, Wray, Moos et al. 1996; Hajeer, Ayoub, Millett et al. 2002) and to investigate repeatability of facial expression in adults (Johnston, Millett, Ayoub et al. 2003). It has also been recommended as a stimulus media for the clinical assessment of residual facial deformity in cleft-repaired adults (Al-Omari, Millett, Ayoub et al. 2003), and for archiving orthodontic study models (Ayoub, Wray, Moos et al. 1997). Most recently, the C3D system has been successfully applied in a case-control study of 3-year-old cleft children (Garrahy 2002; Garrahy, Millett & Ayoub 2005) and in the longitudinal study of normal facial growth of infants aged 3 months to 2 years (White 2005).

1.10 Facial Shape Analysis

Infant cleft facial morphology reflects deformation associated with cleft embryogenesis and adaptative responses to altered function as a result of the presence of a cleft. Morphology, or form, is viewed as a combination of size (dimension) and shape. Size is a quantitative assessment of the magnitude of a parameter e.g. a measurement. Shape refers to the mathematical description of an object, independent of its orientation, relation to reference planes and dimensions (Kendall 1984).

1.10.1 Landmarks

The shape of a face can be described by 3D co-ordinates of anatomically meaningful landmarks. Quantitative analysis of shape relies on the property of correspondence between configurations and this allows facial morphology to be described in terms of equivalent points on the face of each individual.

Landmarks fall into 3 categories (Bookstein et al. 1991):
Type I landmarks e.g. the meeting of skull sutures, meeting of skin creases forming the corner of the eye, etc.
Type II landmarks are defined by geometric surface properties (eg, tooth tip).
Type III landmarks have at least one deficient co-ordinate ie. they can be reliably located on an outline or surface, but not to a very specific location. The tip of a rounded bump would be an example of this.

In terms of homology, most confidence is placed in Type I landmarks, and least in Type III. When describing a complex shape such as the face, a combination of landmark types is commonly required, and so efforts must be made to standardise landmark selection and minimise the 'human error' in landmark identification procedures (O'Higgins & Jones 1998).

1.10.2 Measuring Morphology

1.10.2.1 Traditional morphometrics

Morphometrics comes from the Greek 'Morph' meaning 'shape' and 'metron' meaning 'measurement'. There are various schools of morphometrics, which are characterised by the particular aspect of biological 'form' they measure, and the kinds of biostatistical questions asked. There are two main ways in which landmarks are used to provide information about

form. Measurements between landmarks (inter-landmark distance) provide size information, but do not permit conclusions to be drawn about the shape of an object. Anthropometry is an example of this and describes facial characteristics through linear and angular measurements which are used to define ratios and proportions. Knowledge of facial dimensions is clinically useful, but by definition, the 'shape' of a face cannot be derived from size-based measurements, since this takes no account of the relationship of these measurements to each other.

1.10.2.2 Geometric morphometrics

Geometric morphometrics is a collection of approaches for statistical shape analysis of 3D co-ordinate data. This class of morphometric methods preserve complete information about the relative spatial arrangements of landmarks throughout an analysis (Dryden & Mardia 1998). In comparing shapes, the key idea is to define a measure, which is a distance (the Procrustes distance) between a pair of optimally superimposed shapes. This is calculated as the square root of the sum of the squared differences in the positions of corresponding landmarks in the aligned shape configurations (Dryden & Mardia, 1998) Procrustes methods are commonly used to superimpose configurations by a 'best-fit' method i.e. until the sum of the squared distances between matched landmarks is minimised (Bookstein 1991; Bookstein 1997). The method of aligning two configurations is known as full ordinary Procrustes alignment where configurations are translated, rotated and scaled, and partial ordinary Procrustes alignment where scaling is omitted. Generalised Procrustes analysis is performed where more than two configurations are aligned. Average shape (Procrustes mean) is the least summed squared Procrustes distance to all configurations in a sample. Procrustes distances can used quantify individual shape abnormality by comparison with this 'control' mean shape (Dryden & Mardia 1998).

A single point represents each registered landmark configuration in an abstract 'shape space' of lower dimensionality known commonly as Kendall's shape space, after the man who first described it (Kendall 1984). Shape space does not have the same linear (Euclidean) properties assumed by most statistical techniques and usually data is extracted from the aligned objects that can be treated like linear data i.e. co-ordinates in a tangent space to the shape space. The scatter of points representing individual configurations in shape space are projected into a linearized version of shape space called tangent space. They are now represented as co-ordinates on a plane and conventional statistical methods and multivariate methods such as Principal components analysis can be applied to study

shape variation (O'Higgins & Jones 1998). More recently, researchers have demonstrated that measurements can be made directly in the shape space and simply re-interpreted in a more familiar Euclidean context (Le & Kume 2000).

1.10.3 Measuring Facial Asymmetry

The property of asymmetry of a face is a feature of its shape. The cleft literature has many reports of qualitative as well as quantitative assessments of asymmetry. Qualitative evaluations of asymmetry such as those obtained by panel assessment of 2D photos are subjective (Cussons, Murison, Fernandez et al. 1993; Roberts-Harry et al. 1991). Asymmetry is a 3D phenomenon, and without a quantitative component, a precise evaluation of the magnitude and nature of the asymmetry is not possible. Where 2D data are considered, accurate assessment of the sagittal component of asymmetry is problematic, as it is perpendicular to the plane of the photo or radiograph. Data integrity is also influenced by standardisation of recording of views and images must be taken parallel with the sagittal component of asymmetry.

There are as many methods to describe and quantify asymmetry in a meaningful way, as there are ways to record facial data. The choice ranges from measurements of asymmetry in the horizontal and vertical aspects from frontal photos or PA cephs, to complex calculations of 'centres of gravity' based on 3D co-ordinate systems, or mathematical surface decomposition.

1.10.3.1 2D Asymmetry Assessment Methods

Asymmetry assessments based on the evaluation of directly or indirectly measured distances (Farkas & Cheung 1981; Molsted & Dahl 1990; Mulick 1965), angles (Roberts-Harry et al. 1991), surfaces (Coghlan et al. 1987; Shah & Joshi 1978) or contours (Burke & Healy 1993) on the right and left sides of the face, have advantages and disadvantages. Whilst they are simple to carry out, these methods do not take into account the inter-relationships between the landmarks defining facial features and multiple measurements are required to characterise a facial structure. One may wrongly assume symmetry in an asymmetric case if distances or angles measured are the same size on both sides of the face. This was demonstrated in a study which examined he causes of measurement asymmetry at the level of landmarks in syndromic and non-syndromic individuals (Shaner, Peterson, Beattie et al. 2000). No predictable relationship was found between significant

findings in landmark 3D co-ordinates and measurements between landmarks. In particular, statistical differences in measurements did not infer significant differences in the positions of the actual landmarks between the right and left sides of the face. Various indices have been developed to attempt to overcome some of these limitations (Amaratunga 1988; Chebib & Chamma 1981; Farkas & Cheung 1981). Nevertheless, fundamental methodological variations and the sheer number of potential indices limit their use and make direct inter-study comparisons difficult.

Publicly available NIH Image software was used to assess nostril shape and asymmetry including nostril perimeter, anisometry and bulkiness characteristics, of a group of older individuals with repaired unilateral clefts, aged 12-22 years and age-matched controls. Nostril asymmetry was noted in both groups, but it was of greater magnitude in the cleft group. Authors concluded that the presence of a repaired cleft resulted in a more elliptical non-cleft side nostril and greater nostril shape asymmetry (Russell et al. 2000).

1.10.3.2 3D Asymmetry Methods

A 3D co-ordinate system is prerequisite for the accurate comprehension of facial asymmetry. Analysis techniques were described for 3D facial asymmetry data acquired by laser-scanning (Moss, Coombes, Linney et al. 1991). The first method involved identification of landmarks on laser scans and then joining triplets of landmarks to create triangles. The areas of these triangles could be calculated and compared across a defined symmetry midline. Areas could then be plotted graphically and asymmetries between right and left sides of the face could be visualised. This method, whilst detailed, relied on the accuracy of landmark placement. The other method described was that of surface decomposition (Coombes et al. 1991). The facial surface was divided into components with common properties. The signs of Gaussian & mean curvatures were used to classify surface points into one of 8 surface types. Major facial features are composed of the same surface types; however their size and shape will differ from individual to individual. Changes in shape were assessed by grouping pixels of the same surface type together to form 'patches', the features of which were then compared (i.e. area, centre of gravity, length & width etc). The accuracy of measuring orientation and size of surface patch projection was dependent on accuracy of alignment of 3D surfaces. The difference between patches due to registration misalignment was stated to be small compared to the large overall changes seen before and after surgery. This method is useful for within

individual assessments, but might prove difficult to interpret when applied to multiple individuals.

A stereophotogrammetry-based method of assessing asymmetry in 3 planes of space was been described and applied to cleft children (Ras, Habets, van Ginkel et al. 1995a; Ras et al. 1994b). It involved finding the minimal spatial movement, in millimetres, required to attain a symmetrical arrangement of landmarks, relative to a defined symmetry plane. Ras showed clearly that evaluations of asymmetry based on this method would be influenced by choice of reference landmarks and symmetry plane (Ras et al. 1995a). Methods that inadvertently select baseline points that are in themselves asymmetric may produce erroneous results. The choice of asymmetric tragion landmarks as the origin for facial measurements in a study of Caucasian 6-18 year olds was criticised by the authors as contributing to the high level of asymmetry seen (Farkas & Cheung 1981). Asymmetry of tragion landmarks was later confirmed by others (Ferrario et al. 2001; Ferrario et al. 1994b).

The Ras method used the principal that a line drawn between the outer corners of the eyes (exocanthions) is most suitable to define a 'symmetry plane' perpendicular to this line. Others studies agree and have shown that bony landmarks situated at the lateral borders of the orbits are least affected by asymmetries (Farkas & Cheung 1981; Peck et al. 1991). Whilst this may be true for anthropometric or PA cephalogram derived measurements, it does not necessarily translate to 3D methods. Data gathered by different techniques may yield different results (Shaner, Bamforth, Peterson et al. 1998). As an example; Ferrario's 3D study using data derived from hand-digitised facial landmarks showed that the inner corners of the eyes (endocanthions) were the least asymmetric soft tissue landmarks in normal subjects (Ferrario et al. 2001).

In the studies by Ras et al, measuring and positioning error was reported as having little bearing on results, since exocanthion landmarks were separated by a relatively large distance and this would reduce the effect of small errors (Ras et al. 1995a). In contrast, Ferrario noted that the more distant a landmarks' position, relative to an asymmetry plane, the more likely it was to be asymmetric (Ferrario et al. 2001).

Euclidean Distance Matrix Analysis (EDMA) has been applied to the measurement of facial asymmetry in both 2D and 3D contexts (Ferrario, Sforza, Miani, Jr. et al. 1995; McIntyre & Mossey 2002; O'Grady & Antonyshyn 1999). EDMA compares the form of

the two sides of the face, defined by corresponding landmarks. This technique provides an objective measurement of shape difference that does not depend on a remote frame of reference, or superimposition planes. Both sides of the face are compared by calculating a matrix of all possible ratios of corresponding Euclidean distances measured within each side. This represents the shape of one half of the face and a second matrix on the opposite side. A difference matrix is calculated by dividing the values in the second hemiface matrix by those on the first side. If all of the ratios were equal to 1 then there is no shape difference between sides. If the ratios are less than 1, then the second shape is smaller than the first and the converse is true if the ratios are greater than 1.The technique also separates contributions of size and shape, and localises the sites of major variation by suggesting which landmarks are more involved in the form difference (Lele & Richtsmeier 1991). The disadvantage of this method is that the actual geometry information of an object is lost.

1.10.3.3 3D Asymmetry of facial shape in cleft infants

A fundamental consideration in assessing asymmetry in cleft-affected individuals is the observation that in young children with UCLP, increased inter-orbital width is a recognised part of the facial deformity (Garrahy 2002; Yamada et al. 2002a; Zemann et al. 2002). In 3 month old UCLP infants, variable translocation of the infra-orbital rim was demonstrated (Zemann et al. 2002). This would mean that methods that depend on eye landmarks to define symmetry planes may not be suitable for the study of asymmetry this group.

Despite growing numbers of methods to capture 3D facial morphology, there are few geometric morphometric or 'shape' analyses, Furthermore, there are few who have applied these methods to the study of cleft facial deformity in young children. Asymmetries in the ala, nostril and Cupid's bow were reported in UCLP infants (Yamada et al. 2002b; Yamada et al. 2002a). Although data collected consisted of 3D co-ordinates, analysis was limited to linear and angular inter-landmark measurements and asymmetry was assessed by comparing linear dimensions on the cleft and non-cleft sides of the face, and this could not be considered an analysis of facial shape.

A 3D method to assess nasal surface asymmetry was applied to compare nasal form after pre-surgical use of nasal stenting at age 4.5 years (Maull et al. 1999). The method involved nasal impressions and then scanning of nasal casts with a structured light scanner (Virtuoso shape Camera) in 4 directions. 3D models were built and nasal asymmetry evaluated using Procrustes techniques to register meshes. Unfortunately, there was no information on

reproducibility or system error, but this technique offered the advantage that areas of asymmetry could be visualised as a colour-coded display, and 'index scores' were generated, which allowed statistical comparison.

Procrustes shape manifold-based techniques for investigating symmetry within an object (object symmetry) and symmetry between two corresponding objects (matching symmetry) have been recently described (Mardia, Bookstein & Moreton 2000). Bock and Bowman developed an Asymmetry Score based on this work, which quantified the level of asymmetry in individual configurations of landmarks representing the face (Bock & Bowman 2005). An early version of this method was used to assess asymmetry in 3-year-old surgically managed cleft children and non-cleft children (Garrahy, 2003) and those undergoing maxillo-facial surgery (Hajeer, Ayoub & Millett 2004). This method has the advantage that it is independent of symmetry planes and size differences between and within individuals. It was the method of choice for the study of facial asymmetry in cleft infants in this study.

1.11 Summary

- Cleft lip and /or palate is the most common abnormality in the craniofacial region. There are fewer UCL and UCLP children born in Scotland each year, than in other parts of the UK. In Scotland, the ratio of cleft lip and/or palate to isolated cleft palate is 1:1. This is at odds with the UK in general or other foreign centres, where a ratio of 2:1 is more commonly reported.

- An integral part of cleft rehabilitation is the need to provide children with a facial appearance more like their peers, as early in their development as possible and to minimise the number of subsequent revisions, in order that they and their families can better accept their condition. Successful primary procedures are highly desirable and likely to reduce the duration and complexity of ancillary procedures such as speech therapy, orthodontics and maxillary osteotomy.

- A wide variety of deformity arises within the spectrum of the cleft lip/palate abnormality. Qualitative and quantitative differences in the soft tissues surrounding the cleft account for the multitude of varieties of presentation of cleft facial morphology. The assessment and documentation of these differences prior to operation is of

paramount importance, yet traditional methods cannot capture the three-dimensional nature of soft tissue abnormality.

- Initial cleft severity is often cited as a compounding factor in residual facial deformity after surgery. Attempts to separate the influence of the initial defect from the effects of treatment regimes have proved unsatisfactory. There is a need to develop objective 3D measures of cleft severity in soft tissue facial features.

- Little is known about the potential influence of the initial severity of a cleft on the morphological development of soft tissues of the face. There has been no 3D analysis of soft tissue morphology, which has quantified the degree of the initial cleft deformity in Caucasian infants. Furthermore, the influence of initial cleft severity on facial shape outcomes has not been investigated.

- There are no contemporary quantitative studies of facial soft tissue morphology in UCL infants. It has not been established that infants with UCL have a 'less severe' defect in terms of disruption of the facial soft tissues. It has also not been proven that UCL children have better facial soft tissue appearance outcomes than UCLP children.

- With increasing sophistication of non-invasive 3D imaging systems, there is no longer the need to rely on data derived from hard-tissue imaging modality archives when assessing facial soft tissue morphology or residual deformity.

- Digital Colour Stereophotogrammetry (C3D™) has a number of advantages over other 3D data acquisition systems. It has not been applied in the assessment of cleft deformity in infants prior to and following primary surgery.

- Although early body growth may be impaired in cleft infants, there is no information on how this might relate to the early development of the face.

- Linear dimensions are amenable to measurement, and are the basis of many assessments of cleft and non-cleft facial morphology. Knowledge of facial dimensions is clinically useful, but by definition, the 'shape' of a face cannot be derived from size-based measurements, since this takes no account of the relationship of these measurements to each other.

- There are no comparable 3-Dimensional outcome measures of facial shape or specific facial feature shape in the infant cleft population. Linear measurements are influenced by variation in subject age and size, whilst Procrustes methods allow comparison of 3D shape without the clouding effects of size differences.

- Asymmetry is an important outcome measure in cleft lip and palate assessment. The location and magnitude of 3D asymmetry in the infant cleft face prior to repair, and the improvement with surgical intervention and subsequent facial development is unknown.

- Rapid facial growth occurs during the period in which primary corrective surgery for clefts is undertaken. Facial soft tissue development in infancy is largely undocumented in Caucasian children with UCL and UCLP. There is a lack of comprehensive, longitudinal 3D-assessments of facial soft tissue growth in cleft infants.

1.12 Aims

The aims of this study are:

1. To determine the applicability of computerised stereophotogrammetry (C3D) for three-dimensional assessment of facial morphology of infants with unilateral cleft lip (UCL) and unilateral cleft lip and palate (UCLP).

2. To characterise pre-surgical facial morphology in 3 dimensions and determine statistically significant differences between infants with UCL and UCLP.

3. To determine the relationship between facial dimensions and body weight, length and head circumference prior to surgery and to correlate facial and body growth in UCL and UCLP infants.

4. To describe and measure statistically significant changes in facial morphology of each individual following primary surgery, and with growth and determine statistically significant differences between those with UCL and UCLP.

5. To develop measures of initial severity of soft tissue deformity and apply to UCL and UCLP.

6. To quantify the degree of residual shape deformity in UCL and UCLP after surgical repair, with reference to non-cleft controls.

7. To determine the relationship between initial cleft severity and outcome at 2 years of age.

2 3D Technique Development Studies

2.1 Facial Imaging Equipment

2.1.1 The C3D™ imaging system

The C3D™ digital stereophotogrammetry system configured for clinical facial imaging consisted of two camera pods fixed to a rigid frame, which was set-up on either side of a dental chair in a V-shape (Fig 2.1).

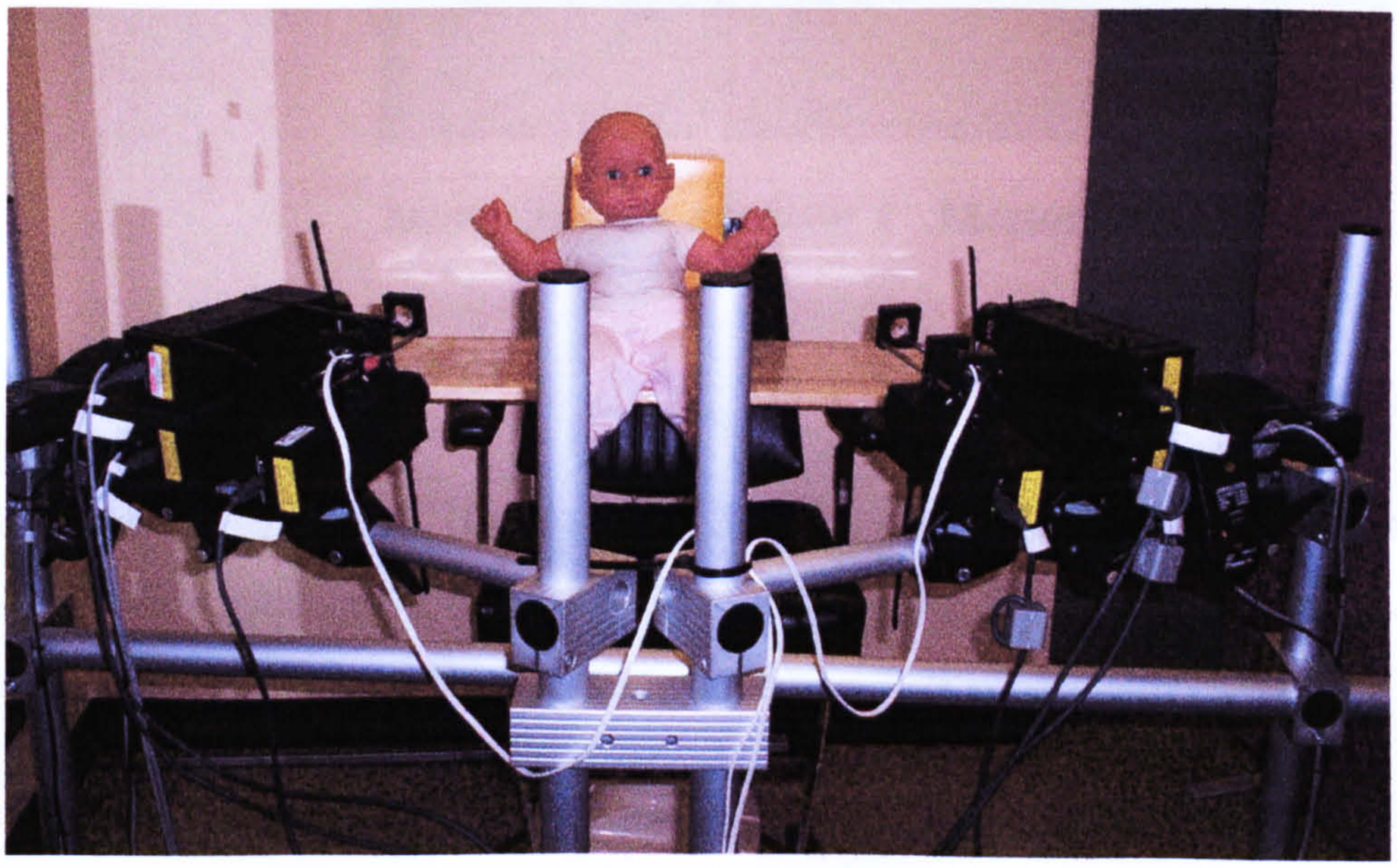


Figure 2.1 V-shaped camera rig setup with doll on dental chair for illustration

The prototype system used in this investigation comprised of several components manufactured specifically for the project. On each pod, two monochrome cameras served to form a stereo baseline. These were synchronized to capture images illuminated by a customised texture-flash, which projected a random speckle pattern onto the face. A third camera captured the natural colour-photographic appearance of the subject under normal white-light flash (Fig 2.2).

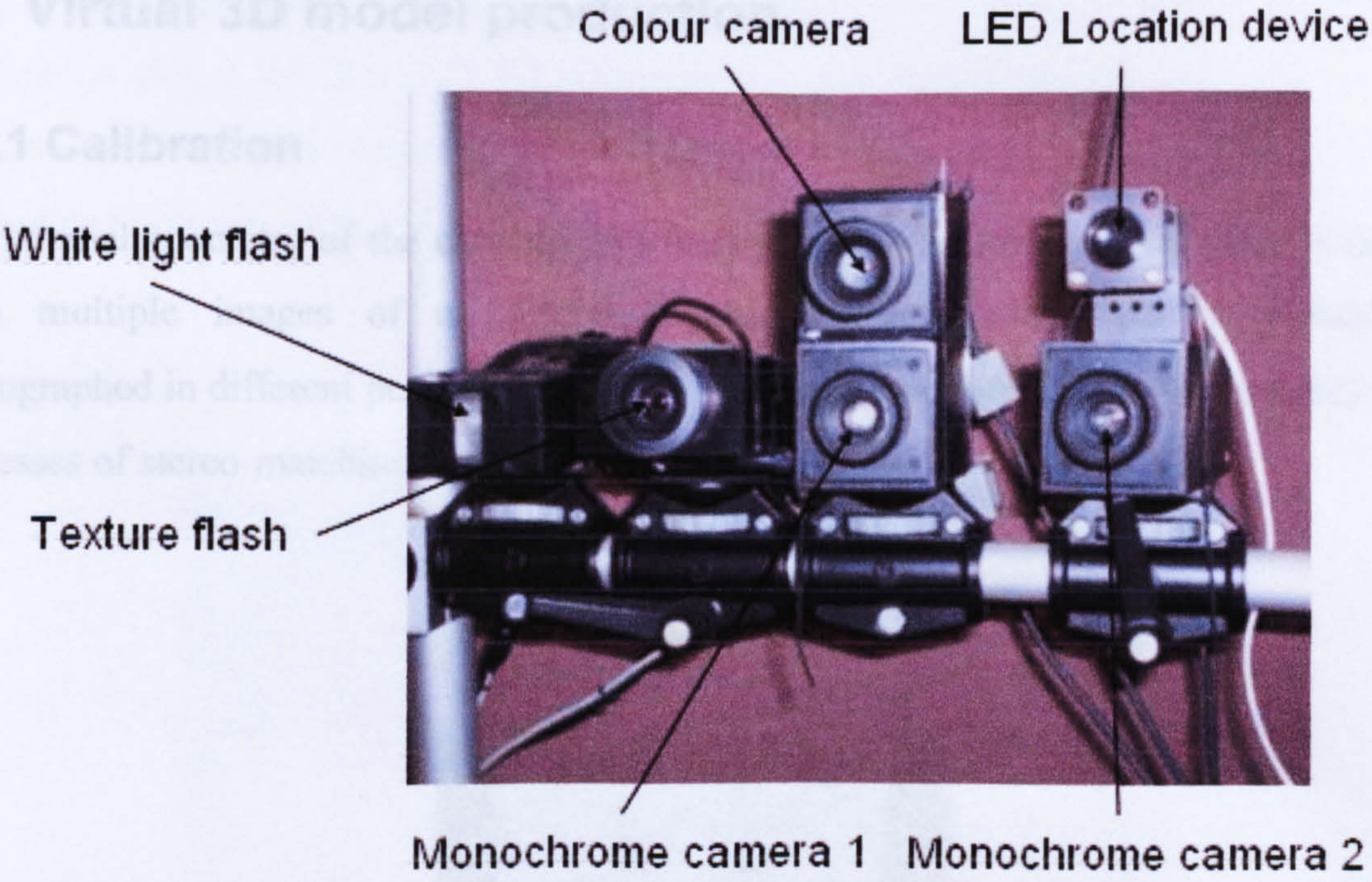


Figure 2.2 Camera pod components

Exposure of the cameras took 10ms, with a 30ms gap between monochrome and colour exposures, giving a total of 50 milliseconds to capture the full face. Cameras and flashes were linked via a USB hub with an un-interruptible power supply to a Dell™ Intel Pentium III™ computer (Windows 98™ operation system) (Fig 2.3).

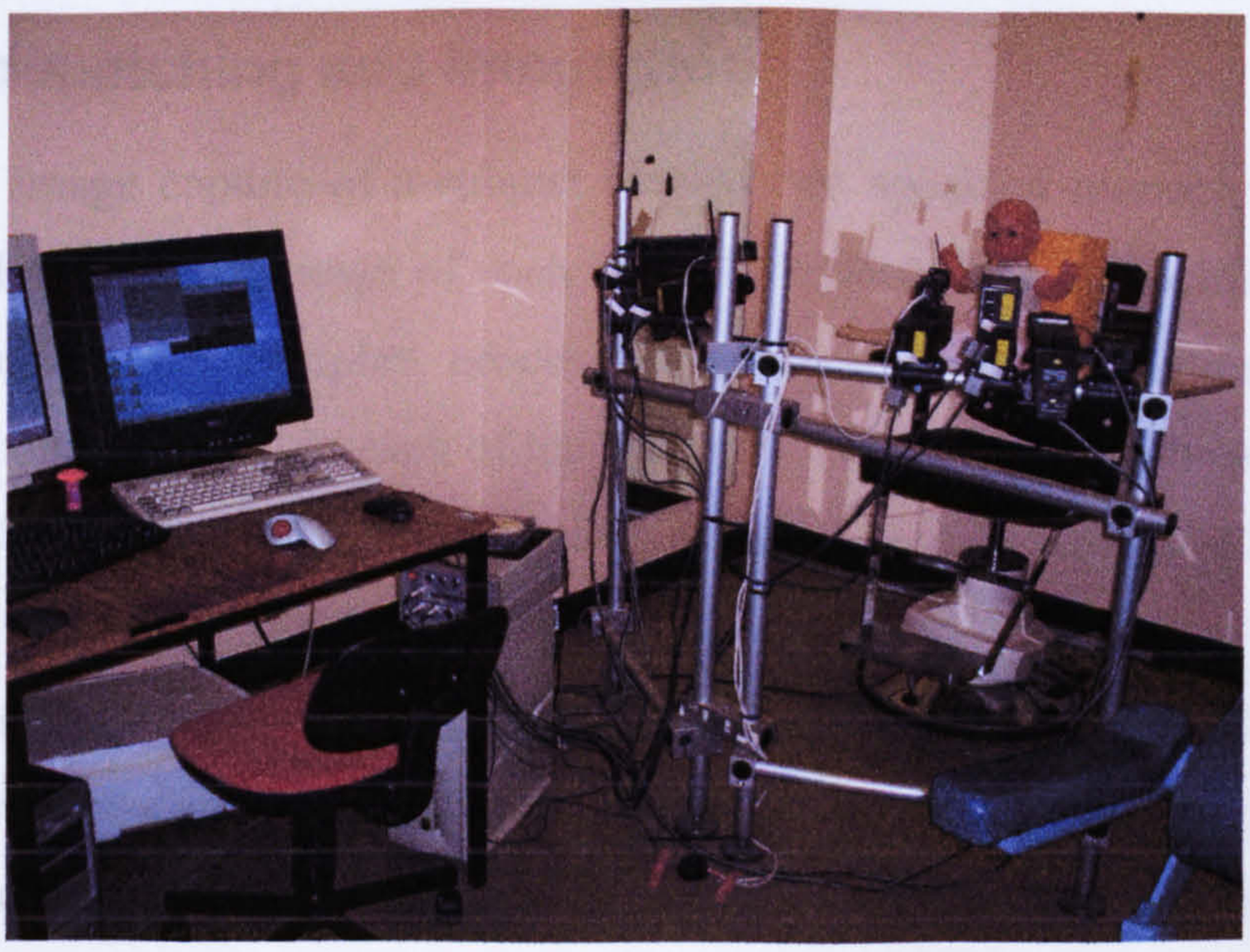


Figure 2.3 C3D™ system. Camera rig, dental chair and computer set-up

C3D™ Imaging software, camera drivers, Check Align© software and Facial Analysis Tool© software were installed.

2.2 Virtual 3D model production

2.2.1 Calibration

The internal geometry of the cameras and their positions relative to each other is derived from multiple images of a calibration object of accurately known dimensions, photographed in different positions (Fig 2.4). This calibration process is fundamental to the processes of stereo-matching and integration.

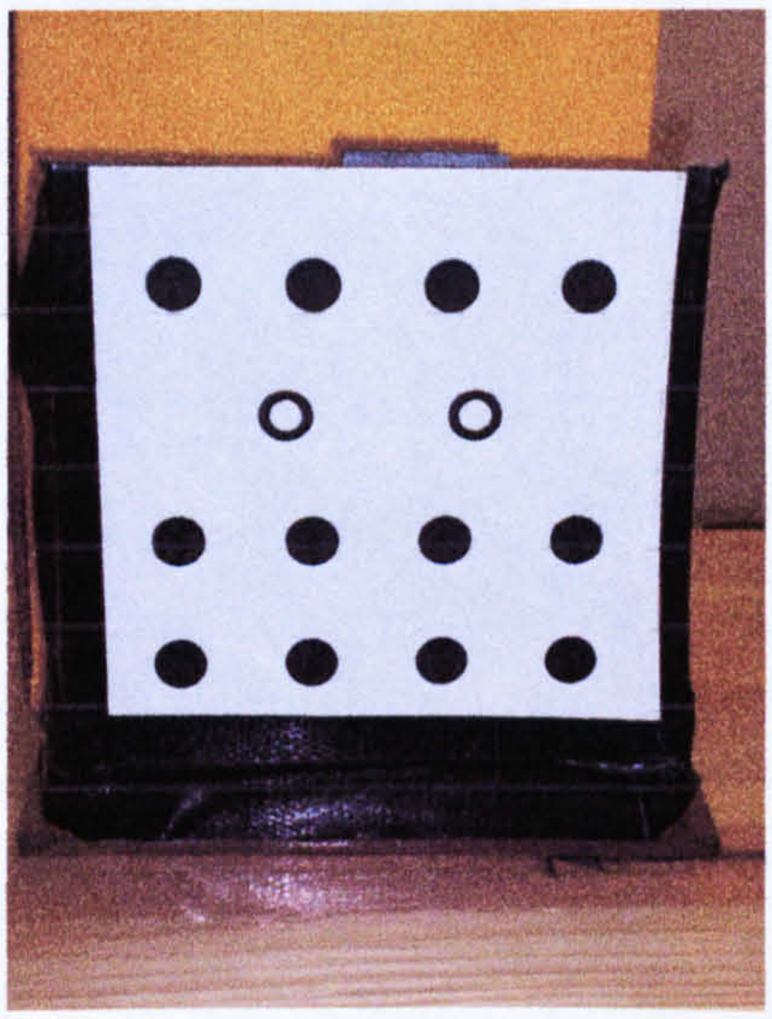
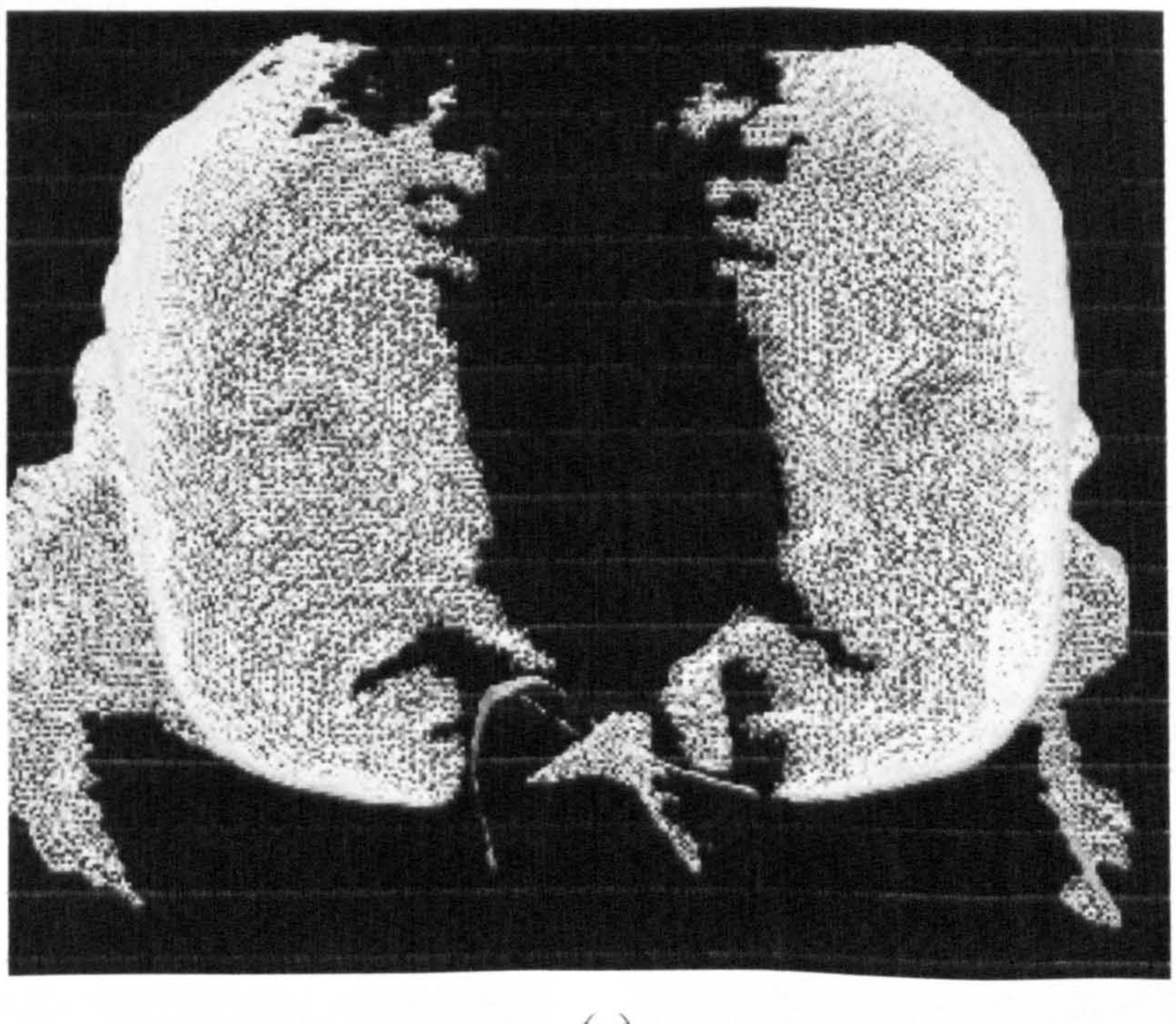


Figure 2.4 Calibration target of known dimensions

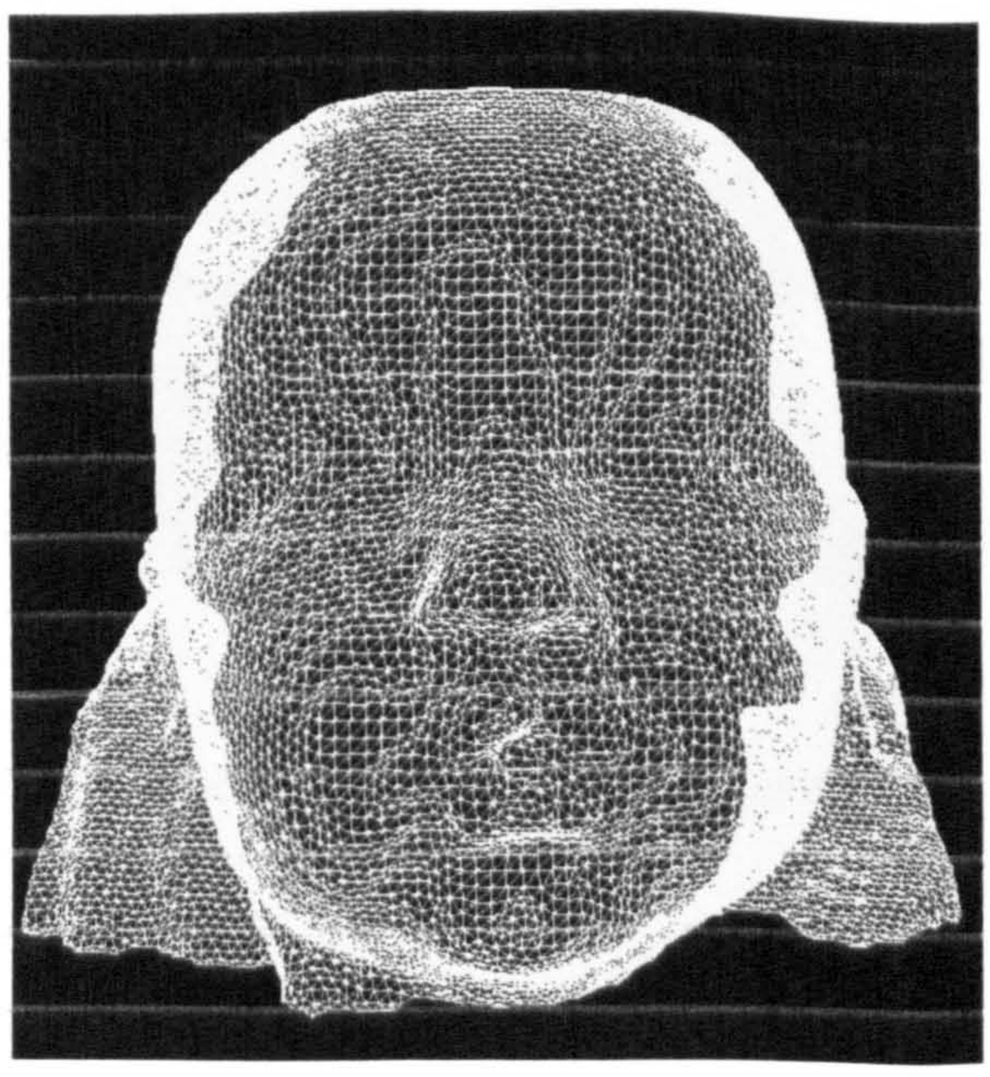
2.2.2 Stereo-matching and Integration

The process of image capture of a subject obtains two speckled monochrome images (a stereo-pair) and one colour image of each side of the face. The monochrome stereo-pair images are used in the complex process of stereo-matching. This involves finding corresponding points (pixels) in each of the monochrome cameras. Each camera will view the same subject from a slightly different perspective. Thus if a subject is photographed by two cameras in slightly different positions, the image of the subject will occupy a slightly different pixel arrangement in each. A particular pixel in one speckled stereo-pair image will match one in a slightly different position in the other. This slight difference or disparity between corresponding pixels allows depth to be calculated by triangulation, if the geometry of the camera system is known (i.e. the calibration). When the calibration is attached, the disparities are used to project a notional ray from each corresponding pair of pixels in the stereo-pair. Thus, the point at which they intersect in space can be computed.

A point cloud is produced in x, y, z space for each pod, which contains only 2.5D information (Fig 2.5a). For true 3D information, point clouds for left and right pods are integrated, transformed into the same co-ordinate frame, and merged into a single triangulated polygon mesh (Fig 2.5b) (Siebert & Marchall 2000).



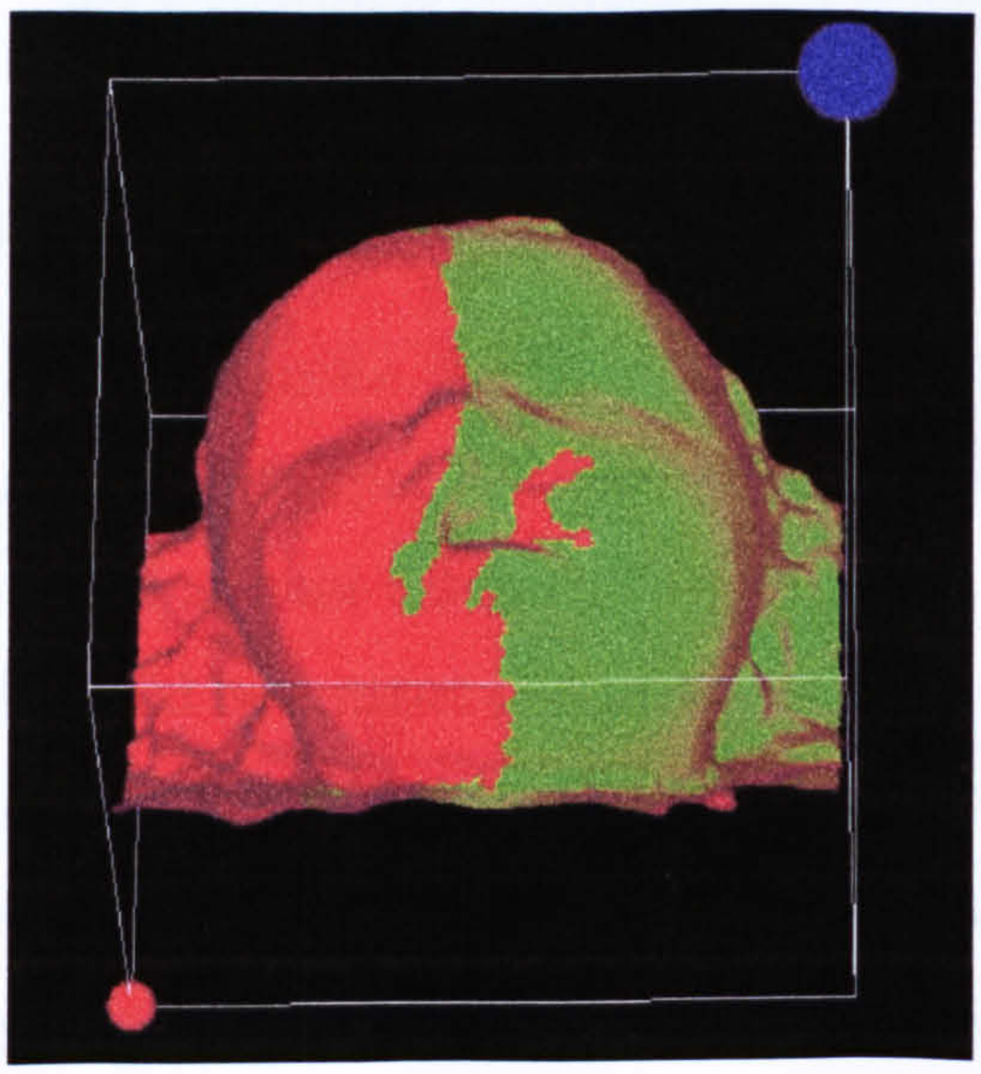
(a)



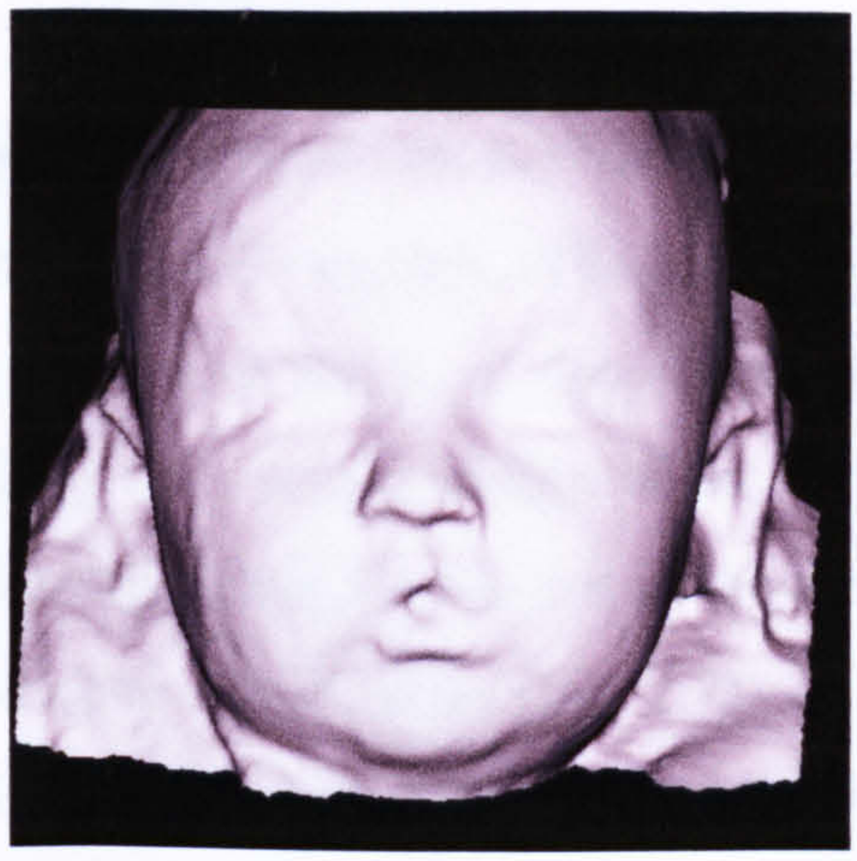
(b)

Figure 2.5 (a) Point clouds for right and left camera pods (b) merged polygon mesh

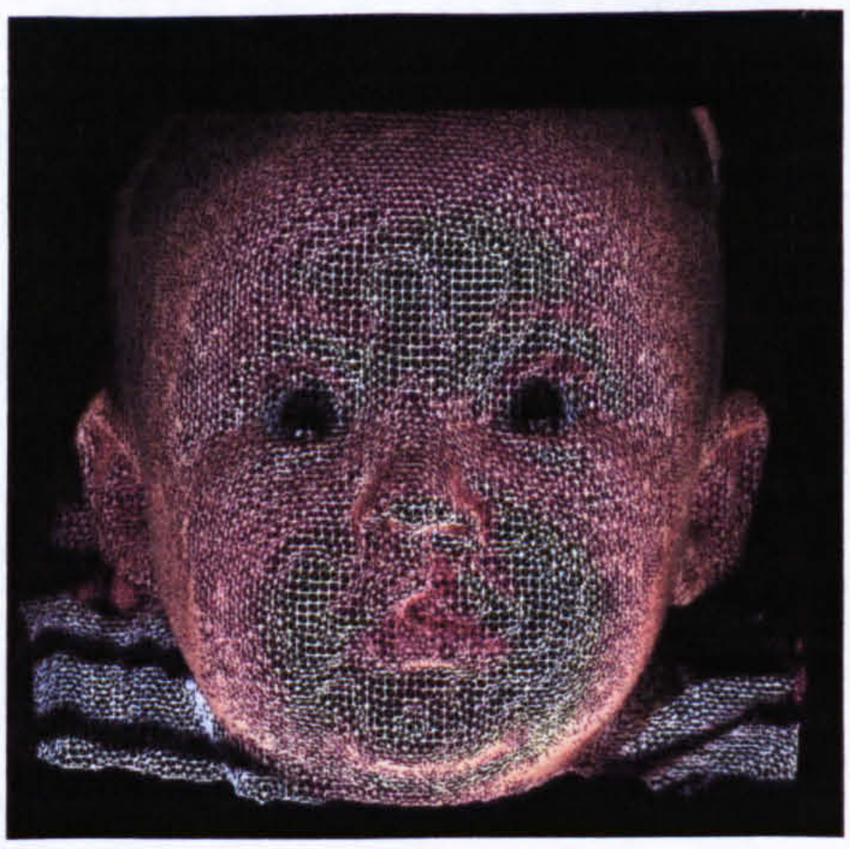
The 3D output can be viewed as a red / green shaded surface, solid surface (range data), or wire-frame (Fig 2.6a-c). Finding the correspondence between each triangle vertex in the polygon mesh and each pixel in the colour images creates the final photorealistic 3D virtual face model. (Fig 2.6d).



(a)



(b)



(c)

(d)

Figure 2.6 (a) Red/green shaded model (b) 3D solid surface model (c) Wire frame (d) photorealistic 3D model

2.3 Landmark Identification

Custom software was required to extract user-defined landmark configurations which represented facial features. Selection of a landmark on a 3D model generated a set of x, y, z co-ordinates, which described the spatial orientation of the point selected. This co-ordinate data could then be used for further analysis.

2.3.1 Facial Analysis Tool©

The Facial Analysis Tool© software (FAT©) was developed to facilitate anatomical landmark identification on the surface of photorealistic 3D models. The user interface consisted of a main window, two auxillary windows and a series of drop-down menus. Models could be rotated and viewed from any perspective. Manipulation of the model in the main window of the FAT© screen resulted in corresponding movement in the auxiliary windows, providing simultaneous profile and 60-degree tilted views (Fig 2.7). A 'zoom' facility enlarged models and improved operator ability to locate and identify landmarks.

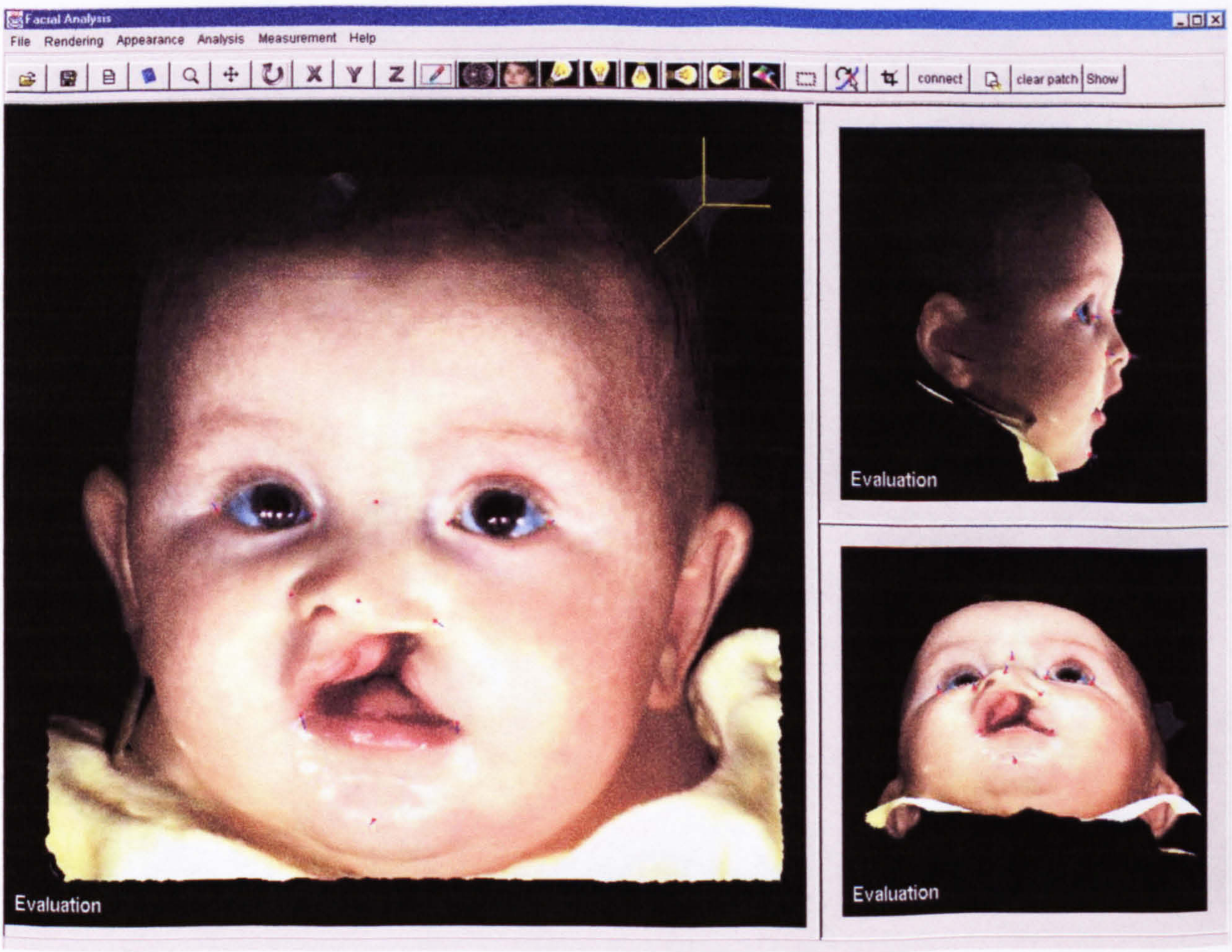


Figure 2.7 Facial Analysis Tool© user interface

A text file containing the desired landmarks and their definitions was created. This was accessed via a drop-down menu option on the Facial Analysis user screen. The operator was prompted to identify individual landmarks one at a time, in sequence. Landmarks were placed using the computer mouse to move the on-screen cursor to the desired location. When the right mouse button was clicked, a red sphere with a blue line indicating the orientation of the point on the model surface, relative to the computer screen (Fig 2.8) appeared on the model. Landmarks could be replaced and deleted by choosing the appropriate option from the editing menu. In addition to a visual display, a set of x,y and z co-ordinates was generated for each point. These were saved and could be recalled and viewed on-screen during landmark placement. The final output was a text file containing all relevant landmark co-ordinates for a particular 3D model that could be recalled and re-displayed.

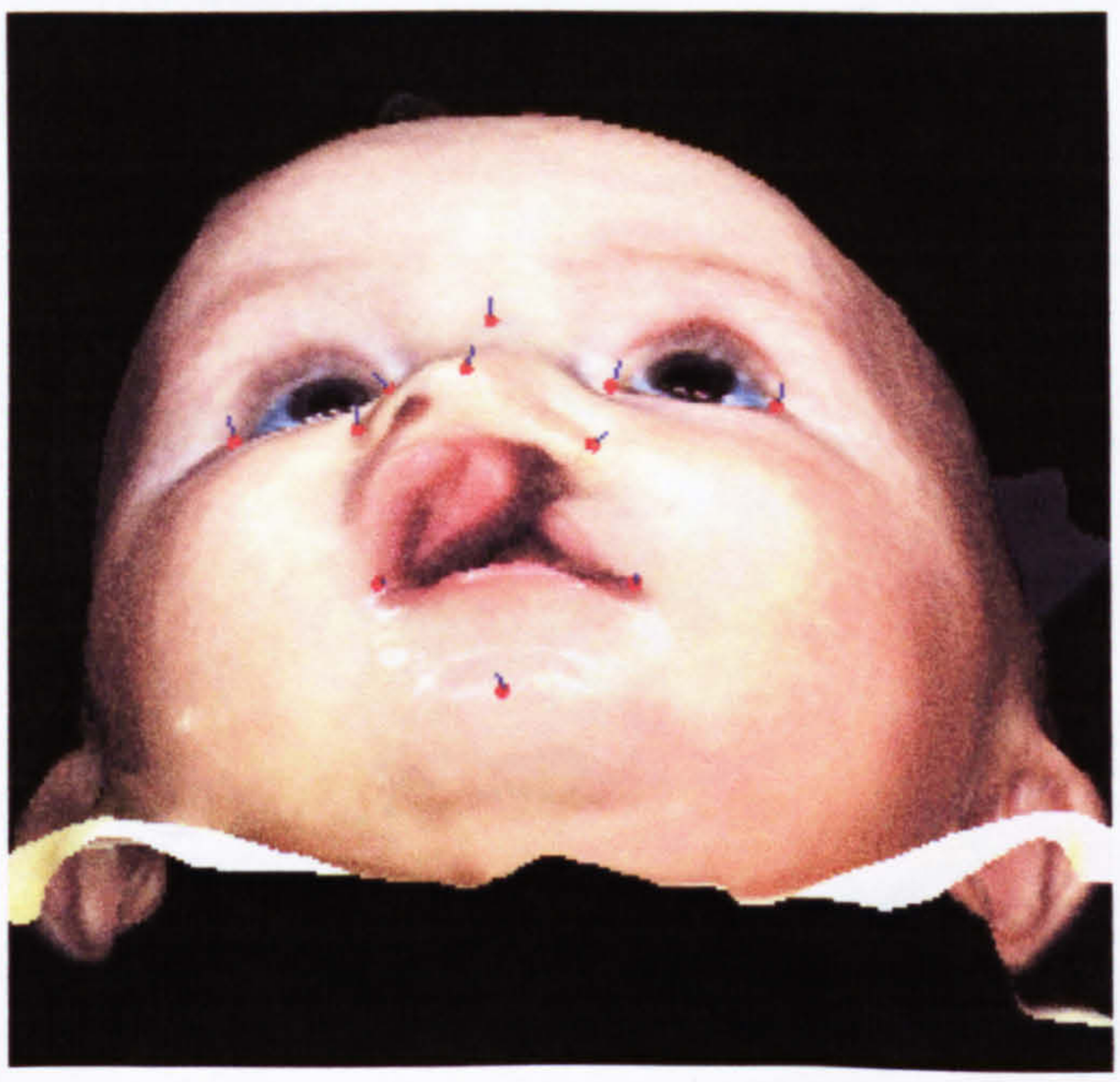


Figure 2.8 3D model with landmarks selected (red dots). Blue lines indicate orientation of point selected on model surface, relative to the computer screen

The first step in using a new 3D-imaging system was to validate the research tool. It was necessary to quantify errors that might arise with image acquisition (capture and registration error), operator error and inherent system instability. System accuracy was determined by measuring inanimate objects (facial casts) with the C3D^{TM} system and a 'gold standard' system of known accuracy, and comparing the two. These studies are described in the 'Validation of the C3D^{TM} System' section. The feasibility of using the system to image infants was explored in a series of clinical development studies. Technique and equipment modifications were made as a result of these investigations and the method was developed and refined. These studies are described in the 'Clinical Development Studies' section.

2.4 Validation of the C3D™ system

2.4.1 Quantification of Errors

Errors associated with 3D-imaging and landmark identification on 3D models can be categorised thus:

1. **Capture error** discrepancies due to errors in the 3D model generated by C3D™.
2. **Registration error** discrepancies due to differences in the position of the 'imaged' object in relation to the cameras.
3. **Operator error** discrepancies due to inconsistencies when locating landmarks on C3D™ models manually.

A study was designed to quantify the errors associated with imaging and locating points on an inanimate object, using the C3D™ stereophotogrammetry system. These key validation studies contributed to a larger project comparing the facial morphology of infants with cleft lip/palate and non-cleft infants. These results have been reported in detail by Ayoub et al. (2003).

Three investigators were involved in the validation process. One investigator photographed the facial casts (AG) and all three were involved in generating the 3D models. Each investigator participated equally in the production of co-ordinate data for analysis. Statistical support was provided by the Dept of Statistics, University of Glasgow.

2.4.1.1 Aims

- To quantify discrepancies due to errors in the 3D model generated by C3D™ (capture error)
- To assess the effect of object positioning on landmark co-ordinate values (registration error)
- To quantify average operator error.

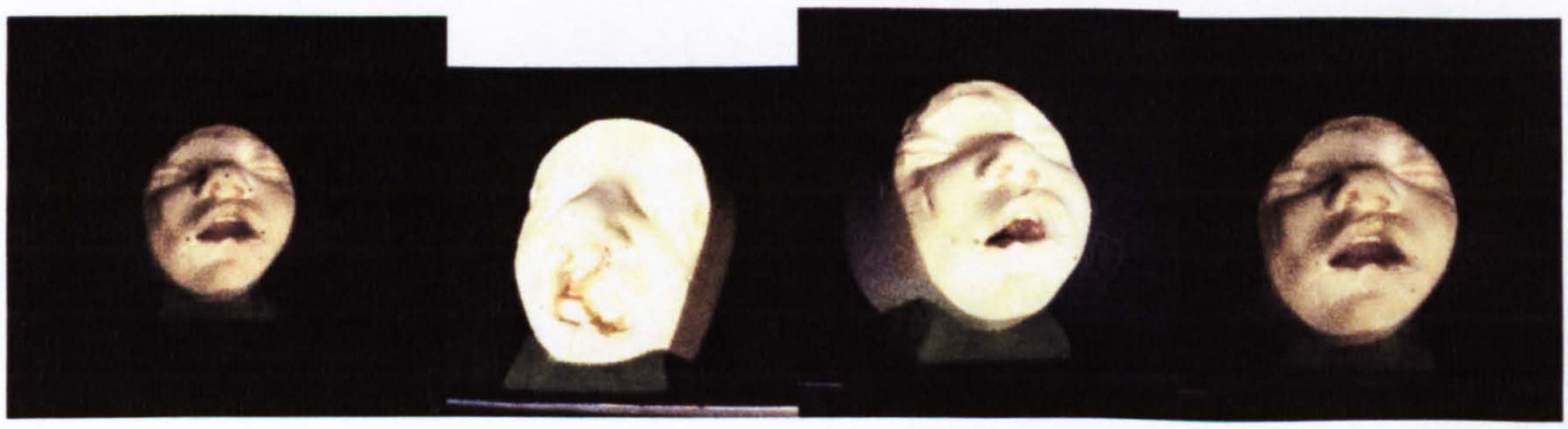
2.4.1.2 Materials

Archived pre-operative facial plaster casts of 21 infants with cleft lip and /or palate were available for study. Each facial cast was marked with a set of 5 ink marks corresponding to the anthropometric landmarks below:

1. Tip of nose (Tip)
2. Left nostril edge (nose L)
3. Left corner of mouth (mouth L)
4. Right corner of mouth (mouth R)
5. Right nostril edge (nose R)

2.4.1.2.1 C3D™ image acquisition

Casts were photographed against a black background, at a pre-determined distance from the wall. Images were acquired 3 times, in each of 4 positions (Fig 2.9), using the C3D™ stereophotogrammetry system. The system was calibrated before image capture and at the end of the imaging session. These were compared and the initial calibration attached to each capture to facilitate 3D model building.



(a) (b) (c) (d)

Figure 2.9 C3D™ models of facial casts in positions a,b,c & d

Casts were imaged in the following positions:

(a) Facing the centre of the camera configuration (Centre), 50cm from wall.

(b) Rotated 20 degrees anti-clockwise (20 degR), 50cm from wall.

(c) Rotated 20 degrees clockwise (20 degL), 50cm from wall.

(d) Facing the centre of the camera configuration (Front), 60cm from wall.

Two hundred and fifty-two 3D models were built from captured images at low resolution; edited, then built at high resolution. A final step was required export models as VRML files for use in the Facial Analysis Tool© software.

2.4.1.2.2 C3D™ co-ordinate data acquisition

Facial Analysis Tool© (FAT©) software was used to identify and manually extract the 3D co-ordinates of the set of ink-marked points. Each 3D model was loaded and oriented to face the operator. Manipulation of the model was at the discretion of the operator.

Three operators located the 5 landmarks on C3D™ models and the three-dimensional co-ordinates were saved to a text file for analysis. Each operator identified landmarks in the same order, every time. To minimize fatigue, models were marked in sessions of 30 minutes. Where an operator had little confidence in the location of a landmark it was not marked on the model. These data were recorded as missing (Table 2.1).

Table 2.1 proportion of missing values, by landmark and model position

Landmark	Model Position				All positions
	Centre	Front	20degL	20degR	
MouthL	4%	7%	9%	7%	7%
MouthR	2%	7%	9%	5%	6%
NoseL	4%	5%	23%	9%	10%
NoseR	11%	5%	9%	47%	18%
Tip	21%	26%	12%	23%	21%
All landmarks	8%	10%	12%	18%	12%

2.4.1.3 Method

2.4.1.3.1 Capture error

Inherent machine instability may contribute to error. Comparison of landmark configurations generated from multiple 3D representations of the same cast in the same position, with the same calibration attached gives an indication of repeatability, and quantifies capture error. Duplicate C3D™ models were built from three successive captures of six different casts, in the same position (centred and 60cm from the wall). Three different operators extracted landmark configurations using the Facial Analysis Tool©. Differences between landmark co-ordinates on the duplicate models were measured and mean values calculated (for each combination of landmark and operator separately).

2.4.1.3.2 Registration error

The potential for registration error in landmark identification was examined by comparing 3D models of the same cast photographed in 4 different positions relative to the camera stations. Since the 3D models of the casts to be compared were located in different places in the co-ordinate system (i.e. same cast in different positions), the configurations of

landmarks derived from these required alignment. Ordinary Partial Procrustes Analysis (O P P A) (Dryden & Mardia, 1998) was applied to rotate and translate the co-ordinates of the C3D^{TM} configurations to maximum superimposition. Scaling was not required, as configurations for individual casts were being compared only to themselves. Pair-wise comparison of landmark co-ordinates obtained from casts photographed in 4 different positions was undertaken. Six comparisons of position for each of 21 casts, averaged across three operators, were made.

2.4.1.3.3 Operator error

Six 3D models of different casts, imaged in the same position, were randomly selected from the available 3D models. Each operator identified a set of landmarks on each model three times. Differences between repeatedly placed landmarks were calculated and these values were averaged over the six models (for each combination of landmark and operator separately).

2.4.1.4 Results

2.4.1.4.1 Capture error

Average capture error for repeated landmark location on duplicate C3D^{TM} models, at the same position, by three operators is show in Table 2.2. Nose R point had the highest error for both operator 1 and 3, resulting in a higher average error value for all operators.

Table 2.2 Average capture error (mm) for each landmark, by operator. (Duplicate 3D images; same position; three operators

Landmark	Operator			All
	1	2	3	
Mouth L	0.36	0.27	0.43	0.35
Mouth R	0.35	0.36	0.56	0.43
Nose L	0.33	0.50	0.68	0.52
Nose R	0.93	0.10	1.50	0.91
Tip	0.39	0.29	0.34	0.34

2.4.1.4.2 Registration error

The average discrepancy between landmark co-ordinates obtained from C3D™ models of casts imaged in different position, relative to the camera set-up, was 0.42 mm (Table 2.3). The 'Nose tip' landmark tended to be affected most by variation in imaging position and displayed the largest differences between positions.

Table 2.3 Registration error (mm). Pairwise comparisons of variation in cast position

Landmark	Centre vs Front	Centre vs 20degR	Centre vs 20degL	20degR vs Front	20degL vs Front	20degL vs 20degR	Total
Mouth L	0.46	0.38	0.32	0.33	0.37	0.31	0.36
Mouth R	0.45	0.34	0.42	0.31	0.58	0.35	0.41
Nose L	0.44	0.36	0.36	0.37	0.43	0.52	0.42
Nose R	0.37	0.44	0.38	0.41	0.39	0.44	0.40
Tip	0.51	0.45	0.58	0.42	0.54	0.48	0.50
Mean	0.46	0.39	0.42	0.36	0.46	0.42	0.42

2.4.1.4.3 Operator error

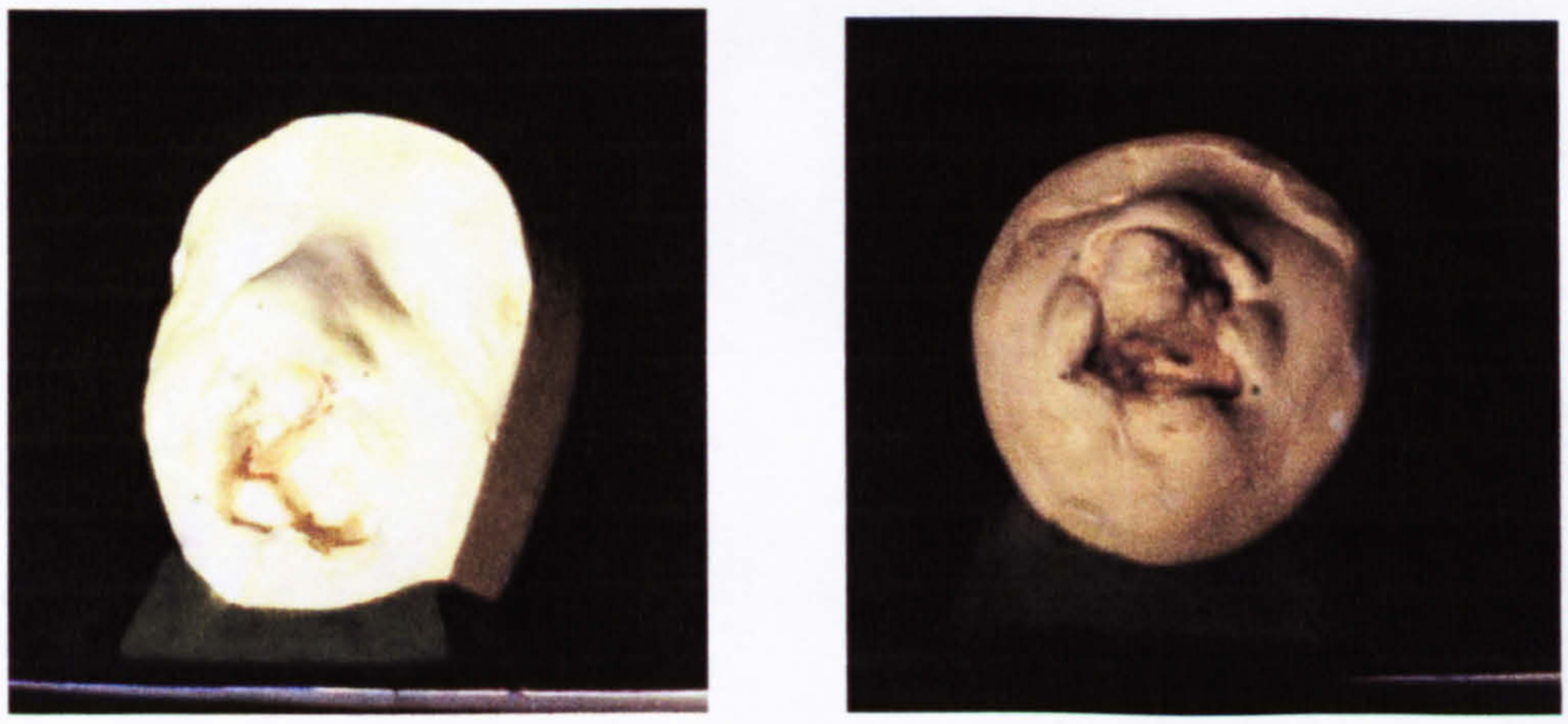
The average discrepancy between repeatedly-placed landmarks was 0.2mm (range 0.14 to 0.32mm). The error associated with 'Nose R' point demonstrated that there was least agreement among operators (0.32mm) associated with the identification of this landmark (Table 2.4). Analysis of variance (ANOVA) demonstrated no statistically significant differences in inter-operator reproducibility (p=0.2).

Table 2.4 Operator Error (mm); Repeatedly placed landmarks, 3 operators

Landmark	Operator			All
	1	2	3	
Mouth L	0.16	0.18	0.24	0.19
Mouth R	0.12	0.14	0.28	0.18
Nose L	0.14	0.08	0.26	0.16
Nose R	0.29	0.15	0.57	0.32
Tip	0.21	0.04	0.19	0.14
Mean	0.18	0.12	0.30	0.20

2.4.1.5 Discussion

A high level of repeatability and reproducibility was demonstrated. The proportion of missing values was high for some landmarks in certain positions. This has potential to affect the perceived accuracy of these points. The decision to omit landmarks that were ambiguous and classify them a missing allowed identification of those landmarks which were difficult to locate. However, this may have potentially introduced bias in the reported accuracy of landmarks that had a high proportion of missing values. This should be borne in mind when interpreting the results. The results of the capture error study demonstrated that generation of 3D co-ordinates from multiple 3D models of the same casts was highly repeatable. Equipment capture error has the potential to introduce a systematic bias in measurement, however attaching the same pre-imaging calibration to each set of images minimised this. When individual landmarks were examined, it was noted that 'Nose R' had the highest error. Two operators displayed high values for this landmark and in addition, 11% of values were missing. This indicates lack of confidence in locating this landmark. The most probable explanation lies in the quality of the facial casts and the lighting conditions during image capture. The casts were light cream in colour and this may have affected image quality due to uneven light reflection.



(a) (b)

Figure 2.10 Landmarks obscured by (a)'bleaching of model (b)shadow

Uneven light reflection resulted in over-exposure and subsequent 'bleaching' of parts of the images (Fig 2.10a). The USB generated fluctuating power levels, which caused the flash intensity to vary, even when the casts were photographed in the same position. A landmark was obscured when it coincided with an area of shadow i.e. the flash was unable to illuminate the object uniformly (Fig 2.10b). Landmarks around the nose in particular, would require careful consideration when finalising the Methods for the main study.

Changing the position in which the casts were imaged had the effect of producing a mean registration error of 0.42mm. There were negligible differences between positions, as demonstrated by pairwise comparison. The tip of the nose was more affected than the other landmarks by changes on position. 21% of these landmarks were missing and again this points to problems with identifying this landmark. The quality of the facial plaster casts was not always good. Some bleeding of the ink landmarks had occurred due to porosity of the cast surface, and some marks were quite indistinct because of past handling. Nevertheless, the potential registration error of an object placed centrally in the photographic field was less than half a millimetre.

Average operator error was very low (0.2mm). This study confirmed that there was least agreement about the location of the Nose R point, however the highest error value associated with this point was 0.57mm. In addition to the problems of model quality and illumination, it is possible that an operator mistakenly located this point or inadvertently moved the cursor when selecting the landmark, resulting in an outlier. Despite this, the error generated by manually selecting ink points on a 3D model of a facial cast could be considered negligible. Location of anatomical landmarks on a photorealistic 3D model would require further clinical evaluation. Imaging of subjects in a standardised position and selection of the best quality 3D model would help to reduce the potential for registration and landmark location error.

2.4.2 C3D™ System Error

C3D™ System error is defined as the discrepancy between the co-ordinate systems generated by C3D™ and a 'Gold Standard'. This can be thought of as overall accuracy of the C3D™ imaging system.

2.4.2.1 Aims

- To quantify system error in terms of the difference between landmark 3D co-ordinate values obtained from the C3D™ system, and benchmark values obtained from an independent source, of known accuracy.

- To examine the effect of variation in object position on the accuracy of landmark identification.

2.4.2.2 Method

2.4.2.2.1 Acquisition of 'Gold Standard' Data

The 3D co-ordinates of ink points on 21 baby casts were determined using the Ferranti co-ordinate-measuring machine (CMM) at the School of Manufacturing and Mechanical Engineering, University of Birmingham. This device consisted of a co-ordinate-measuring machine, a 'traversing frame' and a tactile probe of documented precision (error 9.53 microns). The traversing frame allowed movement along axes at right angles to each other, in 3 planes of space (X, Y and Z axes) and the probe 'sensed' the object to be measured (Spencer, Hathaway & Speculand 1996). The set of landmarks on each cast was digitised twice and benchmark values obtained.

2.4.2.2.2 Comparison of C3D™ and CMM co-ordinates

Each configuration of five C3D™ coordinates was compared with the respective 'gold-standard' configuration (obtained from the CMM). To compare the two data sets it was necessary to standardise the co-ordinate systems. Ordinary Partial Procrustes Analysis (OPPA) was used to align the 3D global positions of each landmark set produced by C3D™, by rotation and translation, to 'best-fit' the benchmark values. As the two co-ordinate systems were calibrated in millimetres, no scaling step was required. The distances (in mm) between each corresponding landmark, after superimposition, represented the discrepancies between the two methods of measuring 3D co-ordinates of facial cast landmarks.

2.4.2.3 Results

Average discrepancy between C3D™ and CMM co-ordinate values was 0.83mm (across 21 casts, 4 positions and 3 operators) (Table 2.5, overleaf).

The lowest difference between C3D™ and CMM co-ordinates occurred when the model was photographed in the '20 degree Right rotated' position (0.64mm). The largest difference between C3D™ and CMM co-ordinates occurred when the model was photographed in the '20 degree Left rotated' position (1.02mm).

Table 2.5 C3D™ System Error (mm)

(Average difference between C3D ™ and CMM co-ordinate values)

Landmark	Position				Total
	Centre	Front	20degL	20degR	
MouthL	0.64	0.64	0.64	0.54	0.62
MouthR	0.55	0.41	0.59	0.46	0.50
NoseL	0.78	0.87	0.88	0.75	0.82
NoseR	1.25	1.00	1.52	0.80	1.18
Tip	1.20	1.12	1.47	0.73	1.14
Total	0.86	0.80	1.02	0.64	0.83

2.4.2.4 Discussion

The C3D™ system was shown to be reliable and accurate to within 1mm of true 3D co-ordinate values. This compares favourably with other three-dimensional imaging systems such as structured light systems, laser scanning and video imaging (Bush & Antonyshyn 1996; Ferrario, Sforza, Poggio et al. 1996; Moss, Grindrod, Linney et al. 1988; Stromland, Chen, Michael et al. 1998).

On first examination, results suggested that the co-ordinates generated by the C3D™ system were most accurate when objects were photographed in a rotated position, facing 20 degrees to the Right, relative to the cameras. However, the high proportion of missing values associated with the 'Tip' and 'Nose Right' landmarks, especially at the '20 degree right' position indicated problems with operator confidence in identifying these landmarks on models imaged in this particular position. This can again be attributed to several factors, including test object quality and photographic conditions. Uneven light reflection resulting in bleaching of images, and fluctuating flash intensity resulting in shadowing are the most likely explanation. Shadowing occurred especially around the nose when casts were imaged in the 20 degree rotated position. This is a recognised limitation of the 2-pod system configuration.

2.4.3 Conclusions of Validation studies

The C3D™ system was demonstrated to be sufficiently accurate for application to facial imaging. The most appropriate position in which to photograph subjects, using the present C3D™ configuration, was with the subject posed equidistant from the camera stations, facing the centre of the set-up. The most anterior limit of the face would be positioned ideally no more than 60cm from the back wall. A small amount of rotational latitude was permissible (+/- 20 degrees from centre). The C3D™ system would require modification to ensure that flash illumination was optimised for facial surface photography in order to minimise areas of shadow and over-exposure of images. Development of a standardised subject position for imaging a range of ages from young infant to primary school age would be required.

2.4.4 Summary of Validation studies

Registration Error

Average displacement error between 3D models of casts photographed in 4 different positions was 0.42mm.

Operator Error

The average displacement of repeatedly placed landmarks by 3 different operators was 0.2mm (range 0.15 - 0.32mm).

System Error (accuracy)

Average distance between landmarks as a result of the discrepancy between C3D™ and CMM co-ordinate values was 0.83mm.

2.5 Clinical Development studies

2.5.1 Standardisation of subject position for image capture

The studies described in this section formed the initial development work for 3D imaging of infants and young children at the Royal Hospital for Sick Children, Yorkhill, Glasgow. Studies were conducted in May 2000. The author also assisted in a development study to determine the working area of the camera kit at Glasgow Dental Hospital, conducted in March 2000, as previously described by (Garrahy 2002).

2.5.1.1 Aims

The aims of this series of development studies were three-fold:

1. To define and standardise optimal subject position, relative to the camera pods.
2. To determine the vertical, horizontal and antero-posterior (AP) limits of the imaging / capture field.
3. To inform as to the need for further equipment / technique modification in order to image infants and young children.

2.5.1.2 Materials

1 'Life-size' baby doll with soft body and vinyl head. Doll's face width = 12cm (ear to ear). Vertex of the head and tip of nose marked.

1 Calibration target .

1 Metal tape measure

1 base-board support for doll.

1 C3D^{TM} 2-pod Facial Imaging System set up in a corner of the room.

1 Dental chair, with adjustable height and swivel facility.

2.5.1.3 Method

Calibration was carried out prior to capture, according to the process described in detail in the Method section. The C3D^{TM} system was set up facing the dental chair (Fig 2.3). A life-size baby doll was positioned on a baseboard fixed across the arms of the dental chair such that the face was centred and visible in each of the 6 camera frames simultaneously (Fig 2.11).

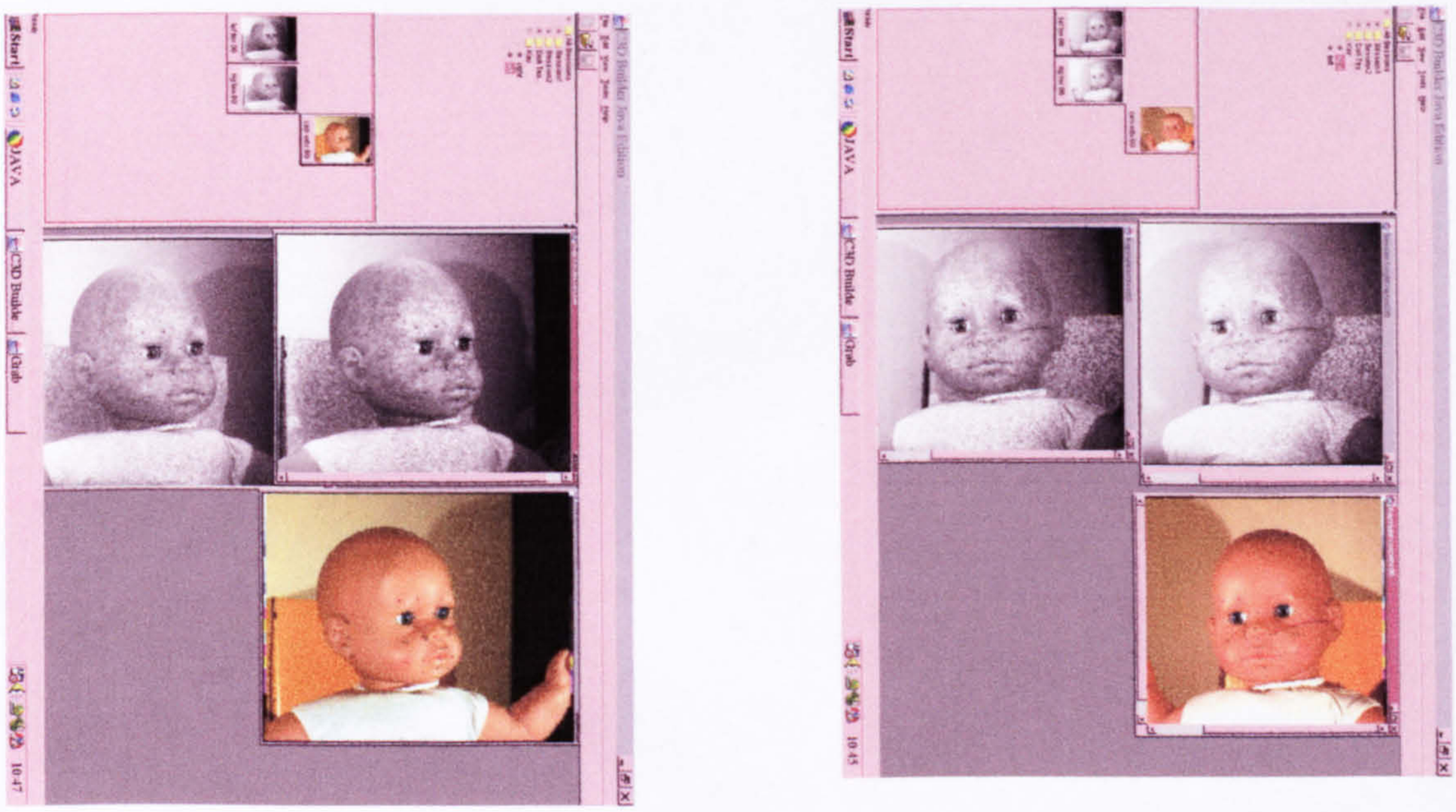


Figure 2.11 Doll face visible in all cameras on left and right pods

A steel measuring tape was used to measure the perpendicular distance of the vertex of the doll's head from the floor, and adjacent walls. This reference position was defined as the 'Start' position or 'position zero' and images were captured.

2.5.1.3.1 Depth of capture field (A-P Dimension)

A steel tape was fixed to the base-board in the antero-posterior direction and the doll advanced forward in increments of 2 cm until the face was no longer completely visible all camera fields simultaneously. Images were captured at each 2cm interval. The process was repeated and the doll moved backwards in 2cm increments from the 'start' position, until the back of the doll's head was at the visible limit of the camera fields.

2.5.1.3.2 Width of capture field – (Horizontal Dimension)

With the tape was fixed horizontally across the front of the baseboard, the doll was moved from its central start position in 2cm increments right, then left. Images were captured at each position.

2.5.1.3.3 Height of capture field (Vertical Dimension)

The perpendicular distance of the vertex of the doll's head from the floor in the 'start' position was considered optimal. This was assessed subjectively as the height at which the entire face / head of the doll was centred and visible in the multiple camera fields.

2.5.1.4 Data processing

Captured images were scrutinised for sharpness of the black and white texture speckled pattern and clarity of focus, since this determined the quality of 3D models produced. 3D models were built and the range data examined. Model quality was assessed subjectively and graded according to the following criteria:

Range Data Quality Reference

Excellent:- Smooth, all features clearly visible (Fig 2.12)

Good:- minor surface irregularities; slightly bumpy texture in limited area (Fig 2.13)

Poor:- very lumpy texture; broken, holes or defects (Fig 2.14)

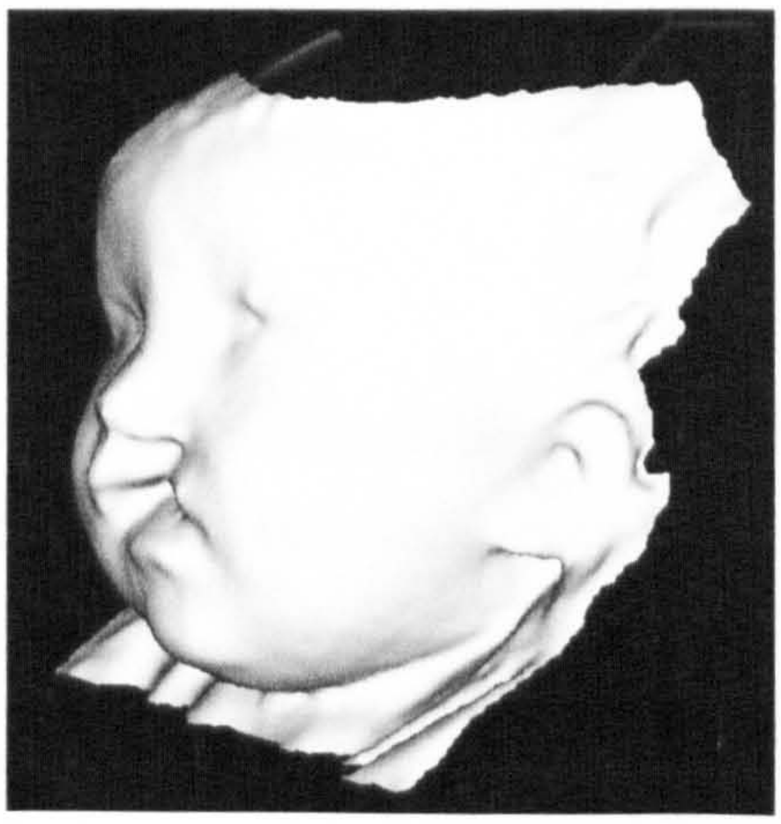


Figure 2.12 Example of 'excellent' range quantity

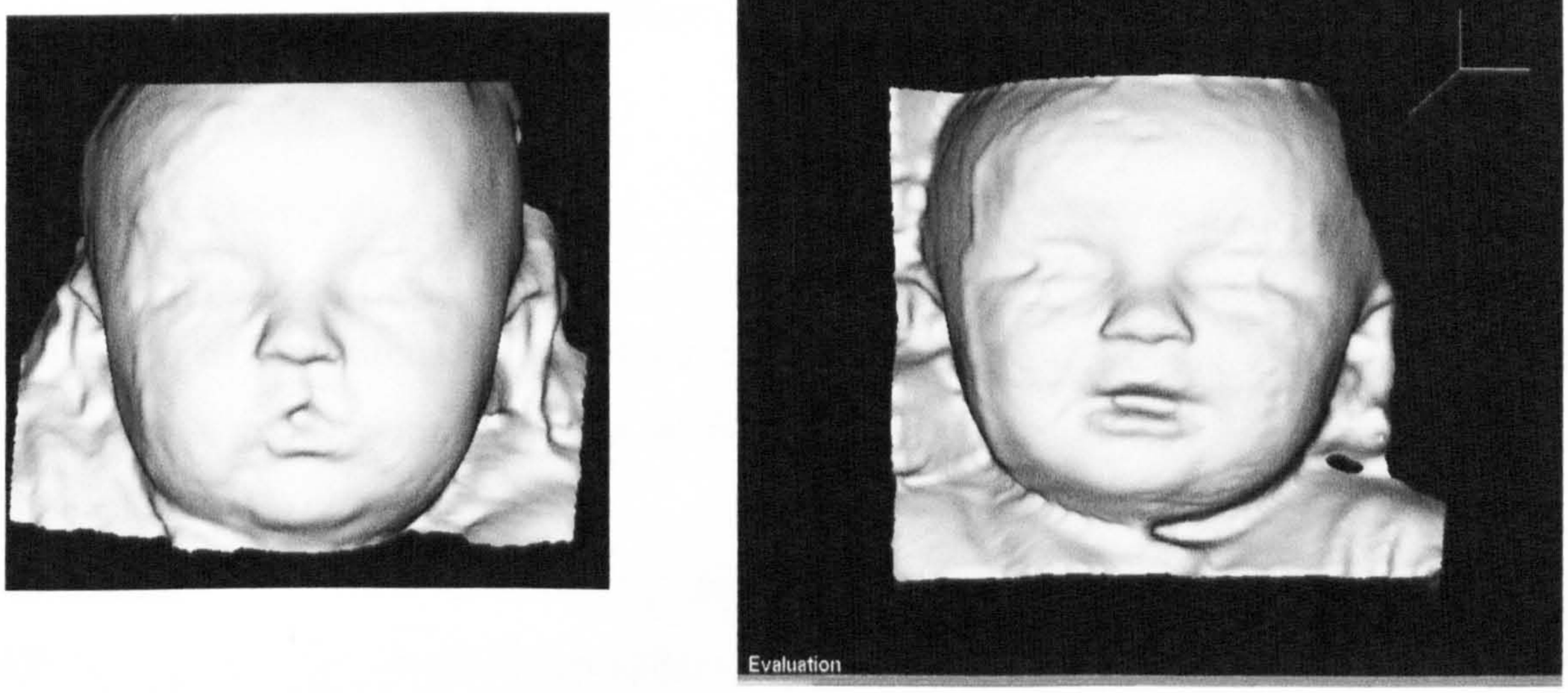
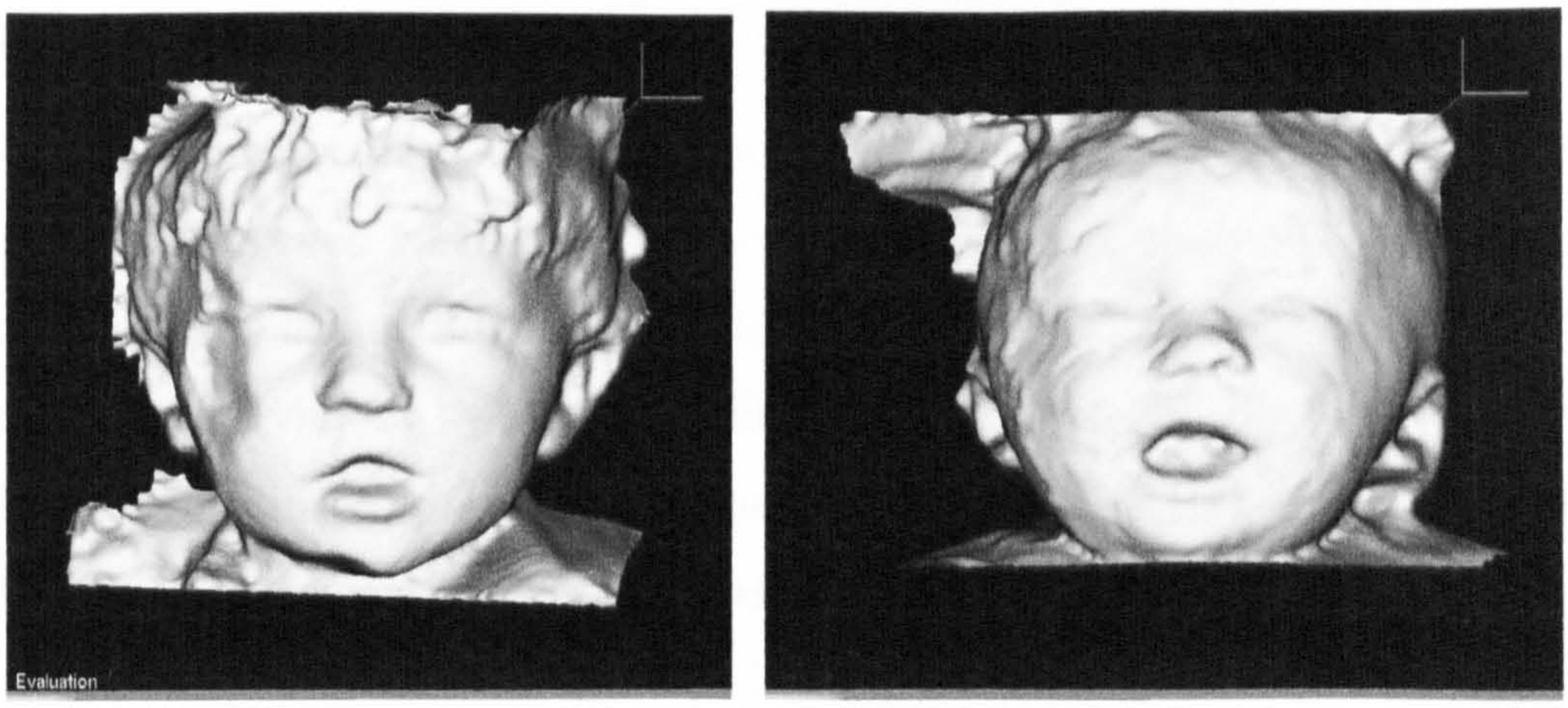


Figure 2.13 Examples of 'good' range quality



(a) (b)

Figure 2.14 Examples of 'poor' range quality (a) defect R cheek (b) lumpy surface texture

2.5.1.5 Results

2.5.1.5.1 Optimal subject position

The position at which the best possible quality range data (grade 1) was achieved was termed the optimal subject position, and determined as:

Vertex of head	R to L	=103cm from side wall
	Height	= 116cm from floor
Tip of nose	AP	= 60cm from back wall
	R to L	=103 cm (range 98-108cm)

2.5.1.5.2 Working Capture Area

The range of measurements at which model quality was subjectively graded as 1 or 2 (excellent - good) delineated the working capture area. This was a kite shape with dimensions:

Horizontal	= 92-114cm (22cm)
AP	= 40-68 cm (28cm)
Height	=96-116 cm (20cm)

2.5.1.6 Conclusions

The face of an infant-sized doll could be imaged with the 2-pod C3D™ system. Poor quality models resulted when a subject was not positioned optimally within the field of capture. Failure to capture the subject in the optimal position resulted in reduced sharpness of texture pattern viewed by the black and white cameras. In a live subject, movement would also result in blurring of the texture pattern. This in turn would produce a poor model. Three-dimensional models of 'good' to 'excellent' quality would be obtained if the subject was imaged within a static working capture area measuring 22cm by 28cm by 20cm. It was anticipated that it would be possible to produce models of superior quality of infant subjects if multiple captures were recorded at each capture session. Results from this study at the RHSC Yorkhill site compared favourably with that carried out at Glasgow Dental Hospital (Garrahy, 2002). Both sites would be used for image capture in the main study. Both systems and settings were identical and the same calibration procedures were performed with identical calibration targets. Therefore equivalence was assumed.

2.5.1.7 Recommendations for 'live' captures

1. Infant subjects would be imaged whilst seated on the lap of an accompanying adult. Adult assistance would be required for young babies who could not fully support their own head weight.
2. Chair base should be fixed, but swivel and height adjustment facility retained to allow accommodation of different sized subjects and parents. A visual marker to be placed on the rear wall to guide re-positioning of the chair before and after each capture session.
3. Visual markers were needed to aid optimal height and AP positioning of the subject, by an accompanying adult.
4. The camera rig should be fixed securely to the floor to avoid accidental movement.
5. A light-based location system should be incorporated on the C3D™ rig to enable operator fine-tuning of subject position within camera fields.

2.5.1.8 System Modifications/Improvements

The position of the chair base was marked out on the floor with black tape. A black tape marker was placed on the wall behind the chair to facilitate re-alignment of the headrest to the same position after seating of the subject. Any movement of the chair from the standard

position could then be observed and rectified during the course of a capture session. A full-length mirror was fixed to the wall adjacent to the C3D™ set-up. Strips of black tape were used to mark height and antero-posterior (AP) field limits on the mirror (Fig 2.15).

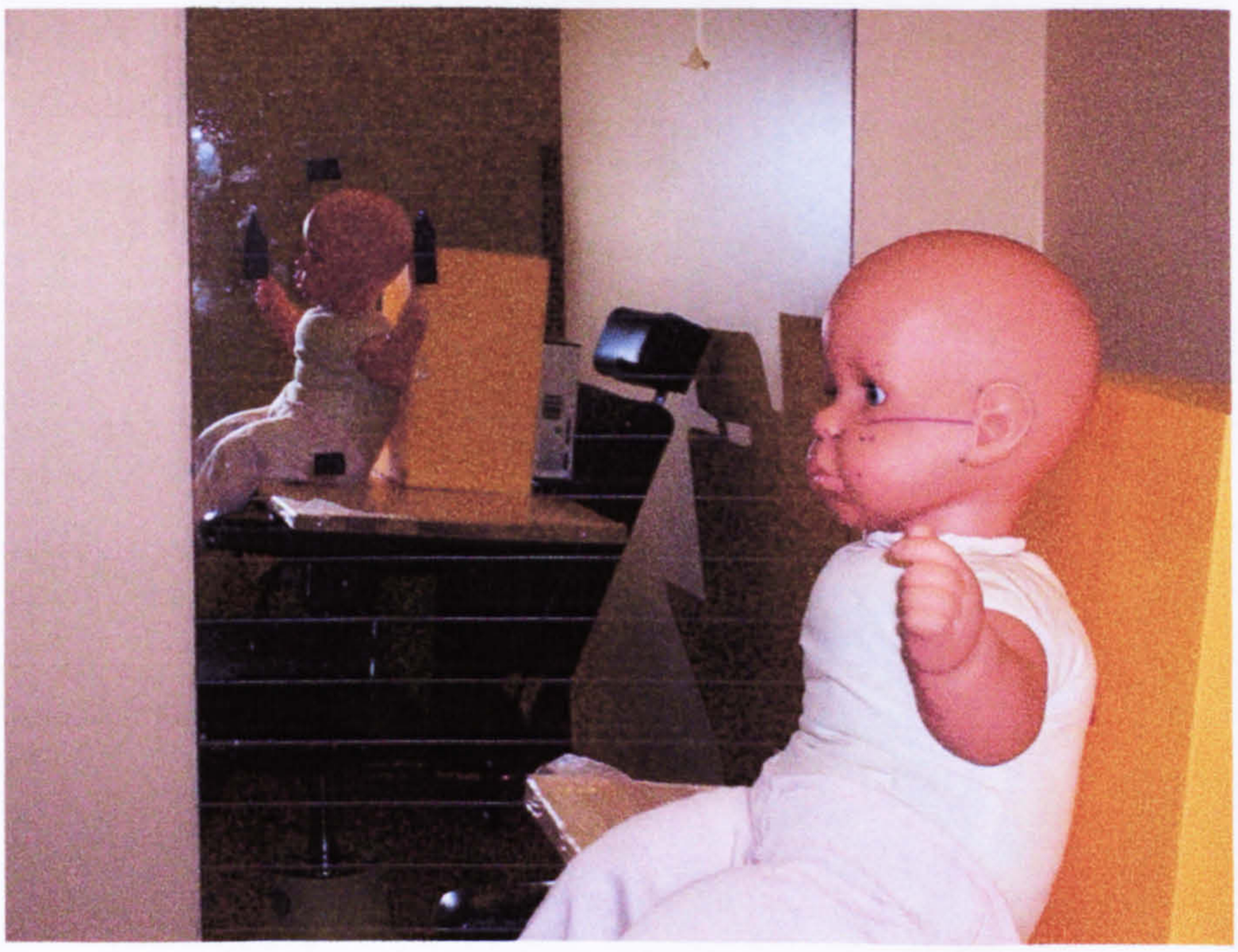


Figure 2.15 Black tape field limit markers on mirror to aid subject positioning

The camera rig was secured in position with floor bolts. The requested light-based positioning system was added to the camera set up. This took the form of a slit-lamp fixed on top of the left and right colour cameras, which projected two lines of light onto the subject's face. These converged in the shape of a cross on the centre of the forehead when the subject was placed in the optimal position. Protocols for calibration, standardized infant facial capture and data processing were developed. These are described in detail in the main Method section.

Having tested the C3D™ system's performance on an inanimate object, the next steps were to evaluate its application to facial imaging and to assess suitability for use in young children with cleft lip and palate. Further evaluation of the feasibility of locating anatomical landmarks on a C3D™ model of an infant face is described in the next section.

2.6 Landmark identification on the infant cleft face

2.6.1 Landmark Feasibility Pilot Study

In order to determine if it was possible to locate anatomical landmarks reproducibly on a 3D model of an infant with facial deformity, a study was designed to measure the feasibility of reliable landmark placement.

2.6.1.1 Aims

- To determine the degree of accuracy to which anthropometric landmarks could be located on a C3D^{TM} model of an infant with Unilateral cleft lip and / or palate, prior to and following surgery.
- To measure the average landmark placement error in millimetres for each landmark and across the whole face.
- To determine ways in which landmark placement error could be reduced.

2.6.1.2 Method

2.6.1.2.1 Power of the study

A clinical reproducibility of 0.5 - 1mm was considered to be the gold standard. A power calculation was preformed to ascertain the necessary sample size. To be 95% certain that the differences detected were real differences, two C3D^{TM} models of each of 11 children were required.

2.6.1.2.2 Sample

Five children with UCL and 6 children with UCLP, who had had 3D images captured prior to lip / nose surgery and after repair, were randomly selected from the main sample (Table 2.6). Twenty-two C3D™ models (11 pre-op models and 11 post-op models) were available for analysis.

Table 2.6 Pilot study sample distribution

Case	UCLP	UCL	Right	Left
001	✓		✓	
003		✓	✓	
005		✓		✓
006		✓		✓
007	✓			✓
008	✓			✓
009		✓		✓
010	✓		✓	
012		✓		✓
014	✓			✓
023		✓		✓
Total	**5**	**6**	**3**	**8**

2.6.1.2.3 Landmarks

Thirty-eight anthropometric landmarks were investigated in this pilot study (Table 2.7, overleaf). Standard anthropometric landmark definitions were used or adapted from other facial morphology studies (Duffy, Noar, Evans et al. 2000; Farkas 1990; Hurwitz, Ashby, Llull et al. 1999). New landmarks were defined to describe estimated crista philtri points adjacent to the cleft.

Fourteen nose landmarks, 12 lip landmarks, 7 eye and forehead landmarks and 5 landmarks on other areas of the face were tested for reproducibility (Table 2.8). Surrogate lip landmarks cph0 and <cph> existed only on the pre-op models and were not included in post-op model markup schedule. Landmark stos, could not be located on pre-op models, and was marked on post-op models only. Landmarks were identified on the models in the same order, on 3 separate occasions. Marking proceeded such that no single model was marked more than once in a session, in an effort to minimize the effect of memory in point placement.

Table 2.7 Anthropometric Landmark definitions

Region	Landmark	Symbol	Definition
Eyes & forehead	Endocanthion	enL, enR	point at inner commissure of the eye
	Exocanthion	exL, exR	point at outer commissure of the eye
	Trichion	tr	point in midline of forehead, at the hairline
	Glabella	g	point of maximum convexity in midline of supra-orbital ridges
	Nasion	n	deepest point of concavity of bridge of nose in midline
Nose	Alar Crest	acL, acR	most lateral point in the curved base line of ala
	Alare	alL, alR	most lateral point on alar contour
	Alare Outer	al0L, al0R	point on outer aspect of ala, at its thinnest point
	Pronasale	prn	most protruded point of apex of nose
	Subalare	sbalL, sbalR	point at lower limit of alar base where it joins skin of upper lip
	Subnasale	sn	point of maximum concavity in midline where columella base, meets upper lip skin
	Subnasale'	sn0L, sn0R	most lateral aspect of columella at its narrowest & lowest point
	Columella	cL, cR	highest point on columella where nostril starts to curve laterally
Lips	Cheilion	chL, chR	point at each labial commissure
	Crista Philtri	cphL, cphR	point at lowermost extent of philtral ridge, junction of white roll and vermillion of upper lip
	Crista philtri surrogate points *new*	<cph>L, <cph>R	point on vermillion on minor segment, adjacent to cleft (estimated; same distance from ch-cph on non-cleft side)
		cph0R, cph0L,	point on vermillion on major segment, adjacent to cleft (estimated; same distance from cph - ls on non-cleft side).
	Labrale Inferius	li	midpoint of lower vermilion border
	Labrale Superius	ls	midpoint of upper vermilion border
	Sublabiale	sl	point of maximum concavity in midline between the lower lip and chin
	Stomion Superius	stos	Point on lowermost extent of vermillion border of upper lip, in midline, with lips apart
	Stomion Inferius	stoi	Point on uppermost extent of vermillion border of lower lip, in midline, with lips apart
Other	Cheek	chkR, chkL	midpoint of a line connecting ex-ch
	Gnathion	gn	most inferior midline point on chin
Ears	Tragion	tL, tR	notch on upper margin of the tragus of the ear

Table 2.8 Pilot study test landmarks

Region	number	Landmarks
Eyes & forehead	7	enL, enR, exL, exR, g, n, tr
Nose	14	prn, sbalL, sbalR, sn, sn0R, sn0L, acL, acR, cL, cR, alL, alR, al0L, al0R
Lip	12	li, ls, chL, chR, cphL, cphR, cph0R, <cph>R, cph0L, <cph>L stoi, stos
Other	5	gn, tR, tL, chkR, chkL

2.6.1.3 Analysis

Three sets of landmark configurations produced for each model were aligned using a partial Generalised Procrustes technique (no scaling step was required and more than 2 models aligned) (Dryden & Mardia 1998). For each 3D landmark, the average of the x,y and z co-ordinates was calculated. The distance of each of the three repeatedly-placed points from their mean was calculated. Landmark placement error was expressed as the standard deviation of each landmark around its mean. This was defined as the square root of the average squared distance of the points from their mean in millimetres (mm) and represented the radius of the sphere of variability around a particular landmark. Landmarks with low values (<0.5mm) would be interpreted as being highly reproducible. Thus, landmark reproducibility would be quantified in millimetres.

2.6.1.4 Results

Landmark placement errors are shown in Table 2.9 below.

Table 2.9 Pilot study landmark placement error

	Pre-Op Model	Post-op Model	
Landmark	**Av St Dev(mm)**	**Av St Dev(mm)**	**Total**
enL	0.32	0.31	0.31
enR	0.39	0.36	0.37
sn0L	0.41	0.48	0.45
exR	0.41	0.52	0.47
exL	0.47	0.50	0.49
li	0.45	0.54	0.50
stoi	0.48	0.56	0.52
sn	0.51	0.53	0.52
sn0R	0.42	0.64	0.53
<cph>	0.55	Not marked	0.55
sl	0.56	0.55	0.55
chL	0.49	0.63	0.56
sbalL	0.71	0.44	0.58
ls	0.61	0.57	0.59
chR	0.65	0.55	0.60
cphL*	0.36	0.89	0.62
sbalR	0.67	0.61	0.64
cphR*	0.48	0.81	0.65
acL	0.82	0.70	0.76
stos	not marked	0.83	0.83
prn	0.94	0.74	0.84
acR	0.99	0.77	0.88
tL	1.11	1.17	1.14
tR	1.14	1.16	1.15
n	1.16	1.14	1.15
gn	1.42	1.00	1.21
cph0	1.27	not marked	1.27
al0L	1.27	1.59	1.43
al0R	1.64	1.36	1.50
cR	1.58	2.43	2.01
cL	2.01	2.08	2.05
chkR	3.09	2.15	2.62
chkL	3.02	2.92	2.97
g	2.49	4.43	3.46
tr	51.87	78.59	65.23

2.6.1.5 Discussion & Conclusions of Pilot study

The majority of landmarks had placement errors of 1mm or less, however 12 landmarks had placement errors in excess of 1mm. Some key landmarks such as nasion (n), right and left columella landmarks and alar crest outer landmarks had unacceptably high errors.

Eye landmarks were among the most reproducible (smallest errors). With the exception of the alare outer (al0) points, the landmarks that were least reproducible were located at the periphery of the face.

Four landmarks with exceptionally high errors (chk R&L tr and gn) proved to be the most difficult to digitise on a young infant's face due to the lack of anatomical structures to guide identification in these areas. The glabella (g) landmark did not exist as pneumatisation of the frontal bone is not well-developed in young infants (Markus, Delaire & Smith 1992). The landmarks around the chin were difficult to locate due to infant head position and varying degrees of development of head control. As a result, it was difficult to distinguish the lower border of the chin i.e. gnathion landmark (gn), particularly in the pre-op group. The trichion (tr) landmark could not be reliably identified as many of the infants did not have sufficient hair growth. The tragion of the ear (t) was poorly identified and often omitted from the model mark-up as it was not sufficiently visible. This was a problem of model quality around the ears and was related to the limitations of the 2 pod C3D^{TM} imaging system.

Two landmarks on the ala of the nose (al0R and al0L) were poorly reproducible and new definitions or alternative points were required in order to define this important area. In this pilot study, the position of the model during landmark identification was at the operator's discretion. Standardisation of the model in a particular position might improve operator ability to select the same point repeatedly, where landmarks were difficult to define anatomically. This has been noted with other systems such as laser scanning, which requires a consistent image view because surface measurements between landmarks tend to produce a larger difference if the correct position of the image on the screen is not selected (Aung, Ngim & Lee 1995). In order to reduce this possible source of error, the Facial Analysis Tool© was modified. A facility, which enabled standardised positioning of 3D models for each mark up, was developed and incorporated into the software package. Three points with low errors were first selected [both inner eye points (en - endocanthion) and a lip point (sl - sublabialis)]. A computer-generated plane passing through these points

was used to orient the model relative to the plane of the computer screen. When the model plane was parallel to the screen, this was termed the 'Face On' position. The model could then be oriented to a variety of standardised upward tilt positions (30, 45 and 60 degree) and left and right profiles. Descriptions of landmarks and techniques for locating them were refined. The model position, in which localisation of a particular landmark could be best achieved was defined as the 'standard position' for that point.

2.6.2 Landmark Reproducibility

2.6.2.1 Method

The method previously employed was repeated with some modifications. Landmarks were located in the same order each time with models in fixed, standardised positions. Four landmarks with exceptionally high errors (chk R&L tr and gn) were discarded. Ear landmarks (tragion R & L) were also discarded in favour of four new landmarks which defined the point of insertion of the helix of the ear (obs R&L, obi R&L). Eight additional new landmarks were added to the mark-up schedule (Table 2.10). These were anatomically defined points around the nostril (hnR&L; al0i R&L; al0o R&L) and two chin landmarks (m; pg). Forty-three landmarks were tested in this study (Table 2.11, overleaf).

Table 2.10 New Landmark definitions

Ears	Otobasion Inferius	obiL, obiR	point where earlobe inserts into facial skin
	Otobasion Superius	obsL, obsR	point where upper curve of helix inserts into facial skin
Nose	High point, nostril	hnL, hnR	highest point of nostril on inner margin
	Alare Inner	al0iL, al0iR	midpoint between sbal and c, on inner margin of nostril
	Alare Outer	al0oL, al0oR	point on outer aspect of each ala opposite Al0i
Other	Menton	m	lower border of the chin, in midline
	Pogonion	pg	most anterior point in midline of the chin

Table 2.11 Reproducibility study test landmarks

Region	number	Landmarks
Nose	12	prn, sbalL, sbalR, sn, sn0R, sn0L, acL, acR, cL, cR, alL, alR
Lip	10	li, ls, chL, chR, cphL, cphR, cph0, <cph>, stoi, stos
Eye & forehead	6	enL, enR, exL, exR, g, n
Other	1	gn
New landmarks	12	hnR, hnL, al0iR, al0iL, al0oR, al0oL, obsR, obsL, obiR, obiL, m, pg

2.6.2.2 Results

Average placement error across all models and landmarks was 0.63mm, after modifications to the Facial Analysis Tool. Errors for individual landmarks are displayed in Fig 2.16.

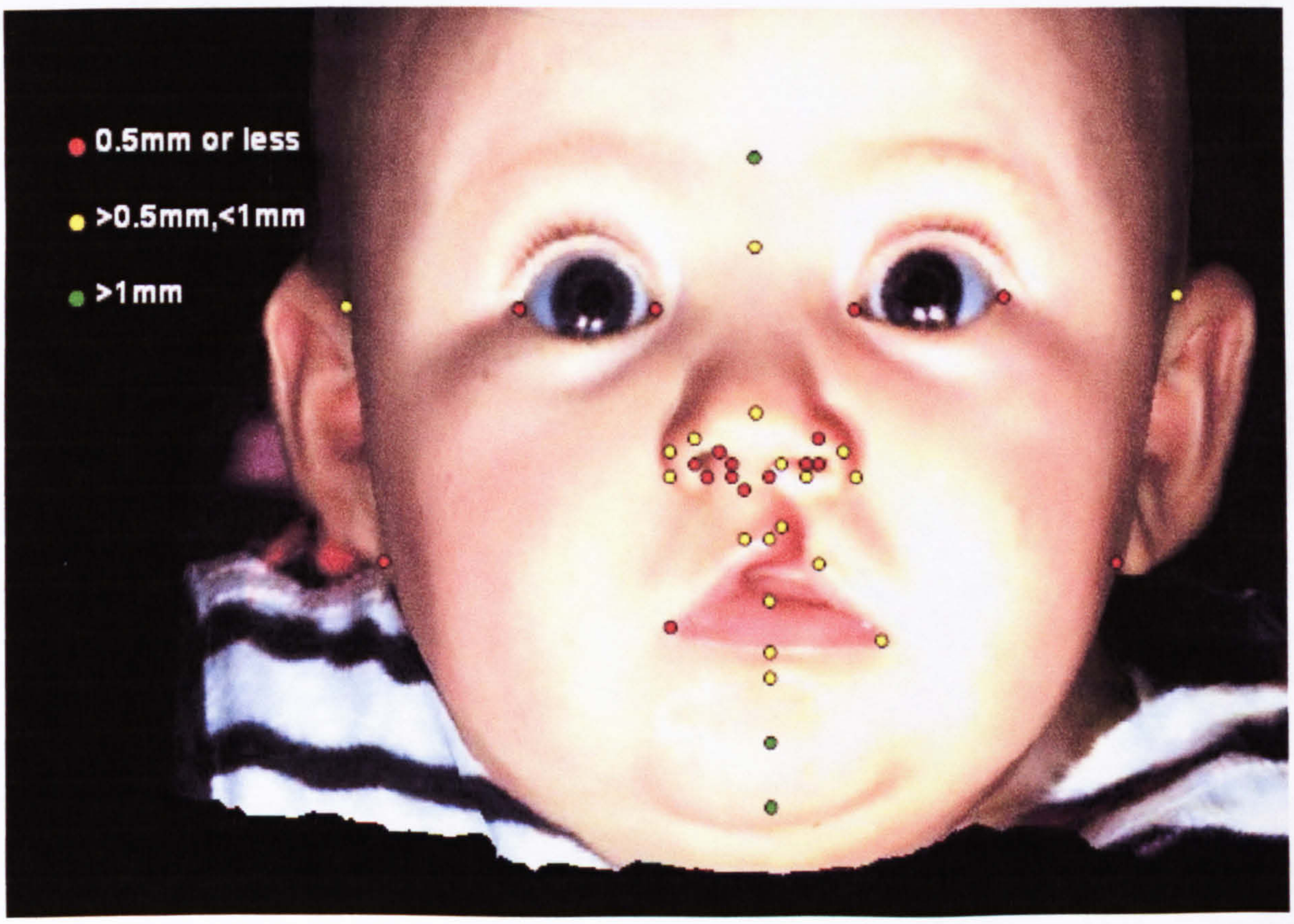


Figure 2.16 Landmark placement errors

Forty landmarks were reproducible, with placement errors of 1mm or less (Table 2.12 overleaf). Eighteen landmarks had placement errors of 0.5mm or less and only three landmarks exceeded 1mm. The new landmarks were among those with the lowest placement errors, with the exception of the chin landmarks (m, pg). Average placement error appeared to be lower for the pre-op models than for the post-op models, however, a t–test showed that this difference was not significant (p=0.26).

Table 2.12 Landmark placement errors (reproducibility)

	Pre-Op Model	Post-op Model	
Landmark	Av St Dev(mm)	Av St Dev(mm)	Total
enR	0.25	0.25	0.25
hnL	0.33	0.24	0.27
cR	0.28	0.31	0.30
sn0R	0.24	0.36	0.30
al0iR	0.34	0.26	0.30
enL	0.33	0.28	0.30
exR	0.37	0.31	0.34
hnR	0.34	0.38	0.36
al0oL	0.36	0.40	0.38
exL	0.34	0.43	0.39
sn0L	0.35	0.46	0.41
obiR	0.27	0.53	0.42
sbalR	0.39	0.45	0.42
al0iL	0.46	0.44	0.45
sn	0.58	0.38	0.47
obiL	0.58	0.43	0.48
cphL	0.54	0.49	0.49
chR	0.39	0.60	0.50
sbalL	0.53	0.49	0.51
al0oR	0.39	0.62	0.51
chL	0.53	0.50	0.52
stoi	0.54	0.50	0.52
obsL	0.54	0.52	0.52
cphR	0.45	0.59	0.53
ls	0.62	0.46	0.54
cL	0.63	0.47	0.55
li	0.54	0.62	0.58
prn	0.69	0.55	0.62
sl	0.72	0.63	0.67
cph0L	0.68	Not marked	0.69
n	0.71	0.77	0.74
<cph>L	0.75	Not marked	0.75
stos	Not marked	0.755	0.76
alL	0.66	0.92	0.78
acL	0.58	1.06	0.82
cph0R	0.88	Not marked	0.88
<cph>R	0.91	Not marked	0.91
alR	0.65	1.20	0.92
acR	0.68	1.12	0.93
obsR	0.95	1.02	0.99
pg	0.83	1.34	1.09
m	1.14	1.62	1.39
g	1.25	4.08	2.74

2.6.2.3 Discussion

Some studies (Kohn, Cheverud, Bhatia et al. 1995; Yamada, Suguhara, Mori et al. 1998), quote their landmark reproducibility as an average for landmarks across the whole face. In the context of measurement of soft tissue parameters, mean placement errors averaged over all landmarks is not a meaningful figure. In this study, some landmarks had smaller errors than others (range 0.25mm to 2.74mm). Three dimensional landmark placement errors associated with laser scanning of the face in adults, were reported as ranging from 1.0 to 2.5mm (Coward, Watson & Scott 1997). As landmarks form the basis of this anthropometric and 3D advanced morphometric analysis, it was considered important to have confidence that manually identified landmarks were as reliable as possible. In the infant cleft face, facial measurements are relatively small and some changes after surgical repair may be subtle, yet clinically significant. Therefore, accuracy in landmark digitisation is mandatory. Confidence in the ability to detect these differences was demonstrated by the accuracy with which anatomical landmarks that could be located on a cleft infant face. Despite system modifications, however, a proportion of landmarks demonstrated residual placement errors of more than 0.5mm. This should be taken into consideration when interpreting the results of surgical changes.

2.6.2.4 Conclusions

The modifications to the landmark location tool (FAT©) and method resulted in a greater proportion of landmarks with acceptable placement errors. Eighteen of these landmarks could be reliably identified on 3D models of infants with pre-op cleft lip and palate and post-op models, with a placement error 0.5mm or less. Menton point (m) and glabella point (g) were discarded from the full analysis as the placement errors associated with these points were unacceptably large.

2.6.3 Landmark Method development

Manual placement errors can be further reduced by increasing the number of times that the points are marked on the models and averaging the results (Houston 1983; Houston, Maher, McElroy et al. 1986). Repeat digitisation of landmarks on multiple occasions (n) would reduce the standard deviation (S) of the mean. With multiple placements of landmarks, the standard error of the mean reduces. In order to bring the placement error (S) for each landmark down to within the acceptable target of 0.5mm in the main study, the

number of times (n) a landmark would require identification was determined according to the formula **S/√n.** Table 2.13 shows the landmark subsets and the number of repeated identifications required:

Table 2.13 Landmarks and number of repeated digitisations required

Error level (mm)	No. repeat placements	Landmark subset
≤ 0.5	**1**	enR, enL, exR, exL, hnR, hnL, cR , cphL, sbalR, sn0R, sn0L, al0iR, al0iL, al0oL, obiR, obiL, sn, chR
0.51 – 0.70	**2**	sl, cphR, ls, stoi, li, chL, sbalL, al0oR, cph0L, prn, cL, cphR, obsL, chL
0.71 – 0.86	**3**	n, alL, <cph>L, stos, acL
0.87 – 1.09	**4**	acR, acR, <cph>R, cph0R, pg, obsR

The models used in this pilot study were also utilised in the main study. However, in the main study, landmark identification was repeated according to the new mark-up criteria and new sets of landmark data were extracted.

2.6.4 Conclusions of Clinical Development and Landmark Reproducibility studies

The Facial Analysis Tool© was modified to improve landmark reproducibility. A 'standardised position' facility was added to allow consistent orientation of models during landmark identification. Anatomical landmarks could be reproducibly located on photorealistic C3D™ models of infants with cleft lip and palate. A core set of 41 landmarks was defined within the Facial Analysis Tool© and the protocol for landmark location finalised. In the main study, repeated identification of some of landmarks up to 4 times would be necessary to reduce the desired level of error for each individual landmark to 0.5mm or less.

Before starting the main study, the following hardware modifications were implemented: The camera rig was secured to the floor and black tape visual markers added to the walls and floor in the imaging room to delineate the 'ideal' position of the chair and subject. A light-based positioning system was added to the camera set up to assist with correct subject positioning in the camera fields. Flash illumination was optimised for facial skin photography.

3 Methods

3.1 Study Design

3.1.1 Ethical approval & consent

Ethical approval was granted from North Glasgow Hospitals Trust and the Royal Hospital for Sick Children, Yorkhill local ethics committees. Written consent was obtained from parents for the participation of their children in the study and the use of data and images for publication / presentation purposes (Appendices 1&2)

3.1.2 Criteria for Inclusion in the Study

Children were invited to participate in the study if they fulfilled the following criteria:

1. New or recently diagnosed, unrepaired unilateral cleft lip (UCL) - no secondary palate involvement

   OR

   New or recently diagnosed, unrepaired unilateral cleft lip and palate (UCLP)
2. White
3. Resident in Scotland at commencement of study
4. No associated anomalies
5. Cleft condition not associated with a recognised syndrome

3.2 Clinical Protocols

3.2.1 Surgical Techniques

Surgical repair in Scotland is carried out according to nationally agreed CLEFTSiS (Managed Clinical Network for Cleft Lip and Palate Services in Scotland) protocols on timing and surgical technique. Procedures are tailored to individual cases, and the variation in cleft severity requires a degree of flexibility in surgical approach. Children in this study underwent a combination of procedures appropriate to the nature of their cleft defect.

- Cleft lip was repaired by the modified Millard Rotation Advancement procedure with a limited lateral (alar sill/crease) incision. Muscle dissection and reconstruction was a distinct part of the procedure and subperiosteal dissection was limited to that which allowed minimum tension across the repair.
- Where the cleft extended into the nasal floor and primary or secondary hard palate, this was closed via a single layer or two-layer procedure or a vomer flap (Oslo method).

- Primary nasal correction was performed depending on the severity of the deformity of the nose according to the McComb principal.
- Closure of the hard palate was carried out via a midline technique (Veau Wardill) or Furlow double-opposing Z-plasty. Releasing incisions (Von Langenbeck) were avoided where safe to do so.
- An Intravelar Veloplasty was used to repair the soft palate as a distinct procedure.

3.2.2 Timing of surgery

Primary repair of the lip and nose was planned for approximately 3 months of age, followed by palate closure at 9 months, according to CLEFTSiS nationally agreed protocols. The surgical timings and procedures for children in this study were documented and verified with reference to locally held Cleft Team computer records and the nationally administered CLEFTSiS Audit database.

3.3 Sample

3.3.1 Identification & Recruitment

New cleft births were identified through Cleft Support Nurses in two Cleft Centres (Glasgow and Edinburgh), and Speech and Language Pathologists involved in the Cleft Teams in Glasgow and Aberdeen. Secretaries to the plastic and paediatric surgeons in Glasgow and Edinburgh provided information about timing of planned surgery. Further children were identified via date of birth and postcode from the SCALP Database / CLEFTSiS Register held in Perth Royal Infirmary, Scotland, the Patient Information Management System (PIMS) and "new baby" Cleft Registration Book held in the Oral Orthopaedic clinic, at Glasgow Dental Hospital.

A letter explaining the nature of the project and an invitation to participate was sent to the family of each child who was identified as eligible for inclusion in the study (Appendix 2). Parents were asked to return a tear-off slip for consent to take part using an enclosed stamped addressed envelope. On receipt, parents were contacted by telephone or in person when they attended The Joint Cleft Clinic at the RHSC, Yorkhill, or Oral Orthopaedic clinic appointments at Glasgow Dental Hospital. Appointments for image capture were arranged at the Dental Hospital or RHSC, as appropriate, and confirmed by letter (Appendix 2).

Families who failed to return the consent slip were contacted by telephone and invited to participate. When children were recruited via this route, consent forms were signed at the first capture appointment. Follow-up appointments were provisionally arranged with parents and noted in a diary kept in the imaging room at Glasgow Dental Hospital. Parents were contacted by telephone and a confirmation letter was sent out to parents 2 weeks before the next capture was due (Appendix 2).

3.3.2 Classification of socio-economic status

The Carstairs & Morris Index of Deprivation is a measure of socioeconomic deprivation commonly used in Scotland, and is based on four census variables which represent material disadvantage (Carstairs & Morris, 1991). These indicators are overcrowding, male unemployment, lack of car ownership and head of the household being in social class 4 or 5. Variables are combined to give a deprivation score for each postcode area in Scotland. From this, seven categories (DEPCATs) are derived which range from most affluent (DEPCAT 1) to most deprived (DEPCAT 7) (McLaren & Bain 1998). Distribution of the Scottish population by DEPCAT based on the 1991 census was reported by McLoone (1994) (Appendix 3). The DEPCAT distribution of cleft children in this study was compared to that of the Scottish population. In addition, DEPCAT distribution by cleft type was examined.

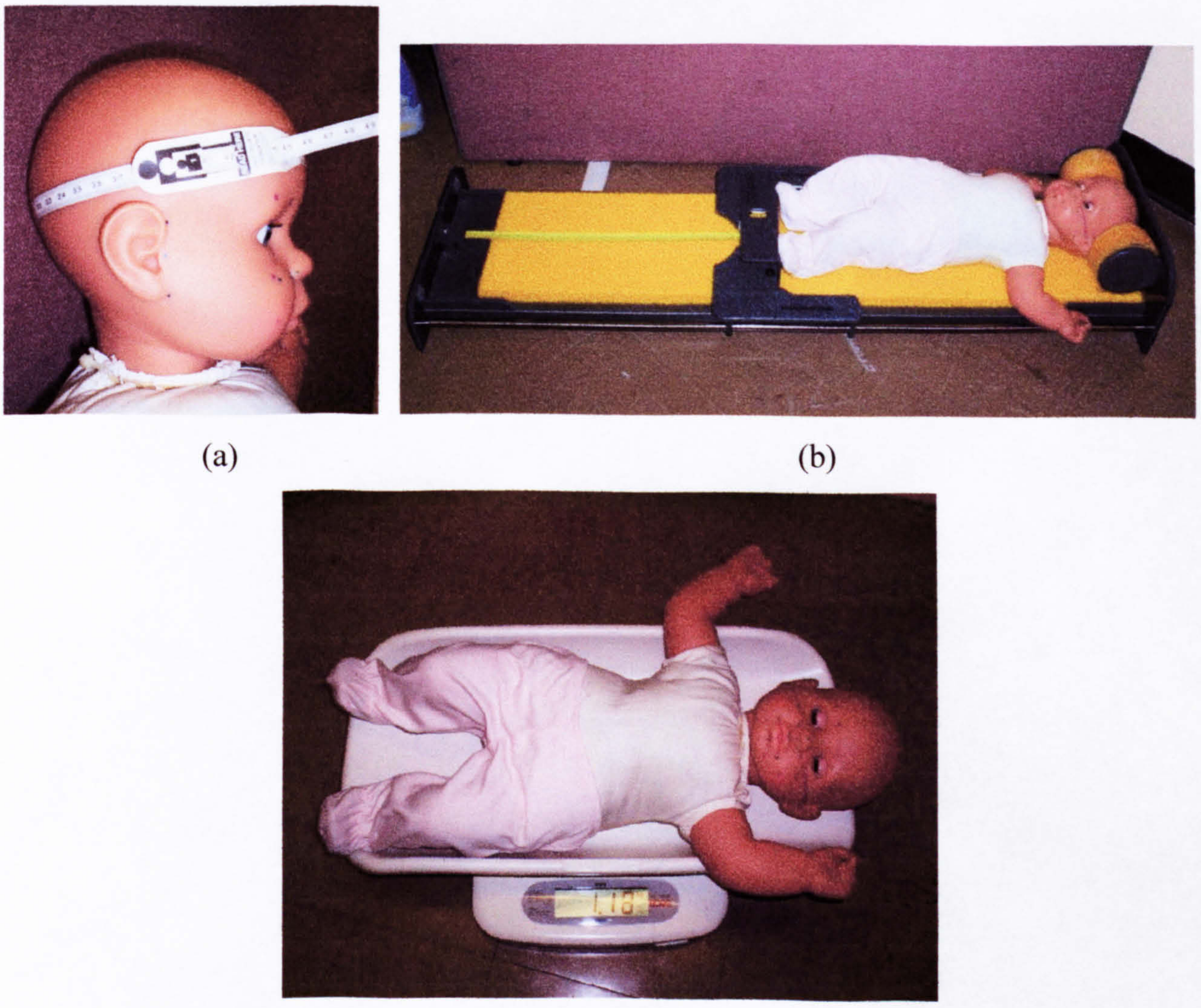
3.4 Imaging / Capture Protocol

The imaging protocol was designed to fit around the surgical protocol. 3D images were planned at four time points:

Pre-op	prior to primary lip/nose repair and as close to 3 months as possible
Post-op	age 6 months, or within 2 months of primary lip/ nose repair
1 Year	within age range 10-14 months
2 Years	within age range 20-28 months

3.5 Data Collection

3.5.1 Somatic Data Collection



(a) (b)

(c)

Figure 3.1 (a) Head circumference measurement with plasticized tape. (b) Infant length measurement on Kiddimetre device. (c) Infant weight measurement on electronic scales

A clinical auxologist from The Royal Hospital for Sick Children, Yorkhill, Glasgow provided hands-on training in current infant measuring techniques and equipment use. The methods used were those recommended by the UK90 cross-sectional reference data growth charts (Child Growth Foundation 1996, Appendix 5&6). Head circumference was measured with a Lasoo© plasticized paper measuring tape, to the nearest millimetre. The tape was positioned such that it lay on the forehead, midway between the hairline and eyebrows, and wrapped around the occipital prominence at the back of the head (Fig.3.1a). Infant length was recorded in the supine position using a Kiddimetre© measuring device (Fig 3.1b). The infant was positioned against the fixed headboard with the legs straight and the heel of the foot contacting the moveable footboard. Measurements were read off the

integral gauge and recorded to the nearest millimetre. Infant weights were recorded to the nearest tenth of a kilogram with digital weighing scales (Seca 835, Seca Vogel und Halke GmbH &Co, Germany) (Fig 3.1c). The scales were first calibrated to zero with a custom baby cradle attached, and preoperative and post-operative babies were weighed supine, without nappies. Light clothing was permitted. At 1 year and 2 years, children's shoes and outdoor clothing were removed and they were invited to sit, or stand on the scales following removal of the cradle, and re-calibration to zero. Infant height, weight and head circumference were recorded, compliance permitting, at each capture session.

3.5.2 Facial Data Collection

3.5.2.1 C3D System

The C3D system previously described (Chapter 2), was configured for facial imaging in children and used to obtain three-dimensional facial data for analysis.

3.5.2.2 C3D System Calibration Process

A calibration process determined the detailed geometric configuration of each of the six cameras used (2 black & white and one colour camera on each pod) to image the subject. The internal geometry of the cameras and their positions relative to each other is derived from multiple images of a calibration object of accurately known dimensions in different positions.

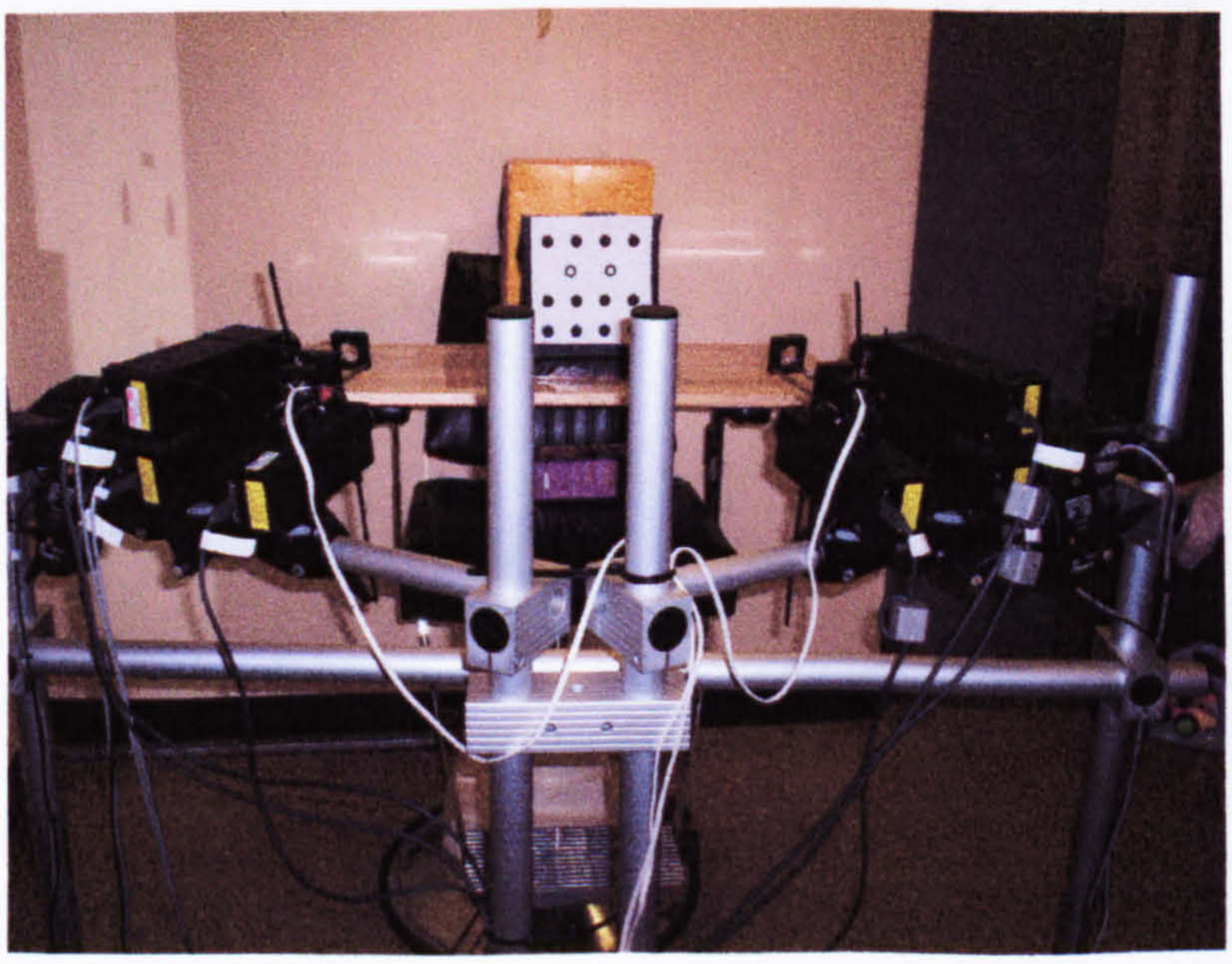
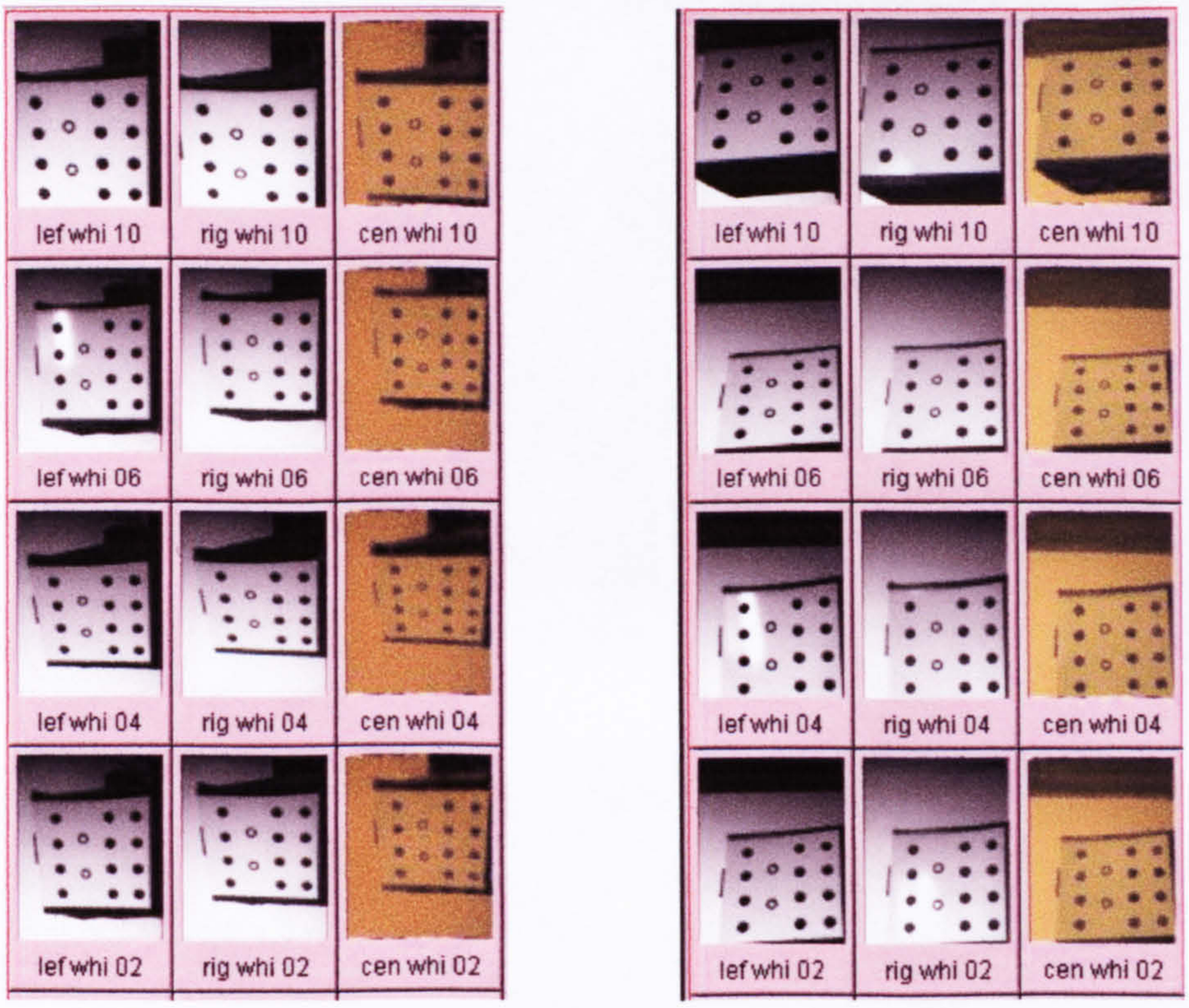


Figure 3.2 Camera rig and calibration target in central position



(a) (b)

Figure 3.3 (a) Calibration images Right camera pod. (b) Calibration images Left camera pod

At the start of the capture session, a calibration plate was imaged in four different positions within the image-target zone (Fig 3.3 a&b), and a calibration file was built using C3D software. A calibration value was produced and noted. A 'poor' calibration value indicated problems with the internal parameters of the cameras such as poorly adjusted focus. The calibration file was saved in the same folder as the subsequent child capture data. At the end of the session, the process was repeated and a 'check calibration' performed to compare the first and second calibration files. Any discrepancies resulting from intrinsic changes in the imaging set-up due to vibration, accidental bumping of the camera rig during the course of the imaging session, etc resulted in a 'poor' check value. Once satisfied that there were negligible differences, the original built calibration file was attached to each set of subject images and the entire session saved to a CD.

3.5.3 Subject Image Capture Method

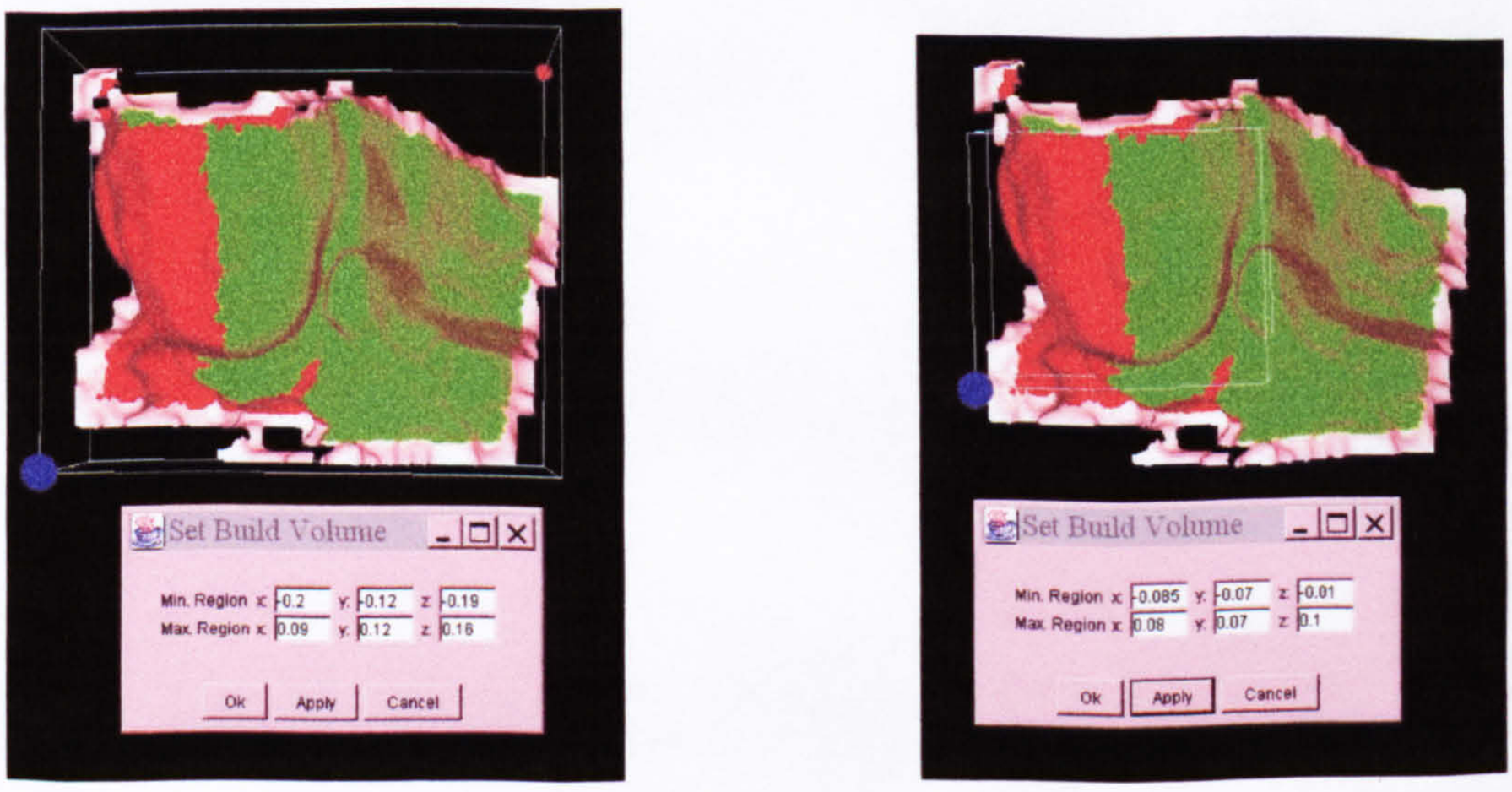
A parent or accompanying adult sat in the dental chair, with the infant on their lap, in the centre of the C3D set-up. Slit lamp location devices were used to standardise the position of the infant in the imaging field and ensure that the subject was visible in all six cameras simultaneously. Infants were photographed at rest, looking slightly upwards towards the operator, in order to capture the submandibular area.

Figure 3.4 Child seated on parent's lap in centre of C3D setup at Glasgow Dental Hospital

Images were captured under standardised lighting conditions. After gaining the child's attention, at least 6 sets of facial images with facial expression at rest (minimal muscle activity), were captured in the same session.

3.5.4 Data Processing

3D models with attached calibrations were built at low resolution (0.005 voxel size) from the best quality image sets. The desired models were edited (Fig 3.5 a&b) to remove extraneous background material and built at high resolution (0.002 voxel size). The best quality, high resolution model for each individual was exported into Virtual Reality Modelling Language format (VRML), in preparation for landmark identification.

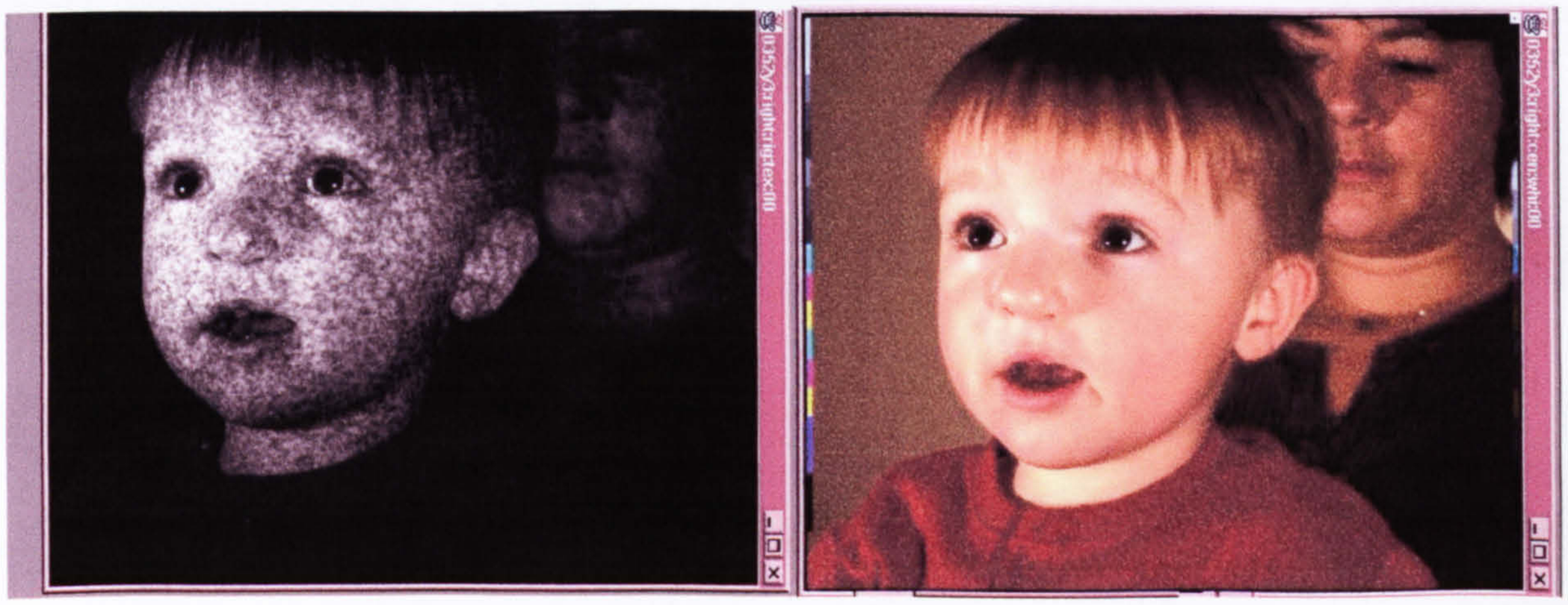


(a) (b)

Figure 3.5 Model editing to remove excess data, prior to rebuild at high resolution; (a) low resolution model pre-edit; (b) after build volume parameters edited

3.5.5 Selection process

Quality checks were performed at every stage from image acquisition through to final 3D model. The quality of the images captured was assessed as each set of images was captured. The child's entire face had to be visible in the frame and the images crisp, with the projected speckled pattern in sharp focus (Fig 3.6 a&b). Image sets which failed to satisfy these criteria were rejected.



(a) (b)

Figure 3.6 (a) Speckled texture in sharp focus (b) Colour image in sharp focus

3D range data was examined for smoothness and integrity. Models were subjectively assessed with reference to the Range Quality Index (Section 2.5.1.4). Evidence of intrinsic or extrinsic movement (blinking, changes in facial expression during image capture, etc) was detected after applying specially written 'Check-align©' software. This programme allowed the operator to compare images from a single pod and check that no movement occurred in the interval between recording of monochrome and colour images. The final part of the selection process involved examination of the integrity of the colour texture map. Good coverage all round face from ear to ear and under chin was desirable. The facial features should be clearly visible, with no blurring, holes or dragging e.g. distinct nostril shape.

3.5.5.1 Summary of Criteria for 3D model selection

1 Subject in optimal position in frame.

2 Facial expression - at rest

3 Texture pattern sharply focussed on R&L black and white images

4 Colour images not overexposed, sharply focussed.

5 Calibration error (0.09 pixels or less)

6 Check calibration (0.09 pixels or less)

7 Low resolution-built model - red/green data clearly demarcated. No holes in model.

8 Range data smooth, no holes, facial features visible.

9 Check-align programme - no gross or fine movement between image capture.

10 Colour mesh, undistorted, no holes, no dragging.

3.6 Facial Data Extraction

3.6.1 Landmark Identification

The Facial Analysis Tool consisted of a custom software package which allowed 3D model manipulation and analysis on the computer screen, as previously described. When loaded, models were simultaneously displayed in the profile view and in the 60 degree tilt position in the auxiliary windows (Fig 3.7).

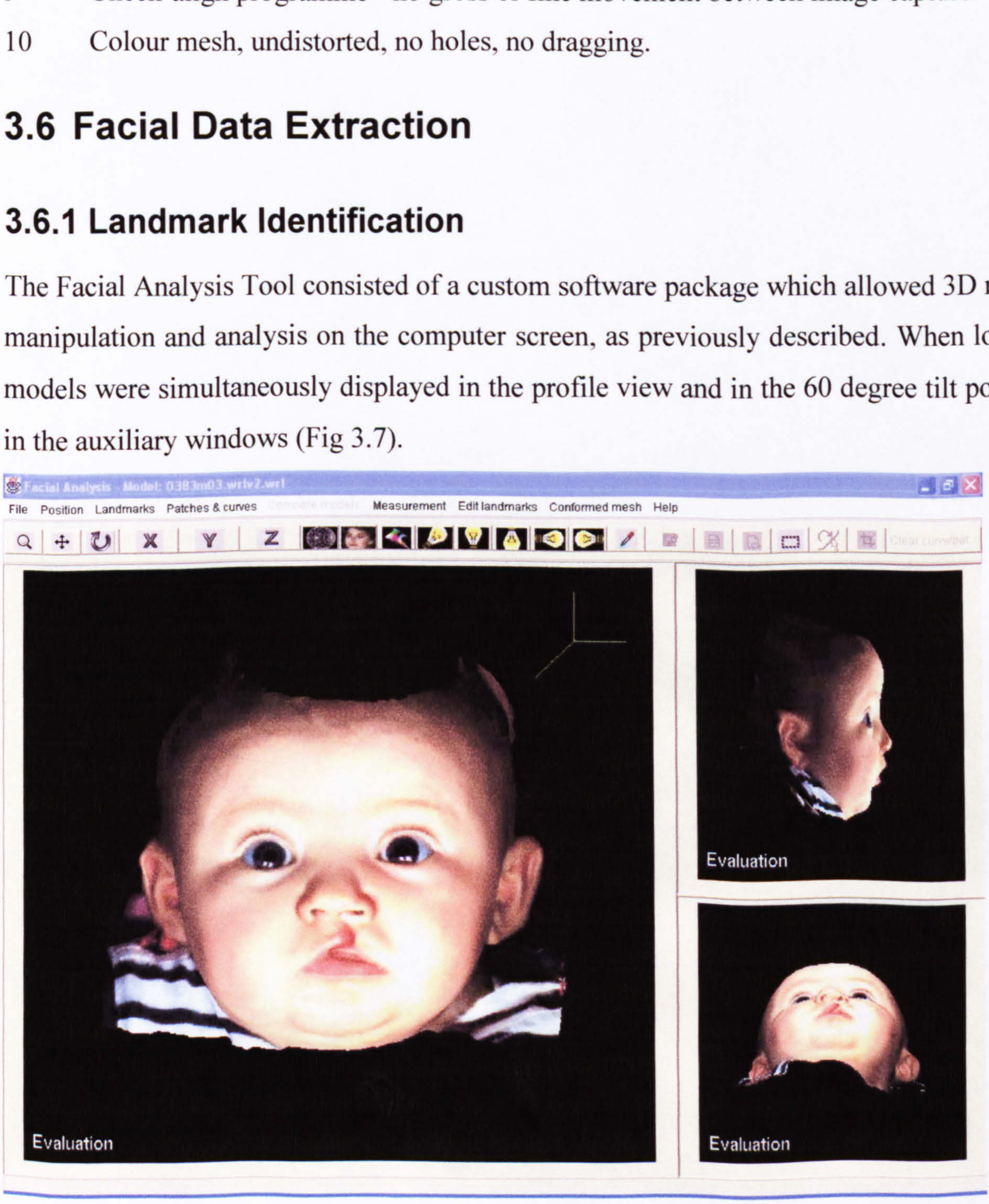


Figure 3.7 Facial Analysis user screen showing main and auxiliary views

3.6.2 Standard Positions

The 'set standard position' facility was used to standardise the position of the model in the main window, in readiness for landmark identification and manipulation. Two eye landmarks (enR, enL) and a lip landmark (sl) were selected on the model. When these were saved, Facial Analysis Tool re-orientated the model such that these three landmarks lay on the same plane. In the 'Face-on' standard position, this plane was parallel to the computer screen. (Fig 3.8a). The researcher was able to manipulate the model and re-orientate it to improve landmark digitisation. Other standard positions: 30 degree tilt (Fig3.8b); 45 degree tilt; 60 degree tilt (Fig 3.8c); left and right profiles (Fig 3.8 d&e) could be selected to facilitate and standardise landmark digitisation.

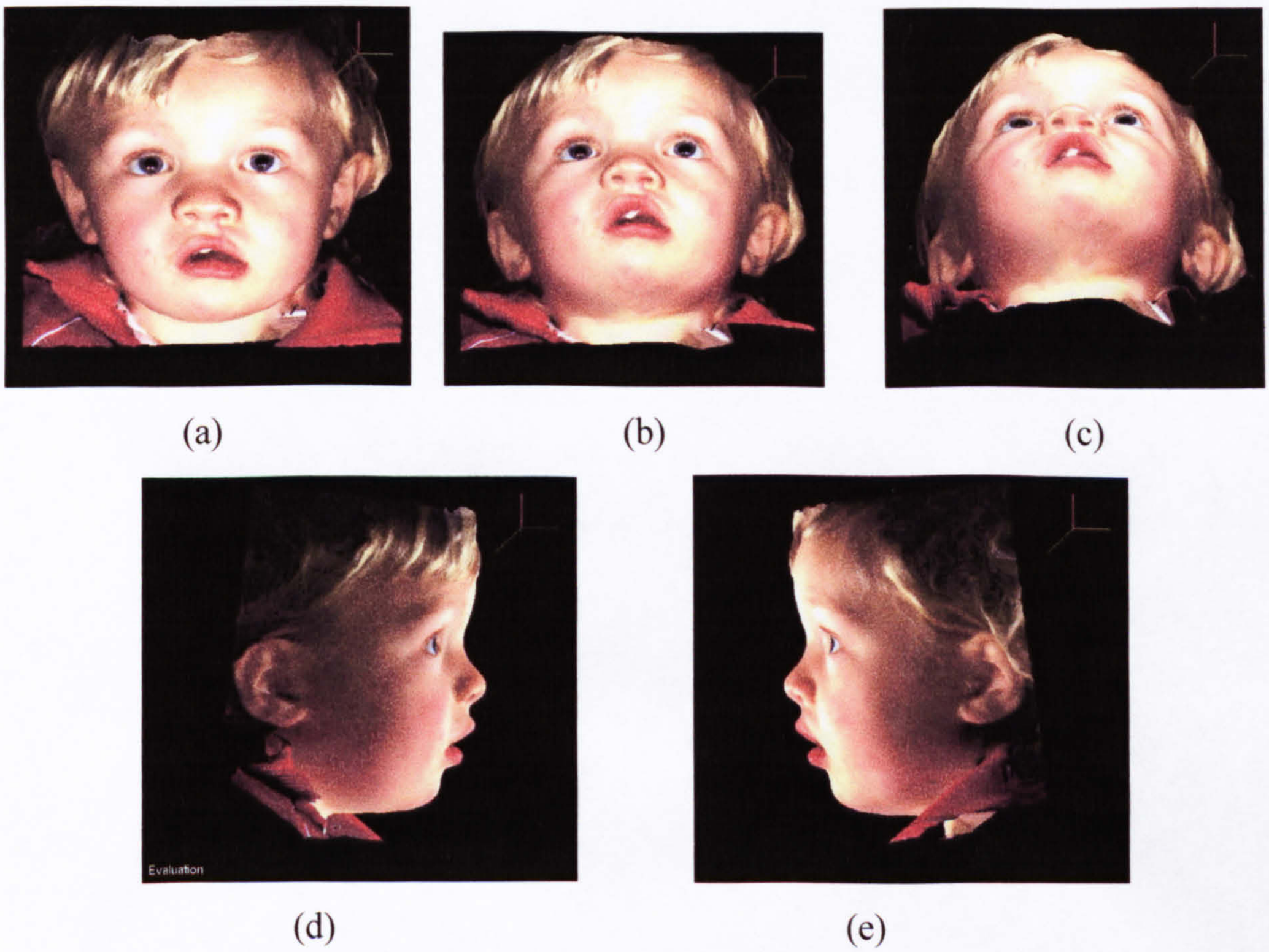
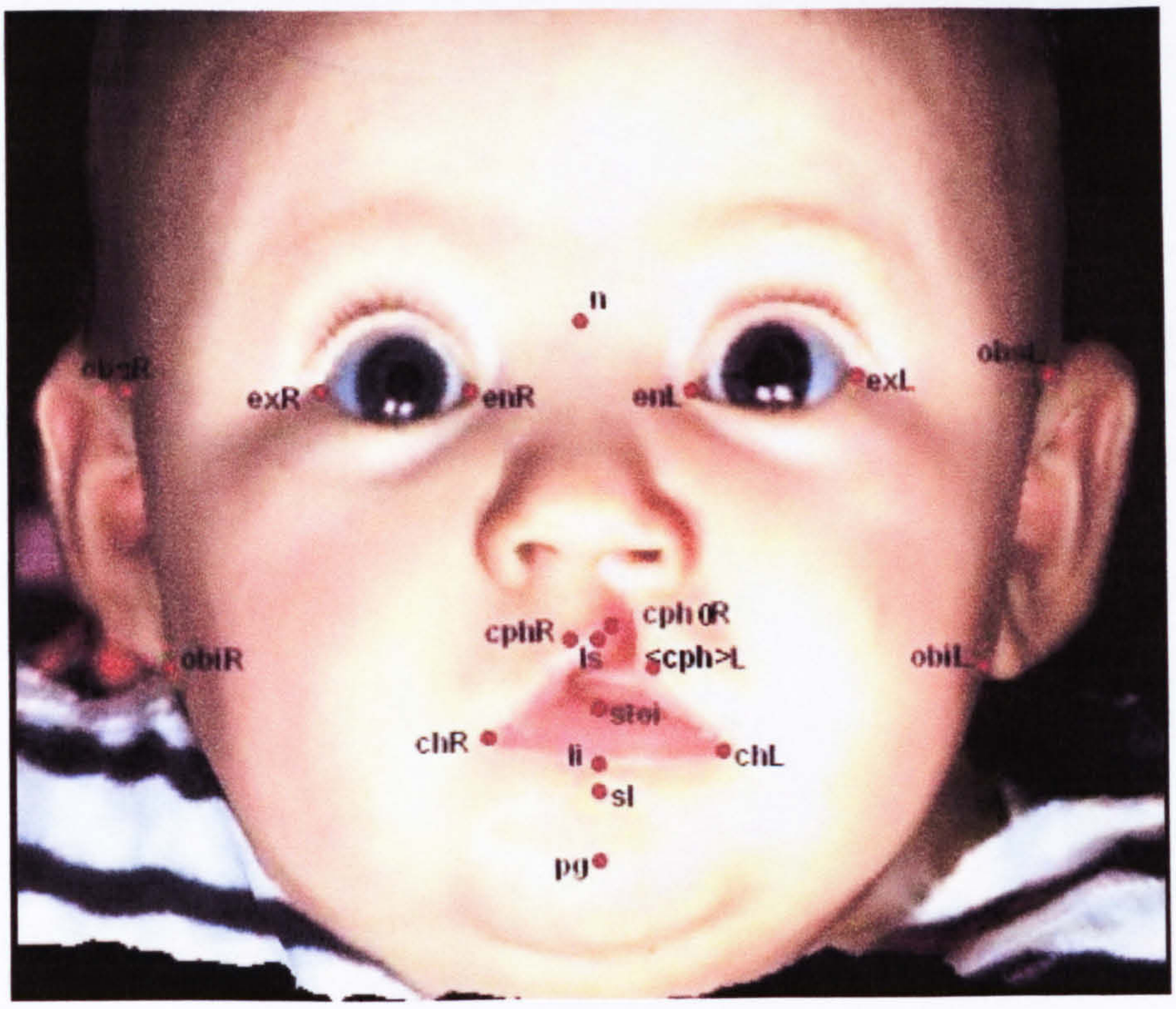


Figure 3.8 Facial Analysis Tool Standard Positions (a) Face on (b) 30° tilt (c) 60° tilt (d) Right profile (d) Left profile

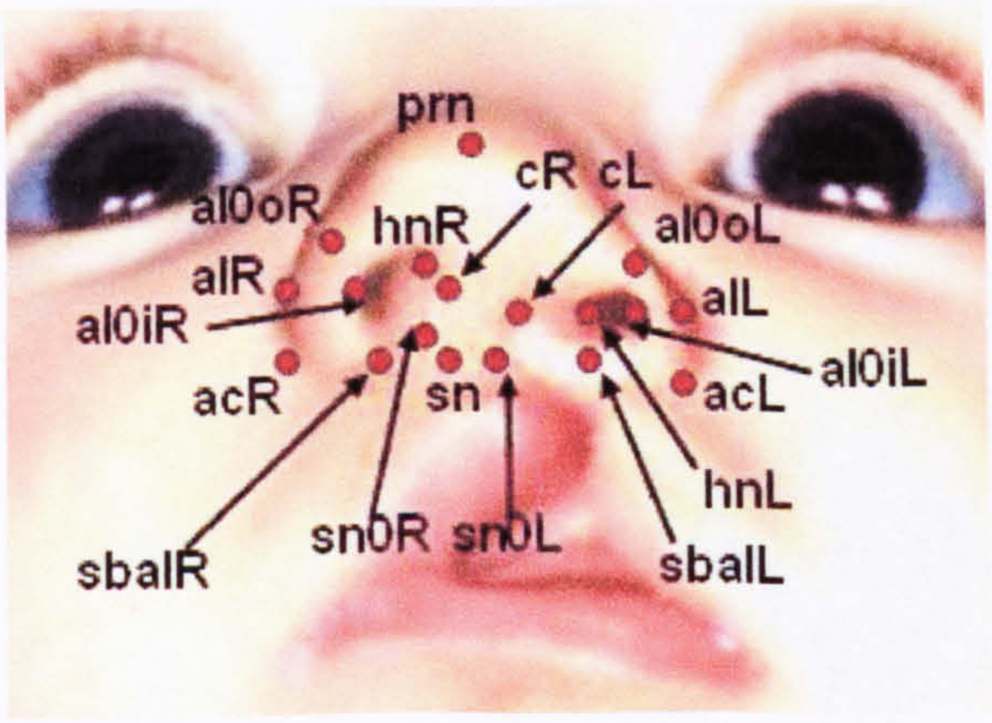
Selection of landmarks generated a set of x, y, z co-ordinates, which described the spatial orientation of facial features. Anthropometric landmarks were identified according to the definitions in Table 3.1. Each landmark was selected on screen using the computer mouse, with the model in the standard position for that landmark. Landmarks for pre-op models are illustrated in the photo key on page (Fig 3.9).

Table 3.1 Landmark definitions (Mark up method)

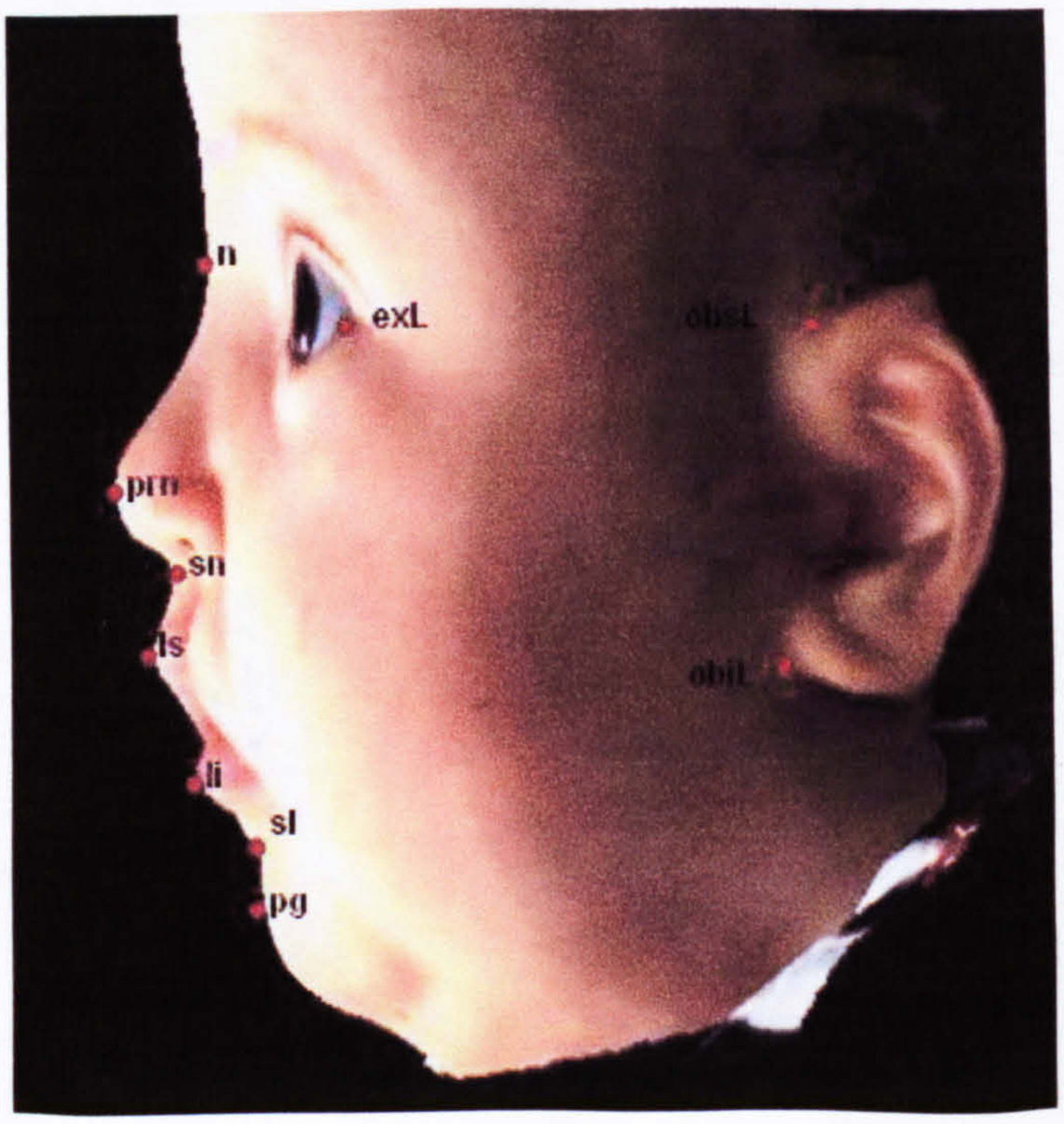
standard position	symbol	landmark	location method &definition
Face on	enR enL	endocanthion	lower & innermost point at junction between upper and lower lids
	exR exL	exocanthion	outer skin junction, where upper lid meets lower. Most lateral extent of lower eyelid
	n	nasion	midline between & slightly above en-en, maximum concavity of nasal bridge,in profile
	li	labiale inferius	lowermost midline point on vermillion
	chL chR	cheilion	most lateral extent of vermillion border of lower lip
	cphR cphL	crista philtri	point at lowermost extent of philtral ridge, junction of white roll and vermillion of upper lip
	ls	labiale superius	point at maximum concavity of philtrum, junction of white roll and vermillion of upper lip
	cph0R cph0L	crista philtri surrogate on major segment	estimated. On major segment adjacent to cleft. Same distance from cph-ls on non-cleft side; pre-op only
	<cph>R <cph>L	crista philtri surrogate on minor segment	estimated. On minor segment adjacent to cleft. Same distance from ch-cph on non-cleft side; pre-op only
	stos	stomion superioris	post-op only. Point on lowermost extent of vermillion border of upper lip, in midline
	stoi	stomion inferioris	point on upper margin of vermillion of lower lip, in midline
	sl	sublabialis	point of maximum concavity at lowermost extent of lower lip skin, in midline. In profile, trace profile of chin and mark point where normal changes direction
	pg	pogonion	most anterior point in midline of chin, marked with normal perpendicular to frontal plane in profile view
60 degree tilt	prn	pronasale	most prominent point on nose tip selected where normal is perpendicular to frontal plane in profile view
	sbalR sbalL	subalare	point where inner rim of nostril joins upper lip skin. Where this is a wide area lower-most point on curve
	sn	subnasale	midpoint of columella, maximum concavity at junction of lip skin and columella, in profile view
	sn0L sn0R	edge of columellar base	narrowest & lowest point of columella on inner nostril margin / most lateral aspect of columella
	acR acL	alar crest	most lateral point of nose in groove between ala and facial skin
	cR cL	columella	highest point of the columella (reflected onto nostril): where nostril starts to curve round
	hnR hnL	high point nostril	highest point of nostril on inner margin
	alL alR	alare	point of maximum convexity of ala on the alar ridge. Confirm in birdseye view
	al0iL al0iR	alare inner	mid-point on inner margin of nostril, between sbal and c
	al0oL al0oR	alare outer	point on outer ala, opposite al0i point
Profile	obsR obsL	otobasion superioris	point where upper curve of helix inserts into facial skin
	obiR obiL	otobasion inferioris	point where earlobe inserts into facial skin



(a)



(b)



(c)

Figure 3.9 Photo keys for landmark identification pre-op. (a) Upper face & eye, lip, ear and lower face landmarks (b) Nasal landmarks (c) Profile view

Pre-op and post-op model landmarks differed in the lip region. Surrogate lip landmarks created to define the cleft area (<cph>R & <cph>L and cph0R & cph0L) did not exist on post-op models. Table 3.2 summarises the lip landmarks for each type of model.

Table 3.2 Lip Landmark Mark-up

Pre-op models		Post-op models
Right Cleft	**Left Cleft**	**All Clefts**
li	li	li
chL	chL	chL
chR	chR	chR
cphL	cphR	cphR
ls	ls	ls
cph0L	cph0R	cphL
<cph>R	<cph>L	stos
stoi	stoi	stoi

Landmarks were systematically identified on the 3D models, in the same sequence. The entire set was identified once, followed by identification of three further subsets of landmarks. Table 3.3 shows the subsets of landmarks that required repeated location and the number of repetitions necessary to achieve 0.5mm or less placement error.

Table 3.3 Landmark subsets for repeated location

Repetition	Landmark subset
2	sl, cphR, ls, stoi, li, chL, sballL, al0oL, obsL
3	n, alR, alL, cph0R, cph0L
4	acR, acL, <cph>R, <cph>L, pg, obsR

Four landmark files were generated for each model and merged using a specially written computer programme, which averaged repeat landmark co-ordinate values. The resultant merged file contained the working 3D (x,y,z) co-ordinate data for an individual, at a particular time-point and could be re-called and displayed on the 3D model (Fig 3.10).

Figure 3.10 Merged landmark file displayed on 3D model

3.7 Data storage

Subject data was identifiable by a coded file naming system. Names, personal details and somatic data were stored in an Access database written for the purpose of the study by the University of Glasgow Statistics Department. Identifiable information was stored separately from the 3D model data. Data were stored on CD.

3.8 Data Processing

3.8.1 Missing data

All global landmark co-ordinate files were checked for missing data. Where a landmark was accidentally omitted, the model and landmarks were re-displayed and the missing landmark identified. The new co-ordinate file was then saved.

3.8.2 Facial Dimensions

A core set of facial measurements was developed from the direct and indirect anthropometric studies of Farkas (1990), Hurwitz et al. (1999), and Duffy et al. (2000) (Table 1.4, continued overleaf).

Table 3.4 Linear distances, angles and ratios

Measurement	Landmarks
Upper face & Eyes	
Biocular width	exL-exR
Intercanthal width	enL - enR
Ocular width	exL -enL exR -enR
Endocanthion to nasion	enL -enL enR -enR
Nose	
Horizontal Dimensions	
Alar base width	sbalL-sbalR
Anatomic nose width	acL-acR
Soft nose width	alL-alR
Nasal tip horizontal displacement (angle)	acR-prn-acL
Vertical dimensions	
Nose dorsum length	n-prn
Nasal tip-base	sn-prn
Nasal tip angulation	n-prn-sn
Alar Wing	
Projective alar length	acL-prn acR-prn
Alar wing angulation	acL-prn-sn acR-prn-sn
Columella	
Columella height	sn0L-cL sn0R-cR
Columella thickness	sn0L-sn0R
Columella angulation	sbalL-cL-sn0L sbalR-cR-sn0R
Nostril	
Nostril floor width	sbalL-sn0L sbalR-sn0R
Nostril long axis	sbalL-cL sbal-cR
Nostril width	sn0L-al0iL sn0R-al0iR
Nasolabial angle	prn-sn-ls
Protrusion of upper lip, relative to nasal base	ls-n-sn

Table 3.4 (continued) Linear distances, angles and ratios

Nasolabial Dimensions		
Alar base to corner of the mouth		sbalL-chL sbalR-chR
Nose/mouth width ratio		ac-ac:ch-ch
Philtrum		
Cupid's Bow width	post-op	cphR - cphL
Medial length		sn-ls
Philtral point to alar base	pre-op left cleft pre-op right cleft	<cph>L - sbalL <cph>R - sbalR cphL-sbalL cphR-sbalR
Philtrum paramedial height		sn0L-cph0R sn0R-cphR
Mouth		
Lower vermillion height		stoi-li
Lower lip length		stoi-sl
mouth width		chL-chR
Face height		
Face height		n-pg
Upper face height		n-sn
Others		
Size of soft tissue defect in lip = distance between philtral points	pre-op left cleft pre-op right cleft	cphR - <cph>L <cph>R - cphL
Size of soft tissue defect in nose = difference between R&L nostril floor widths	(sbalL-sn0L)-(sbalR-sn0R)	

Peripheral landmarks in the ear region (obsR&L; obiR&L) were frequently absent from global co-ordinate files. These landmarks proved the most difficult to identify on the cleft models, and were omitted when the operator did not have confidence in the accuracy of placement. Facial measurements were therefore limited to the upper face and eyes, nose, nasolabial and mouth areas. Linear distances (in mm), angles (in degrees) and ratios defining facial parameters were generated from the global 3D landmark co-ordinates using the Facial Analysis Tool© software.

Measurement data were compiled in Microsoft Excel™, and checked for missing values and outliers. Where either was identified, the model was re-displayed and landmark positions checked. Landmarks were edited as appropriate and new co-ordinate files saved. Measurements were then re-generated for that model.

To facilitate direct comparison between children with Right and Left-sided clefts, data were manipulated so that all clefts became Left-sided. In cases where a Right-sided cleft occurred, individual measurements were re-labelled as left-sided measurements. Data were then exported to MINITAB™ (Version13), for analysis.

3.8.3 Facial Shape Analysis

3.8.3.1 Facial Asymmetry

Facial dimensions can be determined by calculating distances between individual landmarks. The study of symmetry considers 3D configurations of landmarks, representing the whole face and its component parts (Fig 3.11) Global asymmetry is the term that describes an overall level of asymmetry in any configuration.

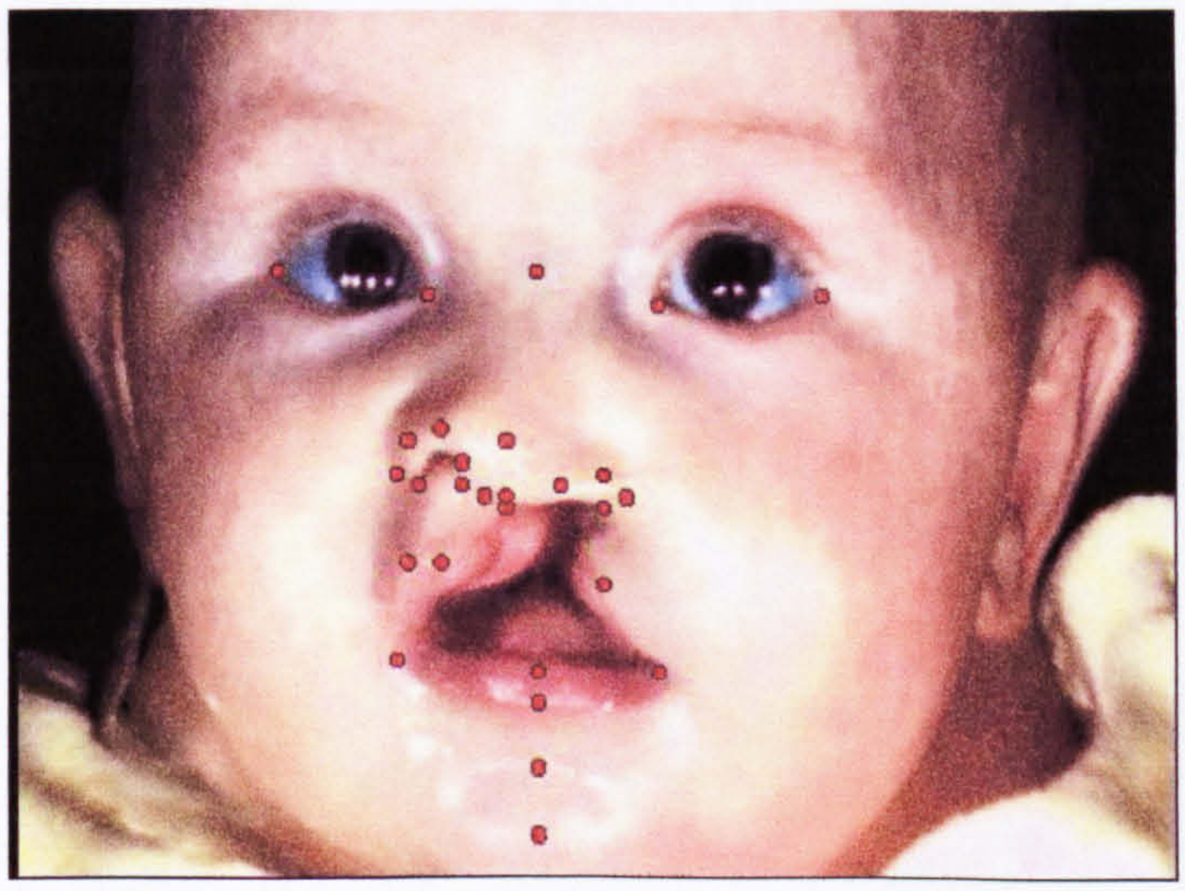


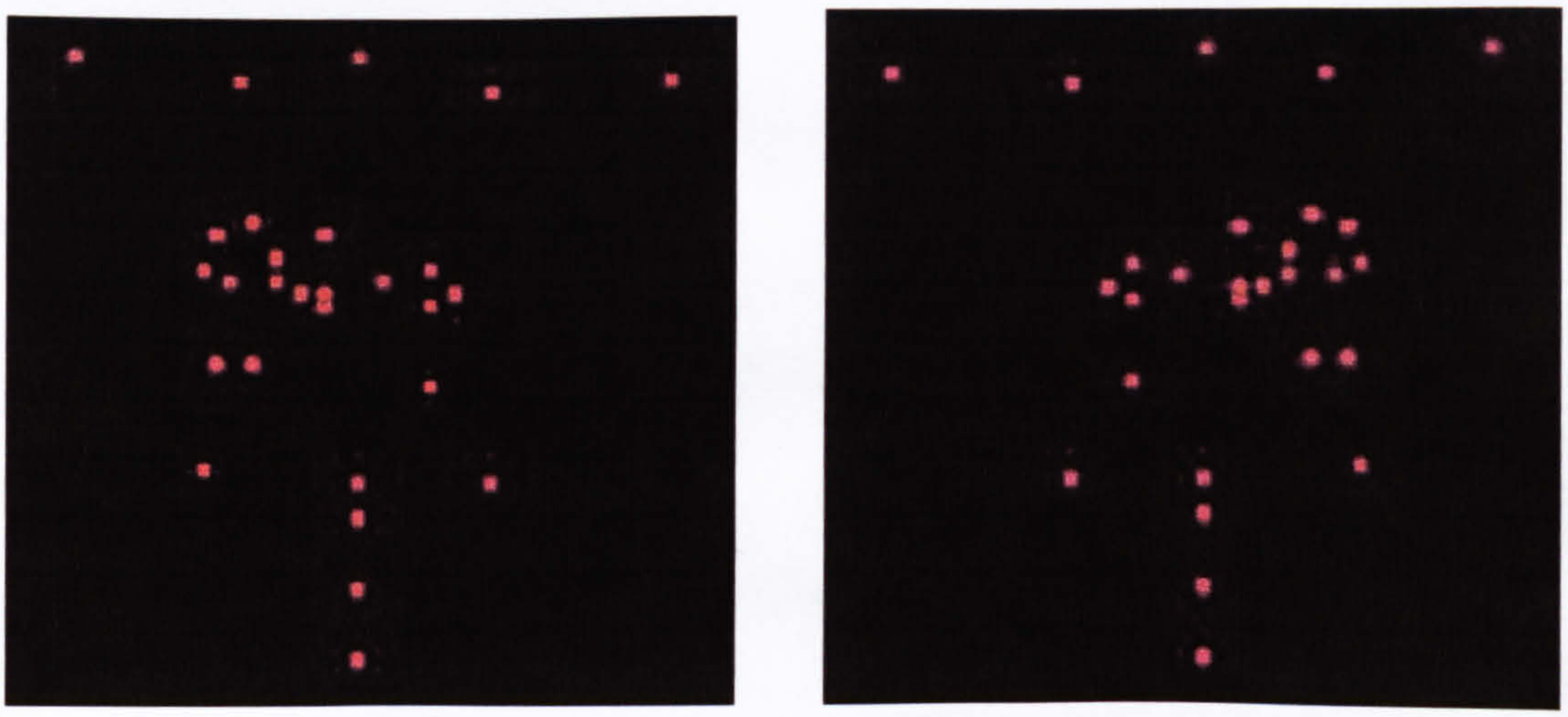
Figure 3.11 configuration of landmarks representing the face

A pilot study revealed that the degree of asymmetry varied according to facial feature and it was possible to locate and quantify these asymmetries, and to measure the effects of surgery and growth of the face (Appendix 10).

3.8.3.2 Asymmetry Score

Asymmetry is the degree to which there is a 'mismatch' between a configuration and its relabelled and matched mirror image (Bock & Bowman 2005). Based on the work of Mardia et al. (2000) an asymmetry score was derived to quantify the level of asymmetry in

landmark configurations (Mardia, Bookstein & Moreton 2000). Configurations were first scaled to an arbitrary common 'unit' size to allow comparison. Each configuration was then reflected and corresponding landmark pairs re-labelled (right became left and vice versa) (Fig 3.12 a&b). This reflected and re-labelled configuration was then 'best-fit' to the original by ordinary partial Procrustes alignment (OPPA) (Fig 3.13). The mean squared distances between the original landmarks and their mirror images were calculated and the average expressed as an Asymmetry Score. If symmetry were perfect, the score would be zero (Bock & Bowman 2005).



(a) (b)

Figure 3.12 (a) original configuration (b) mirror reflection configuration

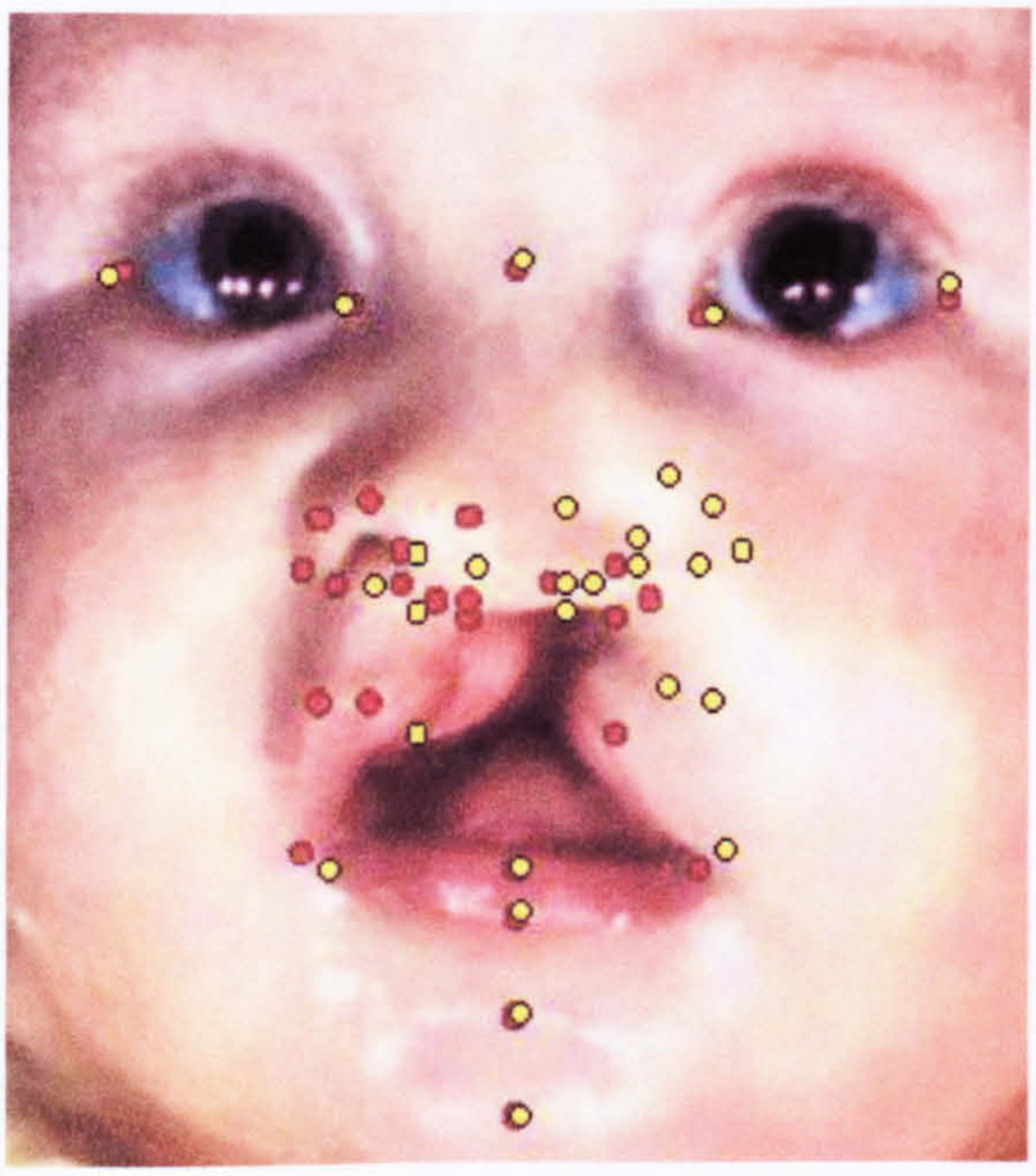


Figure 3.13 original (red) and mirror-image (yellow) landmark configurations, after Procrustes 'best-fit' alignment

3.8.3.3 Facial and Nasolabial Asymmetry

Global Asymmetry Scores were calculated for individual configurations of landmarks representing the entire Face, the Nasolabial area, Upper Face, Nasal Rim, Nasal base and philtrum shape (Table 3.5).

Table 3.5 Global Asymmetry Score landmarks

Global Asymmetry Scores	**Landmarks**
Face	exR enR n enL exR acL alL al0oL prn al0oR al0iR al0iL hnR hnL alR acR sbalR sn sbalL sn0R cR cL sn0L chR cphR ls <cph>L(preop) cphL(postop) chL
Nasolabial area	acL alL al0oL prn al0oR alR acR sbalR sn sbalL sn0R cphR ls cph0R(pre-op) cphL(post-op) sn0L chR chL n
Nasal Rim	acL alL al0oL prn al0oR alR acR
Upper face	exR enR n enL exR
Nasal base	sbalR sn sbalL
Philtrum shape	sn0R cphR ls cph0R(pre-op) cphL(post-op) sn0L

3.8.3.4 Distribution of Asymmetry

In order to determine the distribution of asymmetry in the face and nasolabial region, methods were developed to take account of the relative size and complexity of different facial features and their contribution to overall asymmetry (Bock & Bowman, 2005). Since the Global Asymmetry Score was a weighted average it was decomposed into its component scores, corresponding to constituent facial regions or features.

Global Face Asymmetry Scores were decomposed to assess the relative contribution of different facial regions to the asymmetry of the entire face. Global Nasolabial area Asymmetry Scores were decomposed to assess the relative contribution of specific nose or lip features to overall nasolabial asymmetry.

3.8.3.4.1 Facial Region Asymmetry Distribution

For the purposes of determining which facial regions dominated overall facial asymmetry, global facial Asymmetry Scores were decomposed into upper face, nasal rim, nasal base & columella and upper vermillion (lip) shape. Landmark subsets were defined in Table 3.6 (overleaf).

Table 3.6 Definitions of facial region

Facial Region	Landmark Subsets
Upper face	exR enR n enL exR
Nasal Rim	acL alL al0oL prn al0oR alR acR
Nasal base & columella	sbalR sn sbalL sn0R cR cL sn0L
Upper vermillion shape	chR cphR ls <cph>L(preop) cphL(postop) chL

3.8.3.4.2 Nasolabial Asymmetry Distribution

In order to examine the distribution of asymmetry in the nasolabial area in more detail, nasolabial area Asymmetry Scores were decomposed into nasal rim, nasal base and philtrum shape. Landmark subsets are defined in Table 3.7

Table 3.7 Definitions of nasolabial features

Nasolabial Features	Landmark Subset
Nasal Rim	acL alL al0oL prn al0oR alR acR
Nasal base	sbalR sn sbalL
Philtrum shape	sn0R cphR ls cph0R(pre-op) cphL(post-op) sn0L

3.8.4 Asymmetry Score summary

Global Asymmetry Scores were calculated for configurations representing the whole face, certain facial regions and specific nasolabial features. Global face and nasolabial Asymmetry Scores were decomposed to show the relative contribution of their component features to overall asymmetry. Scores were calculated for each UCL and UCLP child, and compared with those of non-cleft children. Asymmetry Scores and distribution of asymmetry were calculated before primary surgery, after lip / nose repair, at age 1 year and at age 2 years.

3.8.5 Facial feature residual shape deformity at age 2 years

3.8.5.1 Procrustes Distance from normal Score (PDFN)

The concept of 'Procrustes Distance' and was used to quantify the distance of each cleft case from the control mean shape, for different facial features (Dryden & Mardia 1998). Distances between shapes are not measured in the same way as differences in facial dimensions, and consequently are not expressed in conventional metric units such as millimetres. The shape of an object is described as a quantity that does not vary when the object is moved (translated), rotated, enlarged or reduced (scaled) (Bookstein, 1991; 1997). An average shape (Full Procrustes mean) was derived from data from 84 non-cleft 2-year-old Scottish children gathered for a parallel infant facial growth project (White 2005). Generalised Procrustes analysis was performed to align control configurations by finding the 'best-fit', such that the sum of the squared distance between matched landmarks was minimized. Next, individual cleft configurations were aligned with the average shape 'norm' at 2 years (ordinary Procrustes alignment) and Procrustes distance from normal calculated as the square root of the sum of the squared distances between matched landmarks in the cleft configuration and control Procrustes mean configuration. Procrustes 'distances from normal' at 2 years were calculated for facial features defined by the landmarks in Table 3.8.

Table 3.8 Landmark subsets for 'Procrustes distance from normal' at age 2 years

Facial feature	**Landmark Subset**
Nasal Rim shape	acL alL al0oL prn al0oR alR acR
Nasal complex shape	acL alL al0oL prn al0oR alR acR sbalR sn sbalL n
Nostril shape	**sbalR al0iR hnR cR sn0R sbalL al0iL hnL cL sn0L sn**
Columella shape	sn0R cR cL sn0L sn
Philtrum shape	sn0R cphR ls cphL sn0L sn
Upper Lip shape	chR cphR ls cphL chL

3.9 Measures of Cleft Severity

3.9.1 Measures of cleft extent – ratios

Comparison of measurements on the cleft side of a face with those on the non-cleft side is a common method of estimating the severity of a cleft. Ratios were calculated from distances measured between 3D landmarks on cleft and non-cleft sides in the nasal floor and across the cleft in the lip. The vertical discrepancy in the philtrum was measured by the ratio of the non-cleft side philtrum height and philtrum height adjacent to the cleft (Table 3.9). Thus, indicators of severity for each cleft case were obtained, which would be comparable across different individuals.

Table 3.9 Cleft Severity Ratios

Ratio	Distances	Definition
Nostril floor ratio	sbalL-sn0L:sbalR-sn0R	ratio of cleft and non-cleft nasal floor widths
Cupid's bow ratio	cphR-ls:<cph>L-ls	ratio of cleft and non-cleft side philtrum points to the centre of cupid's bow
Philtrum height ratio	sn0R-cphR:sn0L-cph0R	ratio of non-cleft side philtrum height and philtrum height adjacent to the cleft

3.9.1.1 3D Measures of severity in the nose

In order to examine the relationship between different features of the nose, in terms of severity of asymmetry, landmark subsets were created to define nasal features. In addition to previously calculated nasal base and nasal rim, asymmetry scores were calculated for columella and nostril shape. Table 3.10 shows the landmark subsets for the nose region. Asymmetry Scores were generated for pre-op models and 2 year old models.

Table 3.10 Asymmetry Score landmarks for Nasal features

Nasal Feature	Landmarks for Asymmetry Score
Nasal Rim shape	acL alL al0oL prn al0oR alR acR
Nasal base shape	sbalR sn sbalL
Columella shape	sn0R cR cL sn0L sn
Nostril shape	sbalR al0iR hnR cR sn0R sbalL al0iL hnL cL sn0L

3.10 Statistical Methods

3.10.1 Comparison of Somatic measurements in pre-op cleft lip & palate children with UK Growth Reference norms.

Weight, height and head circumference for cleft subjects were plotted on UK90 growth charts (Child Growth Foundation, 1996). Subjects were categorised according to their position relative to the 50th centile line on the charts (above or under average weight, height or head circumference). The proportion of subjects above and below the 50^{th} centile for each parameter were compared by cleft type and by gender and the significance of any differences tested by Fisher's Exact tests ($p<0.05$).

3.10.2 Comparison of Somatic measurements in children with Cleft lip and / or palate.

Weight, height and head circumference for UCL infants and UCLP infants were compared. Differences between groups were tested for significance using Mann-Whitney tests.

3.10.3 Facial Dimensions

3.10.3.1 Facial Characterisation

To characterise facial soft tissue morphology, medians, means and standard deviations were calculated for facial dimensions in UCL and UCLP infants prior to primary lip / nose repair (pre-op), after lip/nose repair (post-op), at age 1 year and at age 2 years.

Differences in facial dimensions between cleft groups were tested for statistical significance by Mann-Whitney tests. Significance was tested at the 99% level ($p<0.01$). Differences between cleft and non-cleft side dimensions for each individual were calculated and differences tested for statistical significance by Wilcoxon signed ranks tests ($p<0.01$).

3.10.3.2 Longitudinal Changes in Facial Morphology with Lip/nose Repair and with Growth

Changes over time with primary lip/nose repair and with growth were measured by calculating the difference between facial dimensions at time one (T1) with those measured at time two (T2). Six time intervals were of interest (Table 3.11):

Table 3.11 Time Intervals for Longitudinal studies

Interval		Characteristics of interest
T1	T2	
Pre-op	Post-op	Facial change with primary lip/nose repair
Post-op	1 year	Facial change after lip/nose & palate repair in the UCLP group Facial growth in UCL after lip/nose repair to age 1 year
1 year	2 years	Facial growth in the year after primary lip/nose and palate surgery
Pre-op	1 year	Facial change from baseline in the first year of life
Pre-op	2 years	Total facial growth from baseline, over 2 years
Postop	2 years	Facial growth after primary lip/repair to 2 years of age

As the number of data sets available for each cleft group, in each time interval was small, a non-parametric approach was adopted in this section.

3.10.3.2.1 Changes in facial dimensions following primary lip/ nose repair

For each individual, Wilcoxon signed ranks tests determined if there were any statistically significant changes in facial dimension after lip/ nose surgery (pre-op to post-op interval). Differences in median change in facial dimensions, after primary lip/nose surgery between UCL and UCLP groups were tested for statistical significance by Mann-Whitney tests. Significance was tested at the 99% level ($p<0.01$).

3.10.3.2.2 Changes in facial dimensions with growth over 2 years

For each individual, Wilcoxon signed ranks tests determined if there were any statistically significant changes in facial dimension after lip / nose repair to age 2 years (post-op to 1 year; 1 year to 2 years; post-op to 2 years). Differences between cleft groups in median change in facial dimensions with growth were tested for statistical significance by Mann-Whitney tests ($p<0.01$). Where appropriate, median change in cleft and non-cleft side dimensions were compared and differences tested for significance by Wilcoxon's signed ranks tests ($p<0.01$).

Changes in facial dimension over the first year (pre-op to1year interval)and total change over 2 years (pre-op to 2years) were tested for significance by Wilcoxon signed ranks tests ($p<0.01$). Differences between cleft groups in median change in facial dimensions with growth were tested for statistical significance by Mann-Whitney tests ($p<0.01$). Where appropriate, median change in cleft and non-cleft side dimensions were compared and differences tested for significance by Wilcoxon's signed ranks tests ($p<0.01$).

3.10.4 Relationship between Somatic dimensions and Facial dimensions in UCL and UCLP

Table 3.12 shows the key dimensions selected to represent growth of the face and body.
To assess the association between these key facial and somatic measurements, the following statistical analyses were used:-

Pearson's Correlation coefficients were calculated to measure the relationship between key facial dimensions and body measurements prior to cleft surgery and at 2 years of age.

Pearson's Correlation coefficients were calculated to measure the relationship between changes in key facial dimensions and body measurements over time. ($p<0.05$).

Table 3.12 Facial and Somatic Measurements

Facial Dimensions	Measurement	Somatic Measurements
Upper face width (binocular width)	exR-exL	Weight (kg)
Upper face height	n-sn	Height (cm)
Total face height	n-pg	Head circumference (cm)

3.11 3D Facial Shape Analysis

3.11.1 Asymmetry Analysis

Analyses of asymmetry distribution and changes in global asymmetry and feature asymmetry over time, were performed using mixed-effects statistical models (Pinheiro & Bates, 2000) to take account of the longitudinal nature of the data. As subjects were observed on multiple occasions, this was accommodated in the model by treating the variation in overall levels of individual subjects as a 'random' effect and the other variables of age (time point), group (UCL, UCLP, control) and component (facial region or nasolabial feature) as fixed effects. The Asymmetry Score data were transformed to achieve approximate normality by applying a fourth root transformation (two square roots) (Bland 1990; Cressie 1995).

Mixed-effects statistical models were applied to assess the significance of differences observed in the distribution of asymmetry across facial regions or nasolabial features and between UCL, UCLP and control groups. Analyses were performed pre-operatively, post lip/nose repair, at age 1year and at age 2years ($p<0.05$).

Mixed-effects statistical models were applied to test the significance of changes in global facial asymmetry and upper face, nasal rim, nasal base and philtrum asymmetry scores over time, for UCL, UCLP and control groups. In addition, Asymmetry Scores were compared between cleft and control groups, at each time point ($p<0.05$).

3.12 Facial Feature Residual Shape Deformity at 2 years

Procrustes 'distance from normal' (PDFN) Scores were calculated for facial features at 2 years of age. Data distributions were checked for normality using histograms. As data were not normally distributed, a logarithmic transformation (log to base 10) was performed. For each nose or lip feature, PDFN Scores were ranked from lowest to highest and plotted to show the distribution of scores for residual shape abnormality in UCL and UCLP children. Median scores were calculated for each cleft type and the significance of any differences tested with Mann Whitney tests. ($p<0.05$).

3.13 Cleft Severity

Data distributions for all variables were checked for normality and a logarithmic transformation (log base 10) was applied to data that were not normally distributed.

3.13.1 Relationship between measures of Severity of cleft extent

The relationship between horizontal and vertical ratios of severity (Nostril Floor ratio, Cupid's Bow ratio and Philtrum height ratio) was investigated by calculating Pearson's Correlation coefficients. Significance level was set at 95% ($p<0.05$).

3.13.2 Relationship between Nasal Asymmetry Severity Scores

The relationship between different 3D measures of severity of nasal asymmetry prior to surgical repair was investigated by calculating Pearson's Correlation coefficients ($p<0.05$) between nasal base, nasal rim, columella and nostril Asymmetry Scores.

3.13.3 Relationship between measures of cleft extent and Asymmetry Scores

The relationship between measures of cleft extent (Nostril Floor ratio, Cupid's Bow ratio and Philtrum height ratio) and nasal base, nostril and nasal rim Asymmetry Scores were investigated by calculating Pearson's Correlation coefficients ($p<0.05$).

3.14 Relationship between initial cleft severity and shape outcomes at 2 years of age

To determine if there was an association between pre-operative measures of cleft severity and the degree of residual deformity at 2 years (Procrustes distance from normal and Asymmetry Scores), Pearson's correlation coefficients (r) were calculated ($p<0.05$). The extent of variability in one variable that could be explained by its relationship with another was calculated as r^2, and expressed as a percentage. The following variables were tested:-

3.14.1 Nasal Region

Asymmetry Scores, prior to surgical repair were tested for correlation with residual Asymmetry Scores at age 2 years in the nasal base, nasal rim and nostril.

Nasal base, nasal rim and nostril Asymmetry Scores, prior to surgical repair were tested for correlation with residual shape deformity (PDFN) Scores for nasal complex, nasal rim and nostrils at age 2years.

3.14.2 Lip Region

Philtrum Asymmetry Score, prior to surgical repair was tested for correlation with residual philtrum asymmetry at age 2 years.

Philtrum height ratio, prior to surgical repair, was tested for correlation with residual philtrum shape deformity (PDFN) Score and overall residual lip shape deformity at age 2 years.

Cupid's Bow ratio, prior to surgical repair, was tested for correlation with residual philtrum shape deformity (PDFN) Score and overall residual lip shape deformity at age 2 years.

4 Results

4.1 Sample Identification and size

Primary recruitment to the study took place from November 1999 to January 2002, in Scotland. During this period, 72 infants born with unilateral clefts were identified (35 UCLP and 37 UCL). Five infants did not satisfy selection criteria (i.e. no longer resident in Scotland, non-Caucasian origin, or associated syndrome) and were excluded. Of the remaining 67 potential recruits, 37 agreed to participate in the study (17 UCLP; 20 UCL).

A second recruitment phase was carried out to augment the cross-sectional data captured at 1 and 2 years of age. A further 43 children, with birth dates between July 1998 and October 1999 were identified and contacted. Of these, four children joined the study at age 1 year and nine joined at age 2 years.

The final study sample consisted of 50 children (27 UCLP; 23 UCL) whose parents consented to 3D Imaging. A schematic diagram of the point at which subjects entered and left the study is shown overleaf (Fig 4.1). Each child did not attend every capture point and so the number of subjects who contributed data at individual time points and between time points vary. Sample sizes and distribution of cleft type are stated in each section.

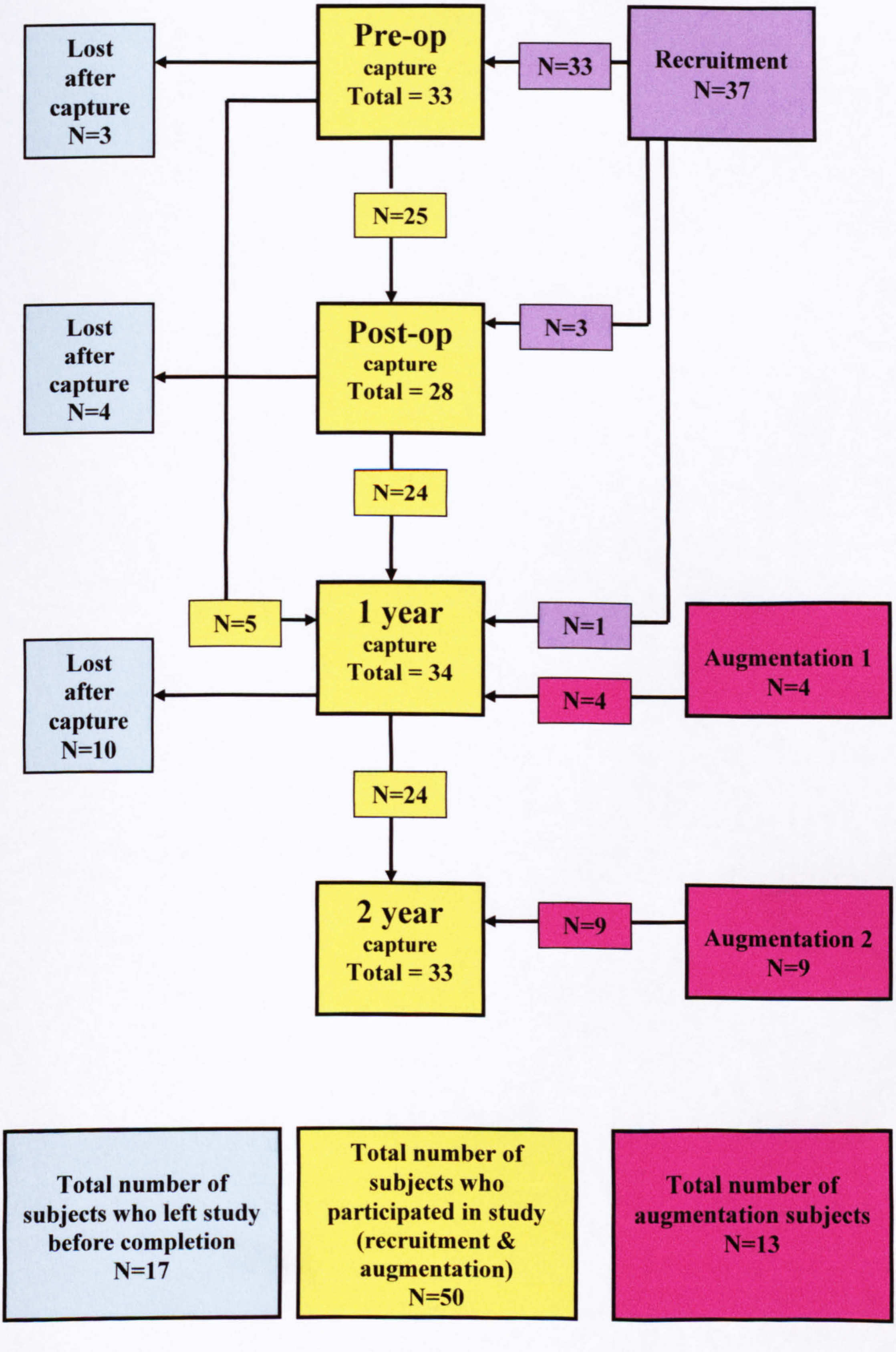


Figure 4.1 Recruitment, data capture and loss from study

Pre-op = prior to lip/nose repair Post-op = after lip/nose repair

4.2 Sample profile

4.2.1 Gender and cleft type

The gender distribution of the cleft groups is illustrated in Table 4.1 The ratio of males to females was approximately 2:1 in the pre-op recruitment group, which increased with the addition of a larger proportion of males than females in the augmentation groups. In the pre-operative group, the majority of UCL infants had incomplete clefts and the majority of UCLP infants had complete clefts (Table 4.2).

Table 4.1 Gender distribution of cleft study sample

	Male	**Female**	**Total**
Pre-op recruitment group (n=37)			
UCLP	12	5	17
UCL	12	8	20
1 year old augmentation group (n=4)			
UCLP	3	0	3
UCL	1	0	1
2 year old augmentation group (n=9)			
UCLP	4	3	7
UCL	2	0	2
Total	**34**	**16**	**50**

Table 4.2 Distribution of complete and incomplete clefts in Pre-op Recruitment group

Cleft extent	**Complete**	**Incomplete**
UCL	3	17
UCLP	15	2
Total	18	19

4.2.2 Socio-economic status

The Carstairs & Morris Index of Deprivation is a measure of socioeconomic deprivation. Seven categories (DEPCATs) are described which range from the most affluent (DEPCAT 1) to the most deprived (DEPCAT 7) (McLaren & Bain, 1998). Cleft children were classified by DEPCAT, according to their postcode at the time of recruitment to the study. The DEPCAT distribution of cleft children in this study was compared to that of the Scottish population (Appendix 3). In addition, DEPCAT distribution by cleft type was examined.

4.2.2.1 Socio-economic status of entire cleft sample

Fourteen percent of the cleft sample lived in DEPCAT 1or 2, compared to 20% of the Scottish population (Fig 4.2, overleaf). Sixty-eight percent of the cleft sample and 62% of the Scottish population were resident in DEPCAT 3, 4 and 5. Almost a third (30%) of the cleft sample were classed as DEPCAT 5, whilst the majority of the Scottish population (25.4%) were DEPCAT 4. The proportion of cleft children in DEPCAT 7 was more than double that of the National population. Two children in the study sample could not be classified (postcode not listed).

4.2.2.2 Socio-economic status of UCL and UCLP groups

The socio-economic status of the UCL infants resembled that of the Scottish population except in DEPCAT 6 and 7 (Fig 4.3, overleaf). The majority of UCLP infants were from more socially deprived areas than UCL or the National population. The proportion of UCL and UCLP infants resident in the most deprived areas (DEPCAT 7) was respectively, 2.5 times and 1.5 times (17% and 11%) greater than the general Scottish population.

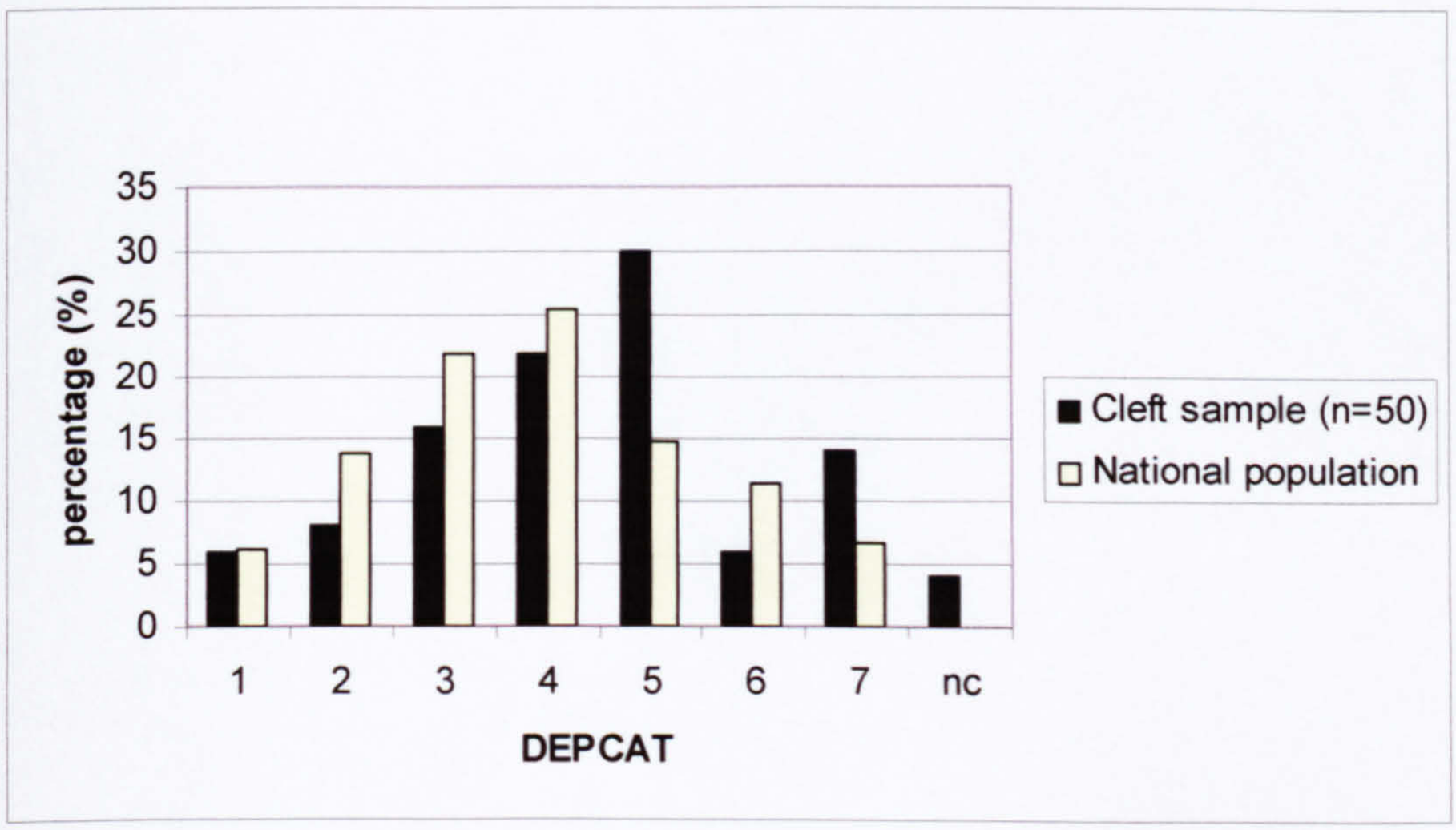


Figure 4.2 DEPCAT of study sample compared to the National population of Scotland, based on 1991 census. (nc = not categorised)

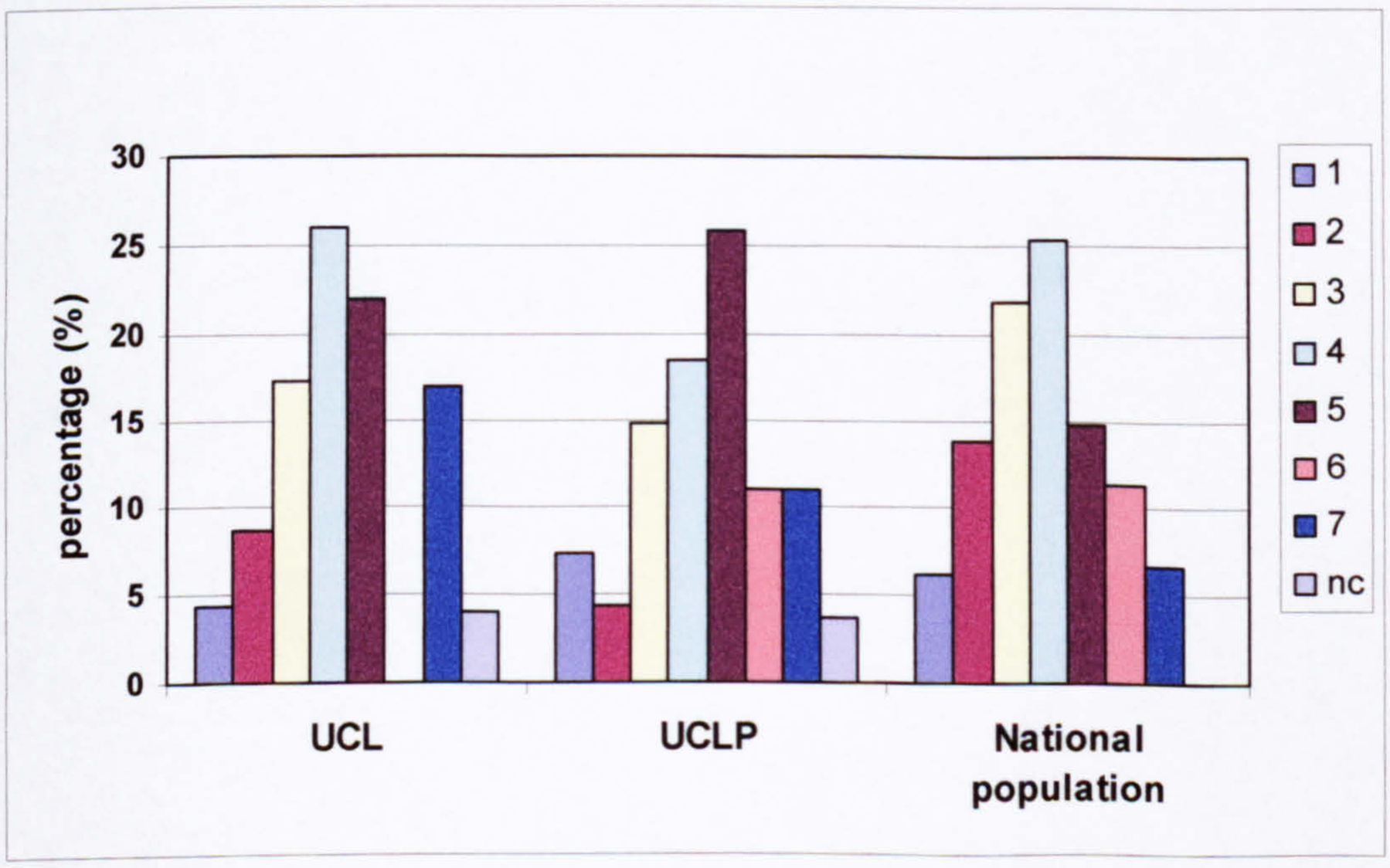


Figure 4.3 DEPCAT distribution by cleft type (nc = not categorised)

4.2.3 Capture Timing

The mean age of the subjects in the study at capture exceeded the original target mean age for each planned capture time-point, though, the mean age fell within the original target capture range (Table 4.3). Most of the variability in age at capture occurred prior to and following primary lip / nose repair. The 1-year and 2-year captures were more homogenous.

Table 4.3 Mean age at capture, compared to target age at capture

Capture time point	Target mean age at capture (months)	Range (months)	Actual mean age at capture (months)	Range (months)
Pre-op	3	2 – 4	3.9	2.75 - 9
Post-op	6	4 - 8	7.1	5.5 - 9.2
1 year	12	10 - 14	13.5	11.5 - 16.2
2 years	24	20 - 28	26.2	25.2 - 27.5

4.2.4 Surgery Timing

Table 4.4 shows the mean age and range in months at which primary surgery was performed for the infants in the study. The average age at the time of lip / nose repair in infants recruited before surgery was almost 5 months. Individual ages ranged from 3 to 9 months (Fig 4.4). In UCLP infants who were recruited prior to lip/nose repair, palate repair was carried out at 9.6 months on average (Fig 4.5). Individual ages ranged from 7 to 15 months.

Table 4.4 Mean age at time of surgery

Lip/nose repair	**Mean age (months)**	**Range (months)**
Pre-op recruitment group	4.9	3.3 - 9.3
1 year augmentation group	4.7	4 - 5.9
2 year augmentation group	4.0	3 - 5.5
Palate surgery		
Pre-op recruitment group	9.6	7.2 - 15
1 year augmentation group	11.3	8.8 - 13.7
2 year augmentation group	9.4	7.5 - 11.2

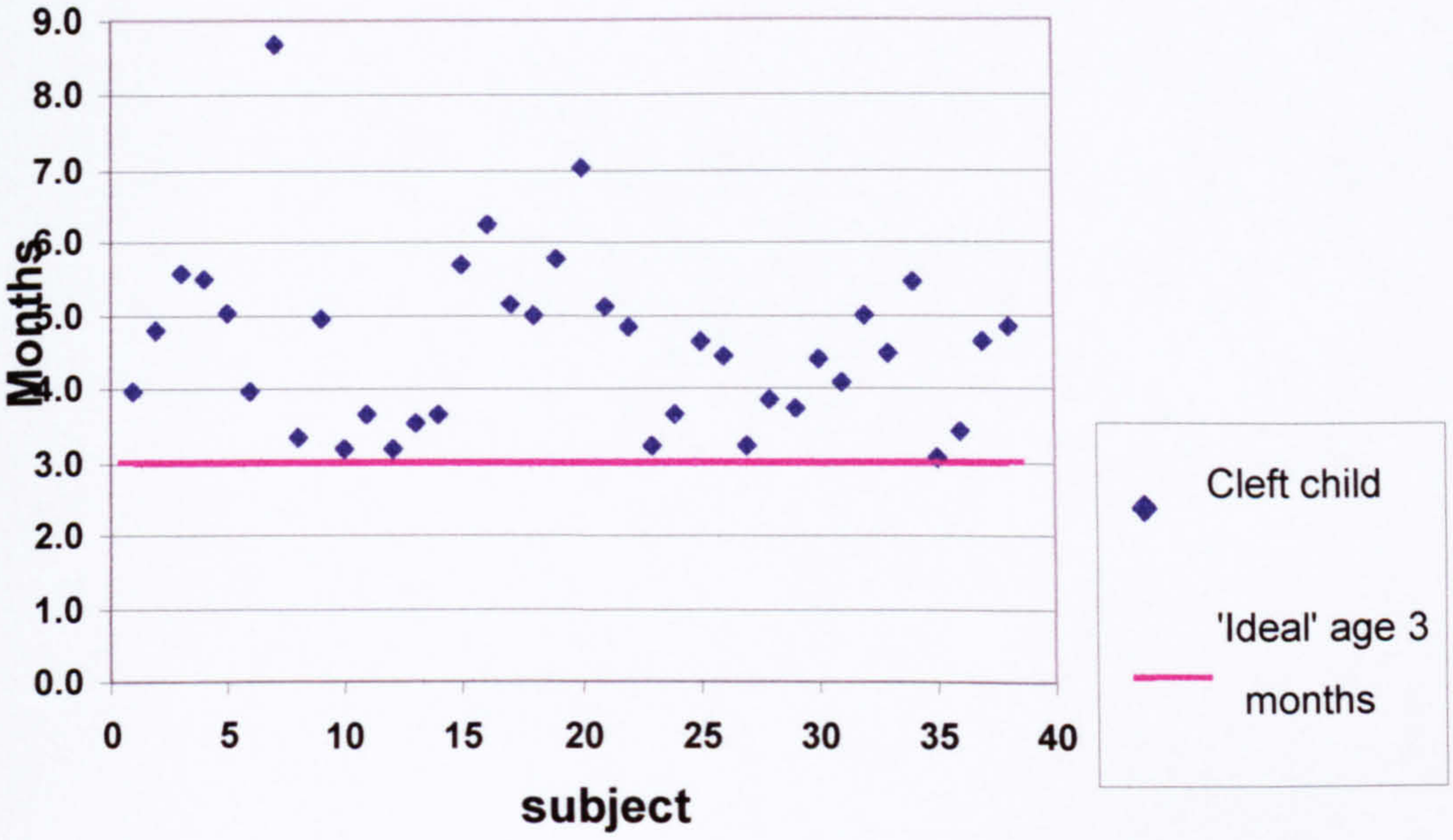


Figure 4.4 Age of pre-op recruitment group at primary lip / nose repair, compared with 'ideal' timing

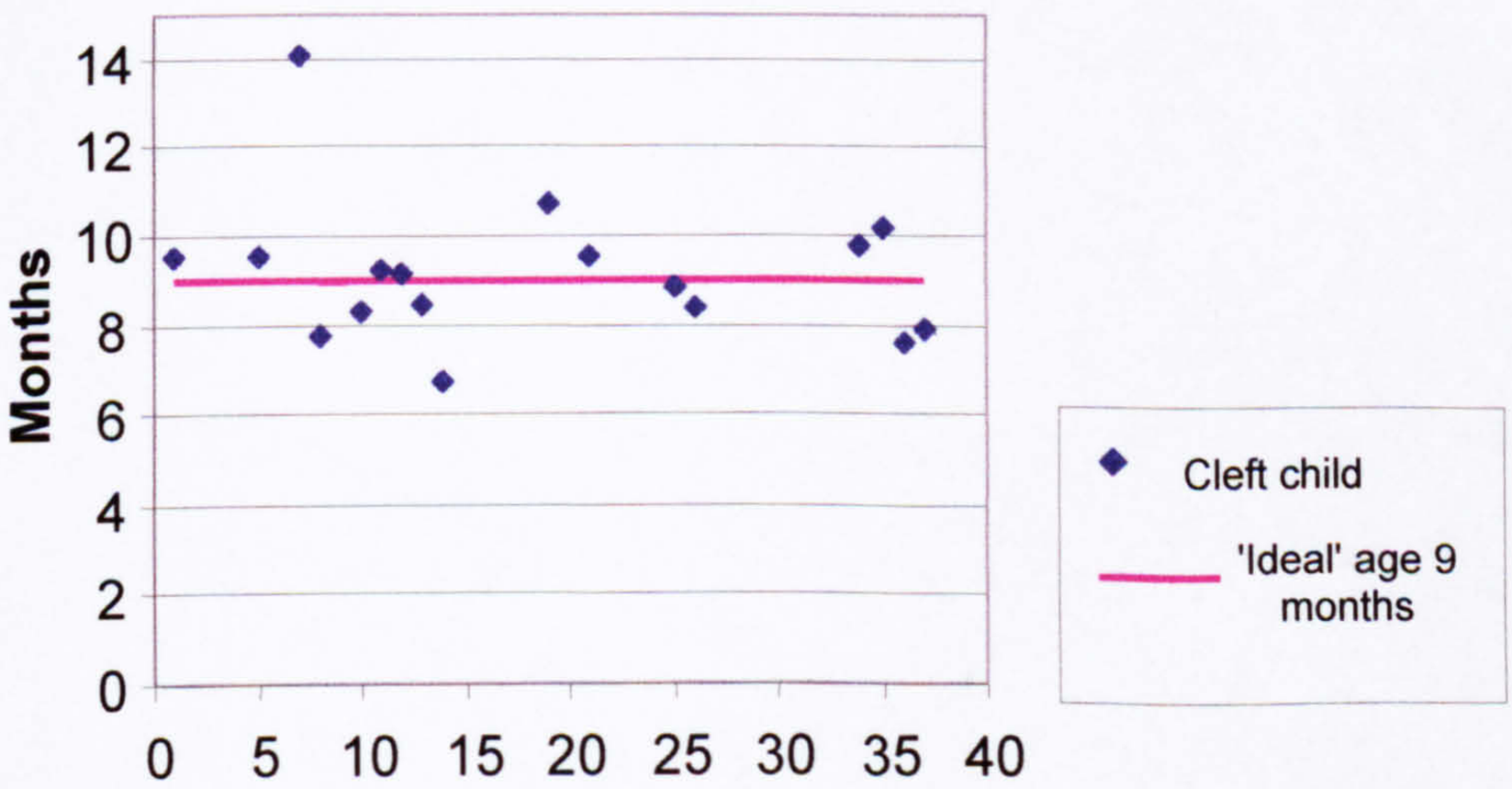


Figure 4.5 Age of pre-op recruitment group at palate closure, compared with 'ideal' timing of 9months

4.2.5 Surgical procedures

The surgical procedures performed on the UCL and UCLP infants in this study are listed in Appendix 4. It illustrates the diversity of primary surgery carried out. The majority of children had a Millard lip repair. One child had a lip adhesion only and one had a Straight line (Manchester) repair. A McComb primary rhinoplasty was the most common primary nasal repair procedure and was performed in both UCL and UCLP infants, however this was not necessary in every case. No primary nasal surgery was performed in 9 out of 20 UCL and 4 out of 17 UCLP infants. Nasal floor closure was via a single layer or 2-layer procedure, where appropriate. An alveolar perioplasty was performed in one case and a vomer flap was documented in five cases for repair of the nasal floor / anterior hard palate (primary palate). Repair of the secondary hard palate was carried out using the Veau Wardill or Von Langenbeck technique. Where no releasing incisions were made, this was noted. Soft palate repair was carried out via the Intravelar Veloplasty, Radical Muscle Dissection or Furlow technique.

4.2.6 Summary of sample profile

The majority of cleft infants in the sample were male (approximately 2:1).

The proportion of cleft infants in the sample who were resident in more socially deprived areas was more than double that of the National population.

The mean age at capture prior to primary lip/nose repair was 3.9 months (target 3 months). The mean age at primary lip/nose surgery was 4.9 months (target 3 months).

The range of surgical procedures carried out in this sample was diverse, however, the majority had a Millard lip repair. A McComb primary nasal repair was necessary in the majority of UCLP infants and in over half of the UCL infants. This was performed at the same time as lip repair.

4.3 Somatic Measurements

4.3.1 Comparison of somatic measurements in UCL and UCLP infants with UK Growth reference norms.

The weight, height and head circumference recorded at the pre-op capture were plotted on UK90 growth reference charts for each cleft infant (Appendices 5&6). Each child's measurement relative to the 50th centile was noted. Comparisons by cleft type and gender were made and the significance of any differences tested by Fisher's exact tests. ($p>0.05$). Weight was not recorded at the pre-op capture for 3 children. Height was not recorded for 4 children and head circumference was not recorded for 6 children.

4.3.1.1 Comparison by cleft type

4.3.1.1.1 Pre-op Weight, compared to UK cross-sectional Growth norms, by cleft group

Compared to UK norms, the majority of children in the study were under the 50th weight centile and would be considered of normal but low weight for their age (Table 4.5). One child whose weight was below the 0.4th centile was outside the normal range (Appendices 5&6). The proportion of underweight children was similar in both cleft groups, however UCLP children's weight tended to be lower than that of UCL children.

Table 4.5 Proportion of sample above and below 50th weight centile, by cleft type

Weight Centile	UCL		UCLP		% of sample recorded (n=30)
	N	%	N	%	
Under 50th	14	82.4%	11	84.6%	83.3%
50th and above	3	17.6%	2	15.4%	16.7%
Total	17	100.0%	13	100.0%	100.0%

4.3.1.1.2 Pre-op Height, compared to UK cross-sectional Growth norms, by cleft group

Compared to UK norms, the majority of children in the study were above the 50th height centile and were above average height for their age (Table 4.6). The proportion of children whose height was below average was similar in both cleft groups; however UCL children tended to be shorter than UCLP children (Appendices 5&6).

Table 4.6 Proportion of sample above and below 50th height centile, by cleft type

Height Centile	UCL		UCLP		% of sample recorded (n=29)
	N	%	N	%	
Under 50th	7	41.2%	5	41.7%	41.4%
50th and above	10	58.8%	7	58.3%	58.6%
Total	17	100.0%	12	100.0%	100.0%

4.3.1.1.3 Pre-op Head Circumference, compared to UK cross-sectional Growth norms, by cleft group

Compared to UK norms, the majority of children in the study were under the 50th head circumference centile and had below average head circumference for their age (Table 4.7). One child was below the 0.4th centile (Appendices 5&6). A slightly greater proportion of UCL infants appeared to have a below average head circumference for their age than UCLP infants, but the difference was not significant (p=0.481).

Table 4.7 Proportion of sample above and below 50th head circumference centile, by cleft type

Head Circumference Centile	UCL		UCLP		% of sample recorded (n=27)
	N	%	N	%	
Under 50th	10	66.7%	7	58.3%	63.0%
50th and above	5	33.3%	5	41.7%	37.0%
Total	15	100.0%	12	100.0%	100.0%

4.3.1.2 Comparison by Gender

4.3.1.2.1 Pre-op Weight, compared to UK cross-sectional Growth norms, by gender

As previously shown, the majority of children in the study were under the 50th weight centile, when compared to UK norms (Table 4.8). The proportion of underweight children was similar in males and females. One female's weight was outside the normal range (below 0.4th centile). Despite this, the weight of males tended to be lower than that of females (Appendices 5&6)

Table 4.8 Proportion of sample above and below 50th weight centile, by gender

Weight Centile	Female		Male		% of sample recorded (n=30)
	N	%	N	%	
Under 50th	9	81.8%	16	84.2%	83.3%
50th or above	2	18.2%	3	15.8%	16.7%
Total	11	100%	19	100%	100.0%

4.3.1.2.2 Pre-op Height, compared to UK cross-sectional Growth norms, by gender

One female was below the normal range for height. However, the rest of the females in the sample were on or above the 50th height centile for their age (Table 4.9). In contrast, more than half of the males in the sample were of below average height (Appendices 5&6). This difference was significant (p=0.004)

Table 4.9 Proportion of sample above and below 50th height centile, by gender

Height Centile	Female		Male		% of sample recorded (n=29)
	N	%	N	%	
Under 50th	1	10.0%	11	57.9%	41.4%
50th or above	9	90.0%	8	42.1%	58.6%
Total	10	100%	19	100%	100.0%

4.3.1.2.3 Pre-op Head Circumference, compared to UK cross-sectional Growth norms, by gender

The majority of males and females were under the 50th centile for head circumference. Slightly fewer females were below the average norm than males (60% and 65% respectively) although this was not statistically significant. Two females had a head circumference that was outside the UK normal range (Table 4.10). Generally, however, boys tended to fall into a slightly lower head circumference centile banding, relative to their UK norm for age, than females (Appendices 5&6).

Table 4.10 Proportion of sample above and below 50th head circumference centile, by gender

Head Circumference Centile	Female		Male		% of sample recorded (n=27)
	N	%	N	%	
Under 50th	6	60.0%	11	64.7%	63.0%
50th or above	4	40.0%	6	35.3%	37.0%
Total	10	100%	17	100%	100.0%

4.3.2 Summary of comparison of cleft sample somatic measurements with UK growth norms

UCL and UCLP infants were of normal but low weight prior to primary lip/nose repair (under 50th centile). There was no difference in the proportion of males and females who were of low weight.

Almost 60% of UCL and UCLP infants were above average height for their age. Females were generally above average height, compared to two fifths of the males.

There were no differences in respect to cleft type in the proportion of infants who were of average or above average height for their age (60%). However, the majority of females (90%) were of average or above average height, compared to just over two fifths of the males in the sample. Infants of below average height were predominantly male.

The majority of UCL and UCLP infants had below average head circumference and there were no differences in the relative proportions of females and males.

4.3.3 Comparison of Somatic Measurements in UCL and UCLP

Weight, height, and head circumference measurements for UCL and UCLP children were compared to each other at individual time points. Data were normally distributed ($p<0.01$).

4.3.3.1 Differences in body measurements, by cleft type

No significant differences were found between UCL and UCLP children in respect of weight, height or head circumference, at any of the time points examined (Table 4.11).

Table 4.11 Somatic Dimensions by Cleft Type

	Time	Cleft type	N	Mean	Median	StDev	SE Mean	p-value
Weight (kg)	preop	UCL	17	5.78	5.70	0.95	0.23	0.60
		UCLP	13	5.61	5.68	0.75	0.21	
	postop	UCL	14	7.45	6.94	1.27	0.33	0.95
		UCLP	11	7.48	7.50	0.77	0.24	
	1y	UCL	12	9.91	10.20	1.96	0.57	0.41
		UCLP	16	9.46	9.60	0.75	0.19	
	2y	UCL	11	13.11	12.80	2.18	0.66	0.15
		UCLP	21	12.23	12.10	1.13	0.25	
Height (cm)	preop	UCL	17	61.55	61.00	4.02	0.98	0.38
		UCLP	12	62.71	63.30	2.32	0.67	
	postop	UCL	14	67.95	68.45	3.71	0.99	0.86
		UCLP	11	68.19	68.00	2.51	0.76	
	1y	UCL	12	76.43	76.00	3.85	1.11	0.47
		UCLP	16	75.52	76.50	2.76	0.69	
	2y	UCL	11	88.64	88.00	4.04	1.22	0.46
		UCLP	21	87.62	87.50	3.38	0.76	
Head Circumference (cm)	preop	UCL	15	40.26	40.20	1.83	0.47	0.55
		UCLP	12	40.70	40.75	1.92	0.55	
	postop	UCL	14	43.14	42.90	2.39	0.64	0.40
		UCLP	11	43.89	44.20	1.85	0.56	
	1y	UCL	12	46.58	46.75	2.11	0.61	0.67
		UCLP	16	46.21	45.90	2.30	0.58	
	2y	UCL	11	48.71	49.00	1.57	0.47	0.35
		UCLP	21	49.83	49.00	3.70	0.85	

(Significance level $p<0.01$)

4.3.3.2 Differences in body measurements, by gender

There were no significant differences between male and female cleft subjects in weight, height or head circumference at any time point ($p<0.01$).(Table 4.12)

Table 4.12 Somatic Dimensions by Gender

	Time	gender	N	Mean	Median	StDev	SE Mean	p-value
Weight (kg)	preop	F	11	5.40	5.50	0.71	0.21	0.14
		M	19	5.88	5.94	0.90	0.21	
	postop	F	11	7.25	7.01	1.00	0.30	0.4
		M	14	7.62	7.41	1.14	0.31	
	1y	F	10	9.52	9.25	1.39	0.44	0.71
		M	18	9.73	9.71	1.42	0.34	
	2y	F	11	11.97	11.70	1.44	0.44	0.2
		M	21	12.75	12.40	1.67	0.36	
Height (cm)	preop	F	10	61.5	60.8	4.0	1.3	0.56
		M	19	62.3	61.6	3.2	0.7	
	postop	F	12	67.1	67.8	2.9	0.8	0.15
		M	13	68.9	68.4	3.3	0.9	
	1y	F	10	75.2	75.3	4.3	1.4	0.38
		M	18	76.3	76.9	2.5	0.6	
	2y	F	11	86.8	87.5	4.3	1.3	0.23
		M	21	88.4	87.5	3.1	0.7	
Head Circumference (cm)	preop	F	10	39.6	40.3	1.5	0.5	0.07
		M	17	40.9	41.0	1.9	0.5	
	postop	F	12	42.3	42.3	1.8	0.5	0.01
		M	13	44.6	44.5	1.9	0.5	
	1y	F	10	45.3	45.5	2.2	0.7	0.06
		M	18	46.9	46.7	2.0	0.5	
	2y	F	10	48.3	48.3	1.3	0.4	0.18
		M	21	49.9	49.5	3.5	0.8	

(Significance level $P<0.01$)

4.3.4 Relationship between weight, height and head circumference in UCL and UCLP infants

Table 4.13 illustrates the relationship between weight, height and head circumference in UCL and UCLP infants prior to lip/nose surgery, after lip/nose repair, at age 1 year and at 2 years old.

There were strong correlations between height and weight at all time points (Pearson Correlation Coefficients 0.7-0.76; $p<0.001$). Head circumference was moderate to strongly correlated with weight, except at age 2 years. (Pearson Correlation Coefficients 0.57-0.76; $p\leq0.002$). There was no correlation between head circumference and height pre-operatively or at 2 years, however a strong correlation was evident post-lip repair and at age 1 year. (Pearson Correlation Coefficients 0.67-0.71; $p<0.001$). No correlation between head circumference and either height or weight was detected at age 2 years.

Table 4.13 Correlation between height, weight and head circumference in cleft sample

Correlation	Pre-op		Post-op		1y		2y	
	Pearson Correlation coeff	P value	Pearson Correlation coeff	P value	Pearson Correlation coeff	P value	Pearson Correlation coeff	P value
Height & Weight	**0.76**	0.00	**0.74**	0.00	**0.72**	0.00	**0.70**	0.00
Head circumference & Weight	**0.57**	0.00	**0.76**	0.00	**0.68**	0.00	0.33	0.75
Head circumference & Height	0.48	0.01	**0.67**	0.00	**0.71**	0.00	0.29	0.12

4.3.5 Summary of comparison of somatic measurements between UCL and UCLP infants at all time points

Irrespective of cleft type or gender there were no significant differences in weight, height or head circumference between children in the sample.

Height and weight correlated at all time points.

Head circumference appeared to correlate more consistently with weight prior to lip / nose surgery, post-operatively and at age 1 year. However head circumference did not correlate with height or weight at age 2 years.

4.4 Characterisation of Facial Soft Tissue morphology in UCL and UCLP infants, prior to surgical repair

In this section, a cross-sectional study of the characteristic facial morphology of UCL and UCLP infants was undertaken. Differences between cleft types, prior to primary cleft repair are presented. In addition, cleft and non-cleft side facial dimensions were compared for each cleft group separately. Characterisation of the facial morphology of UCL and UCLP infants from this study, compared with age matched non-cleft infants has already been published (Appendix 10).

4.4.1 Comparison of Facial Dimensions between cleft groups

Thirty-three of the original thirty-seven babies (Recruitment 1) attended for a pre-operative capture. One data set from this group was corrupted and was excluded. This resulted in **thirty-two** infant data sets, captured prior to lip / nose repair, which were available for cross-sectional analysis (Table 4.14).

Table 4.14 Number of facial data sets for cross-sectional analysis

Time point	UCL (N)	UCLP (N)	Total cleft cases
Pre-op	17	15	32

Figs 4.6 and 4.7 over-leaf illustrate the spectrum of deformity represented by this sample of children with various combinations of unilateral clefts of the lip, nose and palate.

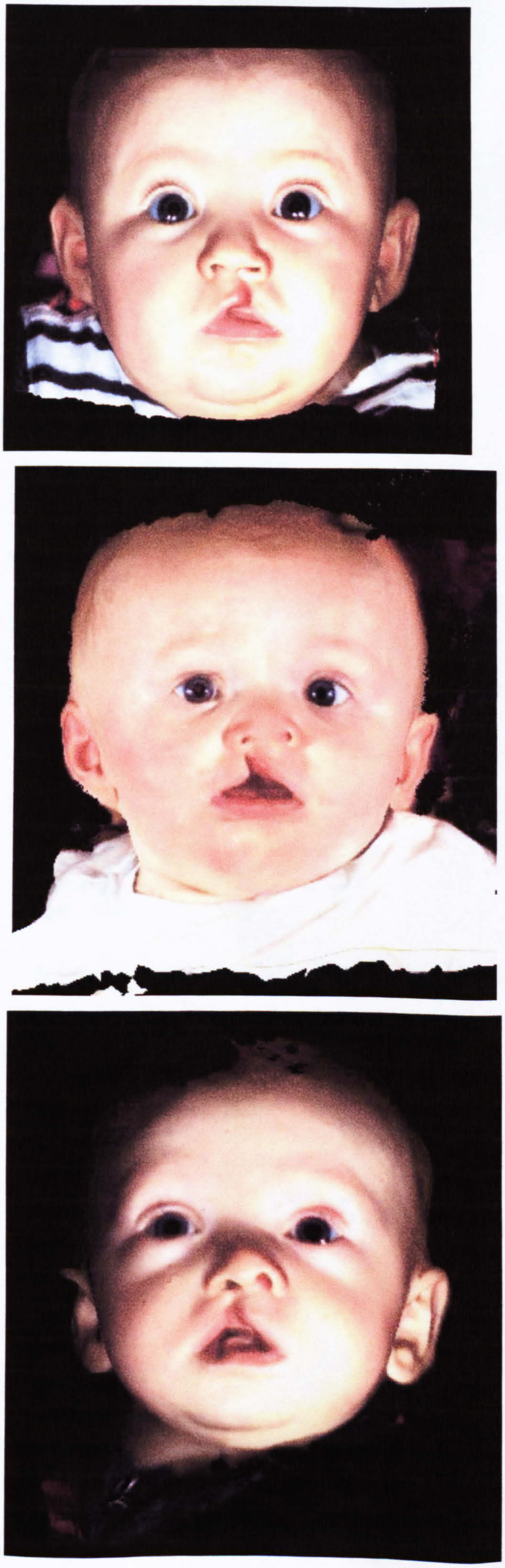


Figure 4.6 The spectrum of deformity in UCL infants

Figure 4.7 The spectrum of deformity in UCLP infants

Table 4.15& 4.16 (page 154 & 155) show means, medians and standard deviations of facial dimensions in UCLP and UCL infants, prior to primary surgery. Differences between cleft groups were observed in several facial dimensions and the significance tested by Mann-Whitney tests ($p<0.01$).

Significant discrepancies between cleft groups occurred mainly in horizontal dimensions and angles in the locale of the cleft. Nasal horizontal dimensions and Cupid's bow width were significantly larger in UCLP infants than in UCL infants, whilst cleft side alar base to commissure distance was shortened in UCLP infants. These are illustrated in Fig 4.8 below and Fig 4.9 overleaf. All other facial dimensions were of similar magnitude in both cleft types.

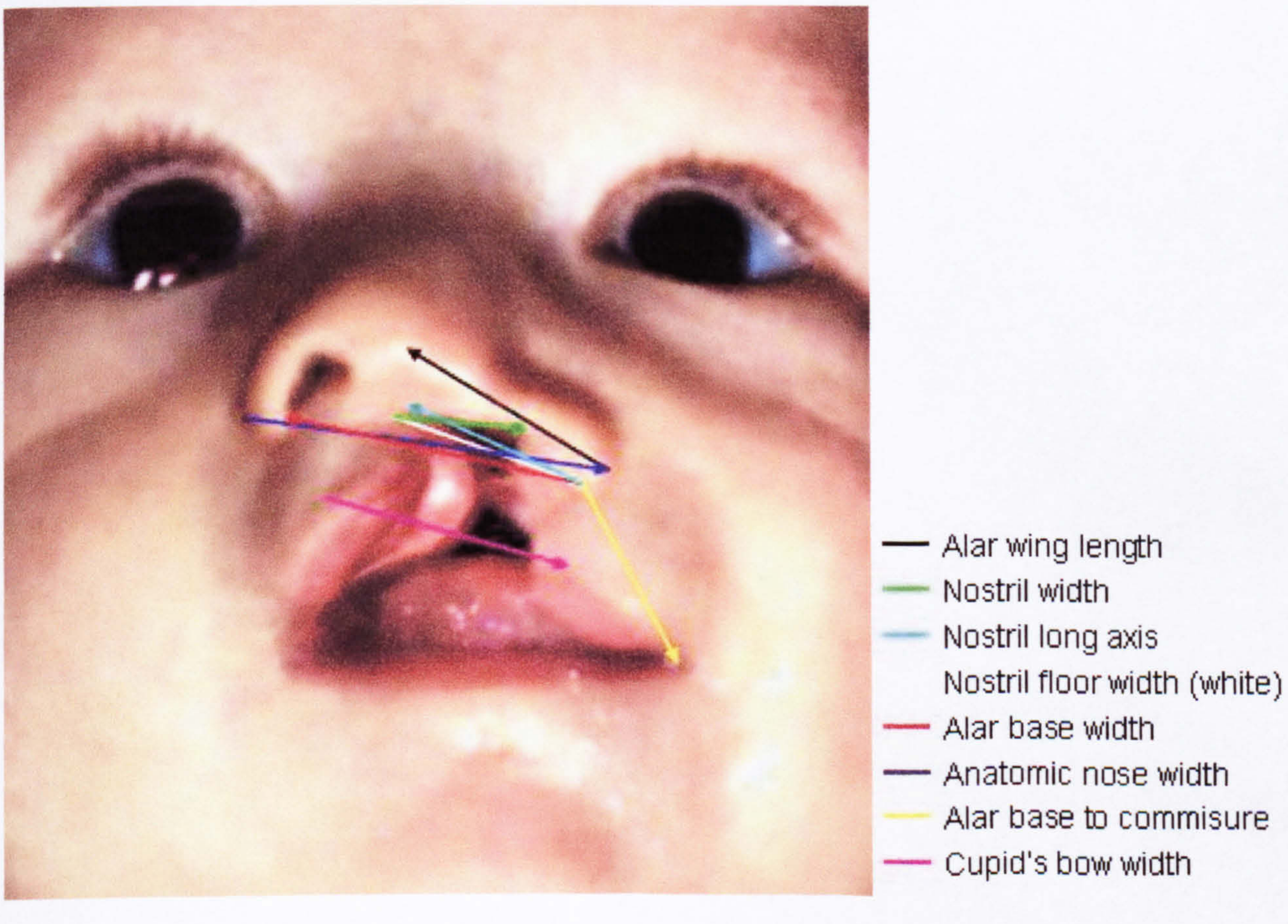


Figure 4.8 UCLP infant illustrating increased linear dimensions and shortened cleft side alar base to commisure distance, relative to UCL infants

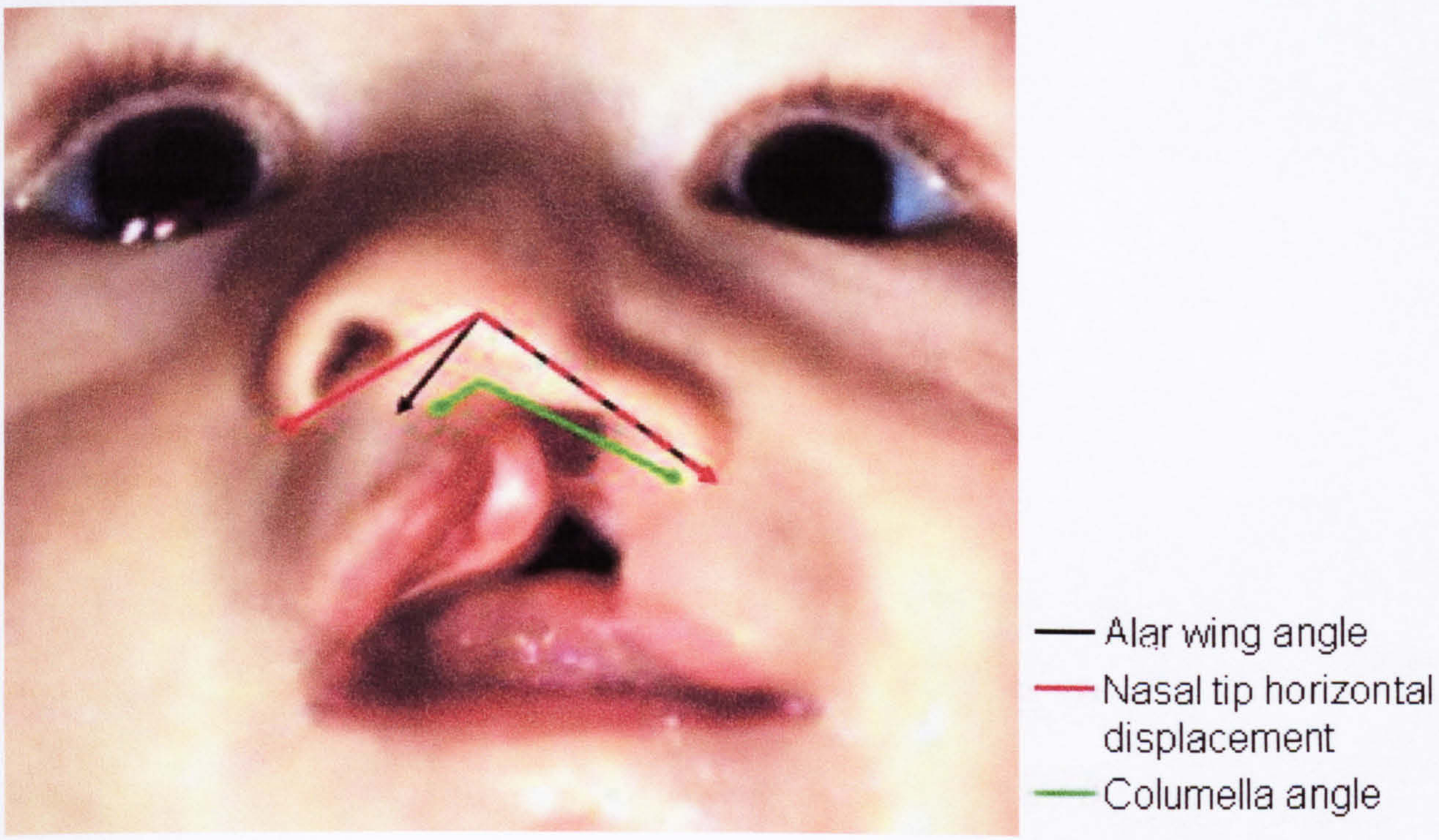


Figure 4.9 ***UCLP infant illustrating increased angles, compared to UCL infants***

Table 4.15 Facial dimensions in UCL and UCLP prior to primary surgery [continued overleaf]

Pre-op Facial Dimensions		UCL=17			UCLP=15	
Measurement	**Distance/angle**	**Cleft Type**	**Mean (mm / degrees)**	**Median**	**StDev**	**p-value**
Upper Face & Eyes						
Biocular width	ExR-ExL	UCL	66.0	65.6	3.8	0.38
		UCLP	67.0	67.7	3.2	
Intercanthal width	EnR-EnL	UCL	26.7	27.2	2.9	0.04
		UCLP	28.5	28.2	1.5	
Ocular width	EnL-ExL	UCL	20.5	19.9	1.8	0.51
		UCLP	20.2	20.4	1.0	
	EnR-ExR	UCL	20.1	19.8	1.8	0.88
		UCLP	20.0	20.1	1.5	
Endocanthion to nasion	EnL-n	UCL	17.0	17.0	1.7	0.31
		UCLP	17.5	17.6	1.0	
	EnR-n	UCL	16.3	16.3	2.1	0.57
		UCLP	15.9	15.8	1.6	
Horizontal Nose Dimensions						
Anatomic nose width	**acR-acL**	UCL	26.9	26.0	3.2	**0.002***
		UCLP	30.3	30.1	2.3	
Alar base width	**sbalL-sbalR**	UCL	16.4	16.8	4.4	**0.000****
		UCLP	23.4	24.0	3.6	
Soft nose width	alL-alR	UCL	23.3	23.1	3.3	0.50
		UCLP	24.0	24.2	2.1	
Nasal tip horizontal displacement angle	**acL-prn-acR**	UCL	98.8	100.9	5.4	**0.000****
		UCLP	106.2	107.1	4.5	
Vertical Nose Dimensions						
Nose dorsum length	n-prn	UCL	21.9	21.4	2.9	1.00
		UCLP	21.9	21.9	1.5	
Nasal tip-base	prn-sn	UCL	9.6	9.8	1.2	0.26
		UCLP	9.2	9.2	0.9	
Nasal tip angle	n-prn-sn	UCL	119.0	119.8	6.2	0.16
		UCLP	122.1	122.9	5.7	
Alar Wing						
projective alar length	**acL-prn**	UCL	18.6	17.9	3.0	**0.001***
		UCLP	21.0	21.0	1.7	
	acR-prn	UCL	16.8	16.7	1.6	0.97
		UCLP	16.8	16.7	1.3	
Alar wing angle	**acL-prn-sn**	UCL	60.9	61.0	7.3	**0.000****
		UCLP	74.3	72.6	7.8	
	acR-prn-sn	UCL	46.2	46.5	7.1	0.38
		UCLP	43.9	43.8	7.3	
Columella						
Columella thickness	sn0L-sn0R	UCL	5.0	4.6	0.9	0.70
		UCLP	4.9	4.7	0.9	
Columella height	sn0L-cL	UCL	1.8	1.7	0.7	0.76
		UCLP	1.9	1.9	0.8	
	sn0R-cR	UCL	2.6	2.6	0.6	0.89
		UCLP	2.7	2.3	1.2	
Columella angle	**sbalL-cL-sn0L**	UCL	73.7	74.8	23.8	**0.003***
		UCLP	106.8	106.1	32.1	
	sbalR-cR-sn0R	UCL	31.9	32.6	10.5	0.91
		UCLP	31.4	24.7	14.4	

*Significant ($p<0.01$)** highly significant ($p<0.001$)

Table 4.16 Facial dimensions in UCL and UCLP prior to surgery [continued]

Pre-op Facial Dimensions		UCL=17			UCLP=15	
Measurement	**Distance/angle**	**Cleft Type**	**Mean (mm / degrees)**	**Median**	**StDev**	**p-value**
Nostril						
Nostril floor width	**sbalL-sn0L**	UCL	8.2	8.3	4.3	**0.000****
		UCLP	15.6	15.4	3.4	
	sbalR-sn0R	UCL	5.0	5.1	0.7	0.26
		UCLP	5.4	5.2	1.3	
Nostril long axis	**sbalL-cL**	UCL	8.9	8.7	3.5	**0.000****
		UCLP	14.8	14.8	3.1	
	sbalR-cR	UCL	6.9	7.0	0.7	0.07
		UCLP	7.6	7.4	1.3	
Nostril width	**sn0L-al0iL**	UCL	6.8	6.6	2.0	**0.000****
		UCLP	9.2	9.3	1.2	
	sn0R-al0iR	UCL	5.1	5.3	1.0	0.42
		UCLP	4.8	4.3	1.2	
Nasolabial Dimensions						
Alar base to corner of mouth	**sbalL-chL**	UCL	20.2	19.6	2.6	**0.002***
		UCLP	18.0	17.8	1.9	
	sbalR-chR	UCL	20.5	19.9	2.6	0.98
		UCLP	20.5	21.2	2.1	
nose:mouth width ratio	acR-acL: chL-chR	UCL	0.9	0.9	0.1	0.06
		UCLP	1.0	1.0	0.3	
Nasolabial angle	prn-sn-ls	UCL	136.6	139.5	10.0	0.83
		UCLP	137.3	137.4	7.8	
protrusion of upper lip relative to nasal base	ls-n-sn	UCL	2.0	1.9	1.2	0.13
		UCLP	2.8	2.3	1.8	
Philtrum						
Cupid's bow width	**cphL-cphR**	UCL	14.8	14.4	3.6	**0.001***
		UCLP	20.0	20.1	4.1	
medial length	sn-ls	UCL	7.0	6.9	1.3	0.67
		UCLP	7.3	7.3	2.0	
Philtrum point to alar base	cphL-sbalL	UCL	8.9	8.2	2.0	0.81
		UCLP	8.7	8.9	1.4	
	cphR-sbalR	UCL	8.8	9.5	1.9	0.23
		UCLP	9.9	8.9	3.0	
Paramedial philtrum length	cph0R-sn0L	UCL	6.3	6.6	1.5	0.05
		UCLP	5.0	4.8	2.1	
	cphR-sn0R	UCL	9.7	9.7	1.7	0.06
		UCLP	11.2	10.4	2.5	
Mouth						
Lower vermillion width	stoi-li	UCL	4.1	4.3	0.9	0.68
		UCLP	4.7	4.7	1.0	
Lower lip length	stoi-sl	UCL	10.0	10.1	1.1	0.29
		UCLP	10.4	10.5	1.4	
Mouth width	chL-chR	UCL	29.9	29.5	3.9	0.21
		UCLP	31.5	31.3	2.8	
Face height						
Upper face height	n-sn	UCL	27.8	27.6	3.3	0.99
		UCLP	27.9	27.8	1.5	
Total face height	n-pg	UCL	60.4	61.3	6.6	0.45
		UCLP	59.0	57.5	3.5	

*Significant ($p<0.01$)** highly significant ($p<0.001$)

4.4.2 Comparison of Cleft and Non-cleft side dimensions

Cleft and non-cleft side median dimensions in the upper face, nose and philtrum were compared for each individual UCL and UCLP child and tested for significance by Wilcoxon's signed rank tests ($p<0.01$). Table 4.17 shows the facial dimensions in which there was a significant difference between the cleft and non-cleft sides, by cleft type.

In general, UCLP infants had larger discrepancies between cleft and non-cleft side dimensions than UCL infants ($p>0.01$). This follows from the previous findings of greater cleft-side dimensions in the UCLP group (Figs 4.8 & 4.9). The largest discrepancies in linear dimensions were recorded in the nostril floor and long axis, followed by the vertical height on each side of the philtrum (paramedial lengths). There was no significant discrepancy in cleft and non-cleft side columella heights in the UCLP group; however, there was a small significant difference in the UCL group (0.8mm). Philtrum point to alar base dimensions on the cleft and non-cleft sides were not significantly different in either UCL or UCLP, however the discrepancy in paramedial philtrum length was significant in both cleft groups. There was a significant discrepancy in cleft and non-cleft side alar base to commissure distance in UCLP infants, due to a shortening of this dimensions on the cleft side. In the UCL group alone, there was no significant difference between cleft and non-cleft endocanthion to nasion dimensions (further examined later), nostril long axis, or alar base to commissure distances.

Table 4.17 Differences between cleft and non-cleft side dimensions, by cleft type, prior to lip/nose surgery

Cleft vs Non-cleft side		UCL (n=17)		UCLP (n=15)	
Measurement	**Distance**	**Median difference (mm or degrees)**	**p-value**	**Median difference (mm or degrees)**	**p-value**
Endocanthion to nasion	en -n	0.5	0.13	**1.7**	**0.001***
Projective alar wing length	ac-prn	**1.7**	**0.005***	**4.1**	**0.001***
Alar wing angle	ac-prn-sn	**14.6**	**0.001***	**32**	**0.001***
Columella height	sn0-c	**0.8**	**0.002***	0.6	0.03
Columella angle	sbal-c-sn0	**42.5**	**0.000****	**80**	**0.001***
Nostril floor width	sbal-sn0	**2.6**	**0.005***	**10.2**	**0.001***
Nostril long axis	sbal-c	1.3	0.02	**7.2**	**0.001***
Nostril width	sn0-al0i	**1.3**	**0.001***	**4.7**	**0.001***
Philtrum point to alar base	cph-sbal	0.1	0.92	0.9	0.26
Philtrum paramedial length	cph (cph0)-sn0	**3.1**	**0.000****	**5.8**	**0.001***
Alar base to commisure	sbal-ch	0.3	1.0	**2.5**	**0.001***

*Significance ($p<0.01$); ** highly significant ($p<0.001$)

4.4.3 Investigation of inter-canthal dimensions

A preliminary study comparing UCLP and UCL facial dimensions with a non-cleft control group has been already published (Appendix 10). It was shown that UCLP infants had increased inter-canthal distance compared to controls (telecanthus), but UCL infants did not. This was attributed to subtle differences in cleft-side endocanthion to nasion (**en-n**) dimensions between cleft groups. Further investigation of the difference between cleft and non-cleft side dimensions prior to and after primary lip/nose surgery, at age 1 year and at 2 years was undertaken (Table 4.18).

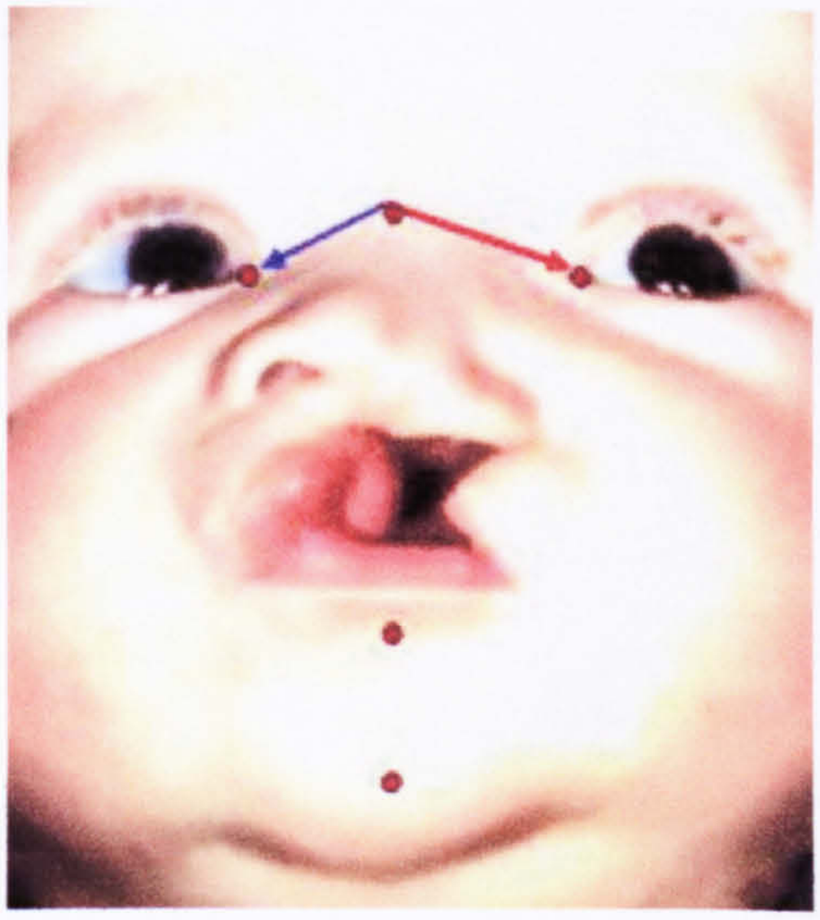


Figure 4.10 UCLP infant illustrating increased** en-n **dimension on the cleft side (red)

Comparison of cleft and non-cleft side soft tissue endocanthion to nasion dimensions (**en-n**) for each child, revealed a significantly wider distance on the cleft side (p=0.001) in UCLP infants only (Fig 4.10). The discrepancy between cleft and non-cleft sides persisted after lip/nose repair (p=0.006), and at age 1 year (p=0.001) in the UCLP group, whilst there was no significant discrepancy in the UCL group. At age 2 years, the discrepancy previously noted in the UCLP group was not evident i.e. there was no significant difference between the cleft and non-cleft sides in either UCLP or UCL children.

Table 4.18 Difference between cleft and non-cleft en-n dimensions, by cleft type

Cleft vs Non-cleft side		UCL		UCLP	
Endocanthion to nasion (en-n)		**Median difference (mm)**	**p-value**	**Median difference (mm)**	**p-value**
Prior to surgery	(n=32)	0.5	0.13	**1.7**	**0.001***
After lip/nose repair	(n=28)	0.4	0.09	**1.4**	**0.006***
1 year	(n=34)	0.2	0.38	**1.1**	**0.001***
2 years	(n=32)	0.2	0.51	0.5	0.16

Significant ($p<0.01$)

4.4.4 Summary of Characterisation of Facial soft tissue morphology in UCL and UCLP infants, prior to surgical repair

UCL and UCLP infants displayed significant nasal and lip deformity.

Facial dimensions in the locale of the cleft tended to be larger in UCLP infants than in UCL infants. Discrepancies in individual cleft and non-cleft side dimensions in the nose and lip were accordingly larger in UCLP infants.

UCLP infants displayed greater deformity in the nose than UCL infants, illustrated by a more flattened and elongated cleft side alar wing, more displaced nasal tip, a more elongated and distorted cleft side nostril, and a more splayed columella position.

In the lip, an increased cleft width and shortened cleft side alar base to commisure distance were the only features that distinguished UCLP from UCL infants.

There was significant discrepancy in the cleft and non-cleft side paramedial dimensions of the philtrum, in both cleft groups, and this was related to a shorter dimension bordering the cleft. However, the distances from the philtral points to the alar base on the cleft and non-cleft sides were similar in both cleft groups.

UCLP infants also displayed significant discrepancy in endocanthion to nasion dimensions in the upper face before surgery. This was still detectable after primary lip/nose repair and at age 1 year, but was not evident at age 2 years.

4.5 Longitudinal Changes in Facial Morphology with Lip Repair and with Growth

Thirty-seven children had data collected at a minimum of two time points, which were incorporated into the longitudinal analysis. Complete data sets (captured at all four time points) were obtained for **nineteen** children. The numbers of subjects represented in each time interval are detailed in table... below.

Table 4.19 Number of facial data sets for longitudinal analysis

Time interval	UCL (N)	UCLP (N)	Total cleft cases
Preop-postop	13	11	24
Post-1y	13	11	24
1y - 2y	9	15	24
Pre - 1y	12	13	25
Pre - 2y	8	11	19
Post - 2y	9	10	19

'Preop' and 'Pre' refer to facial dimensions prior to primary surgical intervention.

'Postop'and 'Post' refer to facial dimensions after primary lip/nose repair.

Longitudinal Results are presented in three parts:

1. Facial dimension changes with primary lip/nose repair (Pre-op compared to post-op).
2. Post-surgical Facial soft tissue growth (changes from postop-1y; 1y-2y; post-2y).
3. Total change, incorporating surgery and growth up to age 1 year and up to age two years are also reported (Pre-1y and Pre-2y).

The magnitude of change in facial dimension in each time interval was calculated for each individual. The amount of change was expressed as median change in millimetres or degrees, and as 'mean percentage change' (%), for illustrative purposes. Wilcoxon signed ranks tests were performed to identify the significance of the change for each cleft individual. Mann-Whitney tests revealed significant differences between cleft groups ($p<0.01$). Changes over time in individual facial dimensions and angles are presented according to facial region. Significant results are highlighted in **bold** and the level of significance indicated by *.

4.5.1 Changes in Facial dimension with primary lip / nose repair

Appendix 7 shows cross-sectional facial dimensions immediately post lip/nose surgery for 28 cleft infants (12 UCLP; 16 UCL). No significant differences in facial dimension were detectable between cleft types at the post-lip / nose repair capture.

The magnitude of the changes in facial dimensions achieved with surgery (pre-post-op interval) are detailed below (11 UCLP; 13 UCL).

4.5.1.1 Upper Face

Tables 4.20 & 4.21 and Fig 4.11 (page 162) show the magnitude of change in upper face dimensions in both cleft groups (combined and separately) during the period encompassing primary lip/nose repair. Median change in upper face and eye parameters after primary lip / nose repair was similar in UCL and UCLP infants.

Biocular width increased by 5.8% (3.8mm) and intercanthal width increased by a similar proportion (5.4%; 1.5mm) pre-postop. Similar increases occurred in eye dimensions on both sides of the face. Cleft side ocular width increased by 5.3% and non cleft side ocular width increased by 6.4% (1.1mm and 1.3mm respectively). The distance from endocanthion to nasion did not significantly increase on the cleft side, nor on the non-cleft side, in either cleft group.

As the upper face and eyes were not involved in the surgery, the percentage change in these dimensions over time represented the amount of growth of the upper face during the lip / nose surgical period. Significant growth of 5-6 % was seen in all dimensions except cleft and non-cleft side endocanthion to nasion distances (en-n), which did not change significantly in either cleft group (Fig 4.12).

Table 4.20 Upper face and eye dimensions changes with primary lip/nose repair (UCL & UCLP combined)

Upper Face & Eyes						
Measurement	**Distance**		**Median Actual Change (mm)**	**p-value**	**Mean.% change**	**Sdev Mean %**
Biocular width		exL-exR	3.8	**0.000****	5.8	3.1
Intercanthal width		enL - enR	1.5	**0.000****	5.4	5.3
Ocular width	**cleft side**	exL -enL	1.1	**0.000****	5.3	4.4
	non-cleft side	exR -enR	1.3	**0.000****	6.4	4.5
Endocanthion to nasion	cleft side	n-enL	0.6	0.018	3.5	6.6
	non-cleft side	n -enR	0.9	0.015	6.0	10.1

*Significant ($p<0.01$)** highly significant ($p<0.001$)

Table 4.21 Differences between UCL and UCLP in Upper face & eye dimension changes with lip/nose surgery

Upper Face & Eyes		UCL	UCLP	Mann-Whitney	
Measurement	**Distance**	**Median change (mm)**	**Median change (mm)**	**99% CI**	**p-value**
Biocular width	exL-exR	4.7	3.6	-1.7, 3.3	0.25
Intercanthal width	enL - enR	1.4	1.3	-1.2, 1.6	0.77
Ocular width	exL -enL	1.3	0.8	-0.5, 1.3	0.18
	exR -enR	1.2	1.4	-0.9, 1.3	0.60
Endocanthion to nasion	enL -n	0.7	0.6	-1.9, 0.9	0.42
	enR -n	0.2	1.6	-2.4, 1.1	0.22

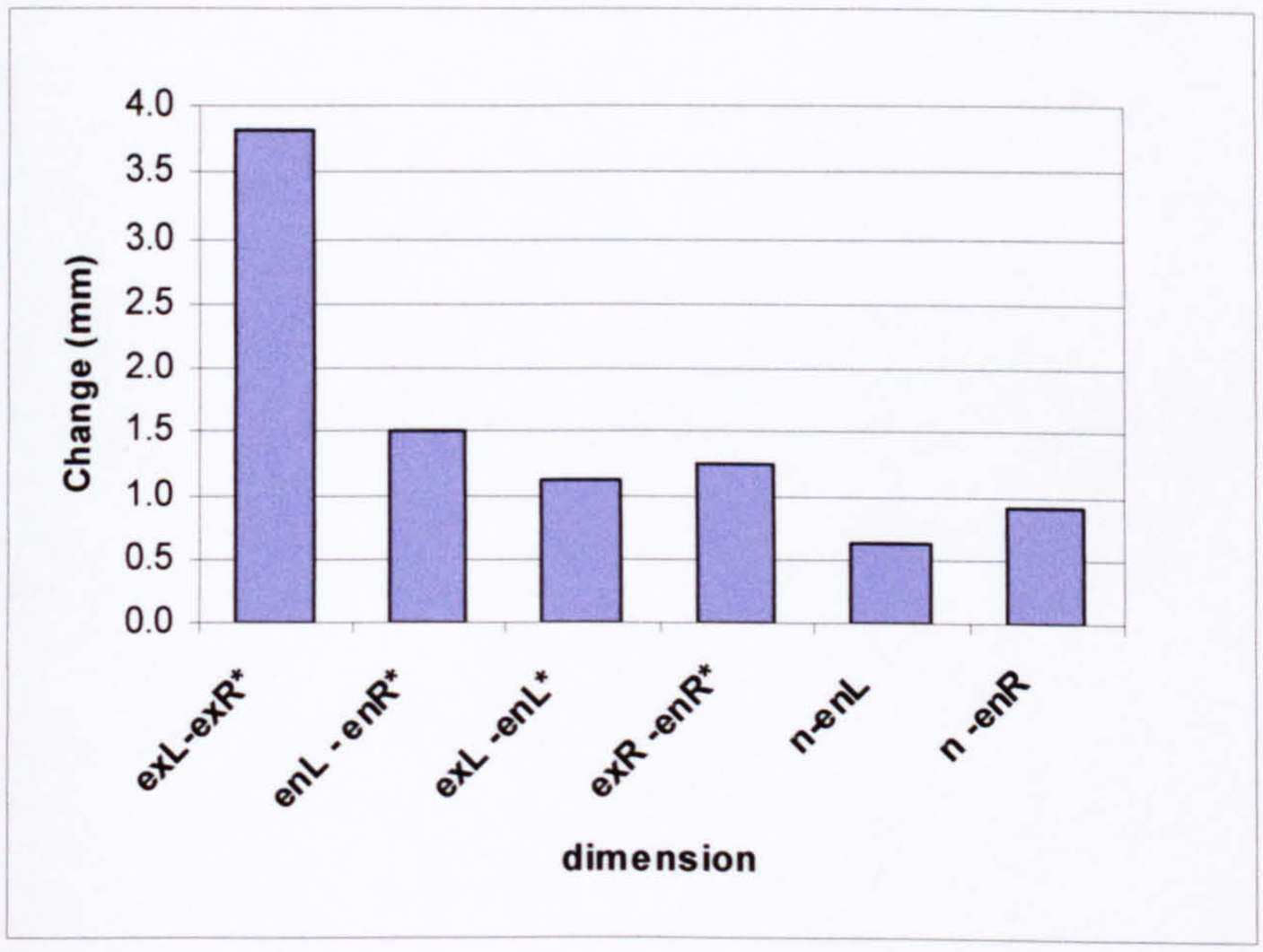


Figure 4.11 ***Median change (mm) in upper face and eye dimensions with primary lip/nose surgery (*significant change)***

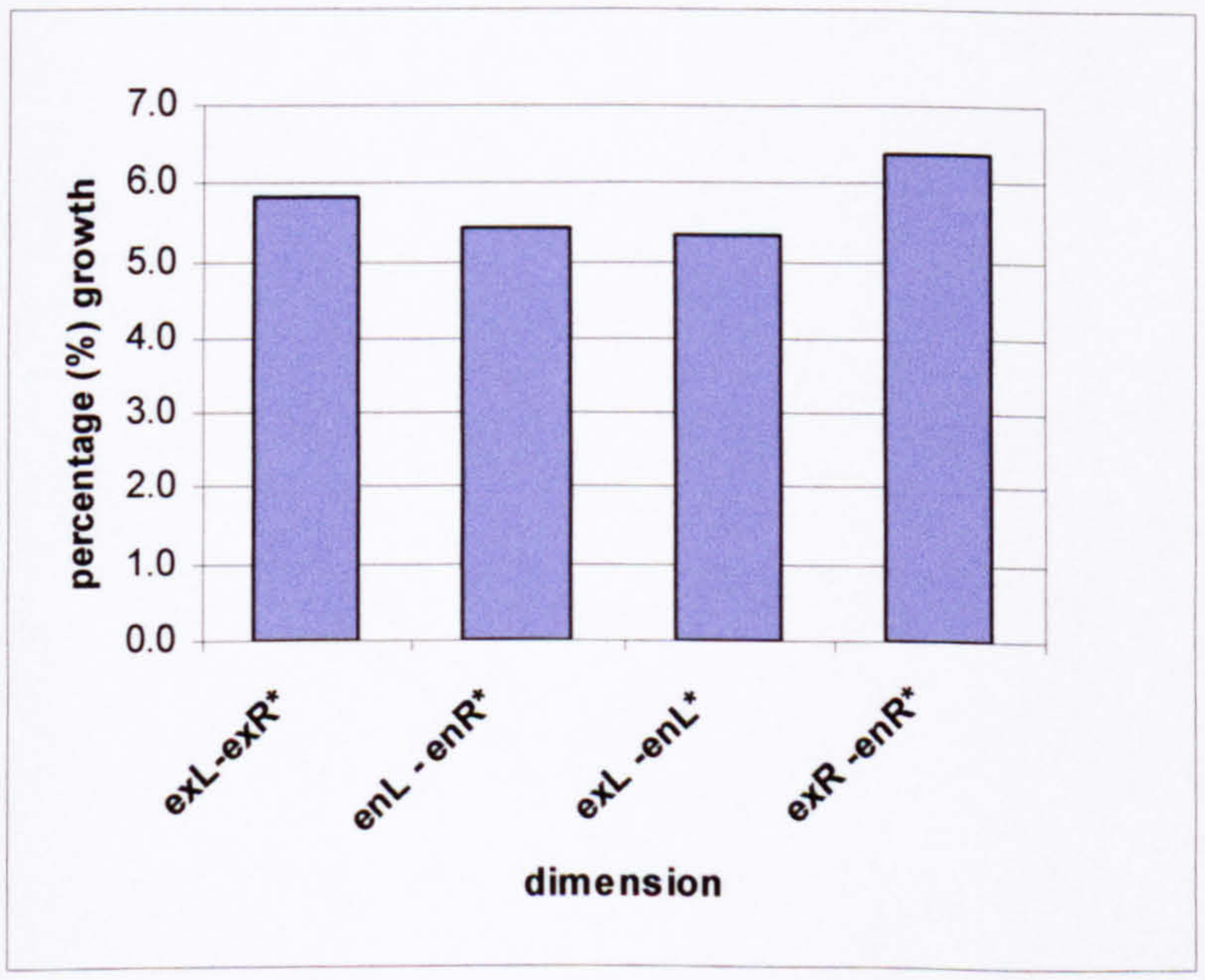


Figure 4.12 ***Percentage (%) growth of upper face and eyes during period of primary lip/nose surgical repair, in UCL and UCLP***

4.5.1.2 Nose

4.5.1.2.1 Horizontal Dimensions

Tables 4.22 & 4.23 (overleaf) show the magnitude of overall change in horizontal nose dimensions with surgery in both cleft groups, and the individual differences between UCL and UCLP.

A significant median reduction in alar base width was achieved with cleft lip /nose repair. In the UCLP group, alar base width was reduced by almost a centimetre (9.7mm) after surgery, compared to just under 2mm in the UCL group. Anatomic nose width did not appear to alter with surgery when pooled cleft data were examined (Table 4.22), yet there appeared to be an increase in length in UCL and a reduction in length in UCL, when cleft groups were examined separately. (Table 4.23). However, neither group experienced significant change when considered separately, although in the UCLP group this just failed to reach statistical significance at the 99% level (UCL p=0.295; UCLP p=0.018). Soft nose width did not significantly alter with surgery in either cleft group. The amount of horizontal displacement of the nasal tip can be gauged by measuring the angle between prn and both ac points. A reduced angle indicates improvement in the orientation of the tip, relative to the base of the nose. Significant reduction in nasal tip horizontal displacement occurred after surgery in the UCLP group only (p=0.004), whilst in the UCL group the change was not statistically significant (p=0.142) (Table 4.23 & Fig 4.13).

Table 4.22 ***Horizontal nose dimension changes with primary lip/nose surgery (UCL & UCLP combined)***

Horizontal Nose Dimensions					
Measurement	**Distance/Angle**	**Median Actual Change (mm or degrees)**	**p-value**	**Mean % change**	**Sdev Mean %**
Alar base width	**sbalL-sbalR**	**-5.1**	**0.000****	**-22.3**	18.6
Anatomic nose width	acL-acR	-0.8	0.134	-2.4	8.0
Soft nose width	alL-alR	-0.1	0.658	-0.7	9.4
Nasal tip horizontal displacement (angle)	**acR-prn-acL**	**-5.5**	**0.001***	**-5.5**	6.4

*Significant ($p<0.01$)** highly significant ($p<0.001$)

Table 4.23 ***Differences between UCL and UCLP in horizontal nose dimension changes with lip/nose surgery***

Horizontal Nose Dimensions		UCL	UCLP	Mann-Whitney	
Measurement	**Distance/Angle**	**Median change (mm or degrees)**	**Median change (mm or degrees)**	**99% CI**	**p-value**
Alar base width	sbalL-sbalR	**-1.7**	**-9.7**	1.8, 10.9	**0.002***
Anatomic nose width	acL-acR	**1.0**	**-2.5**	0.1, 5.0	**0.009***
Soft nose width	alL-alR	0.6	-0.3	-1.4, 4.5	0.07
Nasal tip horizontal displacement (angle)	acR-prn-acL	**-3.4**	**-10.8**	0.1, 14.3	**0.008***

*Significant ($p<0.01$)

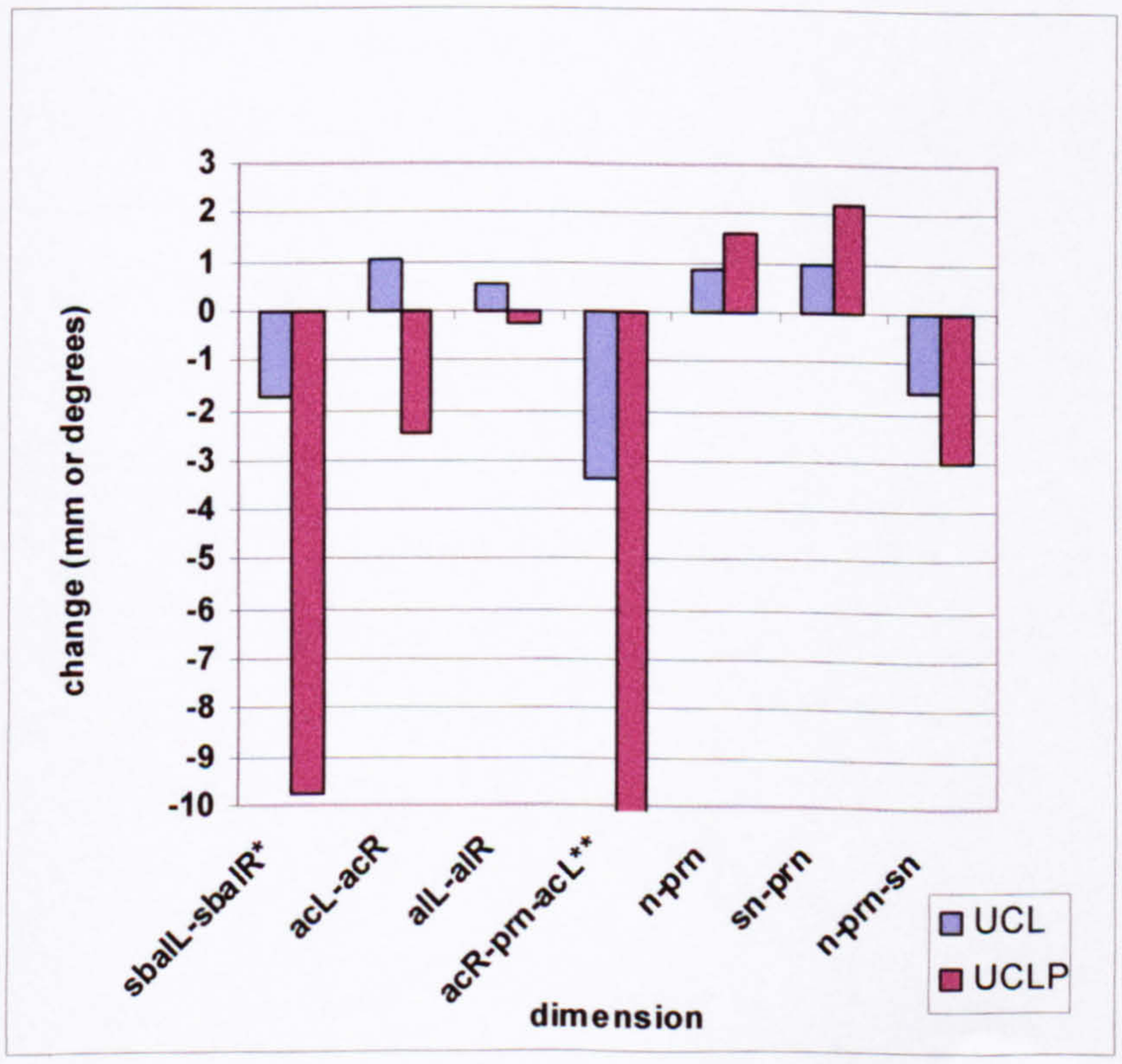


Figure 4.13 ***Horizontal and vertical nose dimension median changes with primary lip/nose/ surgery, in UCL and UCLP. (*significant change, UCL & UCLP; ** significant change UCLP only).***

4.5.1.2.2 Vertical Dimensions

Table 4.24 & 4.25 (overleaf) show the magnitude of change in vertical nose dimensions with surgery in both cleft groups and individual differences between each cleft group.

Significant changes were found in nasal tip –base length and nasal tip angulation. Nose dorsum length (n-prn) did not alter significantly with surgical repair. The degree of protrusion of the tip of the nose is indicated by the distance between the nasal tip and the point at the base of the columella. A median improvement in nasal tip protrusion of approximately 18% was achieved with surgery (1.6mm). The vertical prominence of the tip of the nose, relative to nasion and the base of the columella (nasal tip angle) was improved by a small but significant 2.4% (2.7 degrees), immediately following lip/ nose repair (Fig 4.13).

No statistically significant differences in median change in vertical nose parameters with primary lip / nose repair in UCL and UCLP infants were detected (table 4.25). However, the difference in improvement in nasal tip protrusion of 2.2mm in UCLP, compared with 1mm in the UCL group (Fig 4.13) only just failed to reach statistical significance at the 99% level.

Table 4.24 Vertical nose dimension changes with primary lip/nose surgery (UCL & UCLP combined)

Vertical Nose Dimensions					
Measurement	**Distance/Angle**	**Median Actual Change (mm or degrees)**	**p-value**	**Mean % change**	**Sdev Mean %**
Nose dorsum length	n-prn	1.2	0.02	6.3	11.3
Nasal tip-base	**sn-prn**	**1.6**	**0.000****	**17.8**	15.4
Nasal tip angulation	**n-prn-sn**	**-2.7**	**0.006***	**-2.4**	3.6

*Significant ($p<0.01$)** highly significant ($p<0.001$)

Table 4.25 Differences between UCL and UCLP in vertical nose dimension changes with lip/nose surgery

Vertical Nose Dimensions		UCL	UCLP	Mann-Whitney	
Measurement	**Distance/Angle**	**Median change (mm or degrees)**	**Median change (mm or degrees)**	**99% CI**	**p-value**
Nose dorsum length	n-prn	0.9	1.6	-2.7, 3.2	0.91
Nasal tip-base	sn-prn	1.0	2.2	-2.6, 0.1	0.01
Nasal tip angulation	n-prn-sn	-1.6	-3.0	-4.2, 6.1	0.52

4.5.1.3 Alar Wing dimensions

Table 4.26 (overleaf) shows the magnitude of changes in alar wing dimensions with primary surgery in both cleft groups. Table 4.27 (overleaf) shows differences in median change in alar wing parameters between cleft groups.

Significant changes with surgery were achieved in all parameters except cleft side projective alar length. Following surgery, the cleft side alar wing was not significantly reduced in length. On the non-cleft side, a median gain in length of 9.6% (1.5mm) was found after surgery. The only significant difference between cleft groups was in the magnitude of cleft side alar wing angle reduction with surgery. The UCL group experienced a median reduction of 7 degrees, whilst the UCLP group experienced a huge reduction of almost 25 degrees. No statistically significant differences were detected between cleft groups in the amount of improvement in non-cleft side alar wing angle, which amounted to a 16.4% increase (5.7 degrees).

Table 4.26 Alar wing dimension changes with primary lip/nose surgery (UCL & UCLP combined)

Alar Wing Dimensions						
Measurement	**Distance/Angle**		**Median Actual Change (mm or degrees)**	**p-value**	**Mean % change**	**Sdev Mean %**
Projective alar length	cleft side	acL-prn	-0.8	0.050	-3.8	11.3
	non-cleft side	**acR-prn**	**1.5**	**0.000****	**9.6**	**9.2**
Alar wing angulation	**cleft side**	**acL-prn-sn**	**-13.9**	**0.000****	**-19.7**	**14.1**
	non-cleft side	**acR-prn-sn**	**5.7**	**0.002***	**16.4**	**22.9**

*Significant ($p<0.01$)** highly significant ($p<0.001$)

Table 4.27 Differences between UCL & UCLP in alar wing dimension changes with lip/nose surgery

Alar Wing Dimensions			UCL	UCLP	Mann-Whitney	
Measurement	**Distance/Angle**		**Median change (mm or degrees)**	**Median change (mm or degrees)**	**99% CI**	**p-value**
Projective alar length	cleft side	acL-prn	-0.1	-2.8	0.7, 4.2	0.05
	non-cleft side	acR-prn	1.4	1.3	-2.5, 1.0	0.42
Alar wing angulation	**cleft side**	acL-prn-sn	-7.2	-24.9	3.2, 26.1	**0.001***
	non-cleft side	acR-prn-sn	2.1	5.8	-10.9, 9.1	1.00

*Significant ($p<0.01$)

4.5.1.4 Columella

Table 4.28(overleaf) shows the magnitude of change in columella parameters with primary surgical repair in both cleft groups.

A small, but significant, increase (1mm) was detected in columella thickness after primary surgery. Columella height showed a small but significant increase of 0.8mm on the cleft side after surgery. The non-cleft side columella height increased by 0.5mm, but just failed to reach statistical significance. Primary repair achieved a mean 41% reduction (38 degrees) in cleft side columella angle. On the non-cleft side there was an increase almost 40% (7 degrees) in both groups, but this was not significant at the 99% level.

Table 4.29 (overleaf) shows that the median change in columella dimensions, with primary lip/nose repair were not statistically different in UCL and UCLP infants. Confidence intervals for columella angle demonstrated that there was a large range of variation in columella in both cleft groups, and this could explain why no significant difference was detected between cleft groups.

When dimensions on the repaired side and the non-cleft side after lip/nose surgery were compared, no significant discrepancy between cleft side and non-cleft side columella heights were found in either group. Columella angle was not significantly different on the repaired side compared with the non-cleft side in either group, despite an apparent discrepancy in the UCLP group (p=0.255). (Appendix 7).

Table 4.28 Columella dimension changes with primary lip/nose surgery (UCL & UCLP combined)

Columella Dimensions						
Measurement	**Distance/Angle**		**Median Actual Change (mm or degrees)**	**p-value**	**Mean % change**	**Sdev Mean %**
Columella height	**cleft side**	**sn0L-cL**	**0.8**	**0.001***	**53.7**	**54.7**
	non-cleft side	sn0R-cR	0.5	0.015	25.0	35.1
Columella thickness		**sn0L-sn0R**	**1.0**	**0.003***	**21.3**	**28.1**
Columella angulation	**cleft side**	**sbalL-cL-sn0L**	**-38.6**	**0.000****	**-41.3**	**24.7**
	non-cleft side	sbalR-cR-sn0R	7.0	0.027	39.5	72.8

*Significant ($p<0.01$)** highly significant ($p<0.001$)

Table 4.29 Differences between UCL and UCLP in columella dimension changes with lip/nose surgery

Columella Dimensions			UCL	UCLP	Mann-Whitney	
Measurement	**Distance/Angle**		**Median change (mm or degrees)**	**Median change (mm or degrees)**	**99% CI**	**p-value**
Columella height	cleft side	sn0L-cL	1.0	0.6	-0.6, 1.4	0.25
	non-cleft side	sn0R-cR	0.6	0.6	-1.3, 0.9	0.82
Columella thickness		sn0L-sn0R	1.0	0.9	-1.4, 1.7	0.69
Columella angulation	cleft side	sbalL-cL-sn0L	-29.7	-52.3	-8.5, 65.1.	0.04
	non-cleft side	sbalR-cR-sn0R	2.6	5.9	-30.1, 9.5	0.15

4.5.1.5 Nostril Dimensions

Table 4.30 (overleaf) shows the magnitude of change in nostril dimensions with primary surgical repair in both cleft groups. Table 4.31 (overleaf) shows the differences between cleft groups in the amount of change in nostril parameters with surgery. Significantly greater change occurred in the UCLP group in all cleft side nostril dimensions, and also in non-cleft side nostril width.

After lip/ nose repair, cleft side nostril floor width was reduced by 10.6mm in UCLP and 2.9mm in UCL. Non-cleft side nostril floor width did not change significantly in either cleft group. The long axis of the nostril was measured from the subalare (sbal) point to the top of the columella. Cleft side nostril long axis was significantly reduced with surgery by 8.2mm in UCLP, compared to a 1.9mm in the UCL group (Fig 4.14). Non-cleft side long axis did not change significantly in either group. The third distance measured to characterise the nostril was the nostril width from sn0-al0i points. On the cleft side there was a significant reduction of 3.6mm in the UCLP group ($p=0.004$), but no significant change in the UCL group ($p=0.36$). Non-cleft side nostril width was significantly increased by 1.5mm in the UCLP group ($p=0.005$), but did not change significantly in the UCL group ($p=0.014$). There were no differences in repaired cleft side nostril dimensions, when compared to non-cleft side dimensions in individuals in either cleft group, after primary lip/nose surgery.

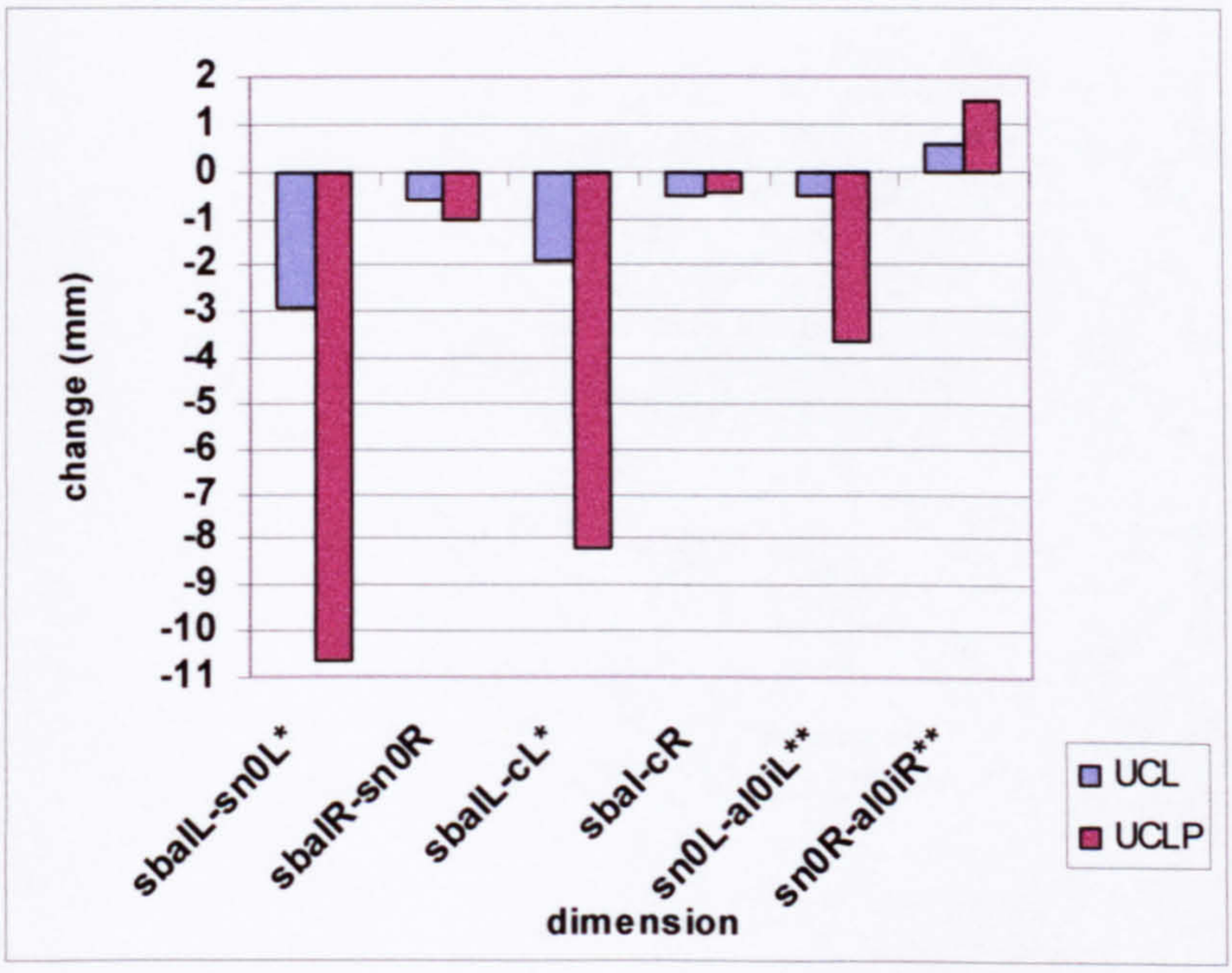


Figure 4.14 ***Nostril dimension median changes with primary lip/nose surgery, in UCL and UCLP. (*significant change UCL & UCLP; **significant change UCLP only).***

Table 4.30 Nostril dimension changes with primary lip / nose surgery (UCL & UCLP combined)

Nostril Dimensions						
Measurement	**Distance**		**Median Actual Change (mm)**	**p-value**	**Mean % change**	**Sdev Mean %**
Nostril floor width	**cleft side**	**sbalL-sn0L**	**-6.2**	**0.000****	**-43.6**	**28.1**
	non-cleft side	sbalR-sn0R	-0.8	0.011	-11.8	22.0
Nostril long axis	**cleft side**	**sbalL-cL**	**-5.0**	**0.001***	**-35.4**	**24.0**
	non-cleft side	sbal-cR	-0.6	0.018	-7.3	17.9
Nostril width	**cleft side**	**sn0L-al0iL**	**-1.7**	**0.000****	**-18.8**	**27.5**
	non-cleft side	**sn0R-al0iR**	**1.0**	**0.000****	**22.9**	**22.6**

*Significant ($p<0.01$) ** highly significant ($p<0.001$)

Table 4.31 Differences between UCL and UCLP in amount of nostril dimension change with lip/nose surgery

Nostril Dimensions			UCL	UCLP	Mann-Whitney	
Measurement	**Distance**		**Median change (mm)**	**Median change (mm)**	**99% CI**	**p-value**
Nostril floor width	**cleft side**	sbalL-sn0L	-2.9	-10.6	3.1, 10.8	**0.000***
	non-cleft side	sbalR-sn0R	-0.6	-1.0	-1.1, 1.7	0.52
Nostril long axis	**cleft side**	sbalL-cL	-1.9	-8.2	3.3, 8.9	**0.000****
	non-cleft side	sbal-cR	-0.6	-0.5	-1.1, 2.5	0.60
Nostril width	**cleft side**	sn0L-al0iL	-0.5	-3.6	1.1, 5.4	**0.000****
	non-cleft side	sn0R-al0iR	0.5	1.5	0.3, 1.8	0.04

*Significant ($p<0.01$) ** highly significant ($p<0.001$)

4.5.1.6 Nasolabial Dimensions

Table 4.32 (overleaf) shows the magnitude of change in nasolabial dimensions with primary surgical repair in both cleft groups. Table 4.33 (overleaf) shows that the median change in nasolabial parameters, with primary lip/nose repair was not significantly different in UCL and UCLP infants.

The distance between the corner of mouth and alar base on the cleft side increased by 4.2mm, and by 3.4mm on the non-cleft side, after lip repair. Nasolabial angle was not significantly altered after primary lip / nose repair in either UCL or UCLP. The degree of protrusion of the upper lip relative to the base of the nose did not alter with primary lip/nose repair in either cleft group. The nose: mouth width ratio was significantly reduced with surgery to the same extent, in both cleft groups.

Table 4.32 Nasolabial dimension canges with primary lip/nose surgery (UCL & UCLP combined)

Nasolabial Dimensions						
Measurement	**Distance/Angle**		**Median Actual Change (mm or degrees)**	**p-value**	**Mean % change**	**Sdev Mean %**
Alar base to corner of the mouth	**cleft side**	**sbalL-chL**	**4.2**	**0.000****	**24.2**	**15.9**
	non-cleft side	**sbalR-chR**	**3.4**	**0.000****	**18.5**	**13.2**
Nose/mouth width ratio		**ac-ac:ch-ch**	**-0.1**	**0.000****	**-11.1**	**12.5**
Nasolabial angle		prn-sn-ls	1.6	0.484	1.2	7.0
Protrusion of upper lip, relative to nasal base		ls-n-sn	0.7	0.061	78.8	147.9

** highly significant ($p<0.001$)

Table 4.33 Differences between UCL and UCLP in nasolabial dimension changes with lip/nose surgery

Nasolabial dimensions			UCL	UCLP	Mann-Whitney	
Measurement	**Distance/Angle**		**Median change (mm or degrees)**	**Median change (mm or degrees)**	**99% CI**	**p-value**
Alar base to corner of the mouth	cleft side	sbalL-chL	2.9	5.1	-5.1, 1.1	0.07
	non-cleft side	sbalR-chR	3.4	3.2	-2.3, 3.1	0.52
Nose/mouth width ratio		ac-ac:ch-ch	-0.1	-0.1	-0.1, 0.2	0.60
Nasolabial angle		prn-sn-ls	0.4	3.1	-15.7, 8.6	0.20
Protrusion of upper lip, relative to nasal base		ls-n-sn	0.7	1.5	-2.7, 0.8	0.07

4.5.1.6.1 Philtrum Dimensions

Table 4.34 (overleaf) shows the magnitude of change in philtrum dimensions with primary surgical repair in both cleft groups. Fig 4.16 & Table 4.35 show significant differences in philtrum dimensions between cleft groups occurred in the amount of change in Cupid's bow width and the paramedial philtrum dimension of the non-cleft side.

Cupid's bow width was reduced following primary lip repair in both cleft groups. Millard repair resulted in reduction of the distance between the philtral points, or peaks, of almost 12mm in UCLP infants and 3mm in UCL infants (Table 4.35). In both cleft groups, the medial length of the philtrum was increased by 1.5mm (20.4%). The paramedial philtrum dimension on the repaired side increased in length by 4.8mm in both cleft groups. On the non-cleft side, a significant increase of 1.3mm occurred in the UCL group only (p=0.008). In contrast, the distance between the philtral point and the alar base on the cleft side was unchanged by surgery in both cleft groups. On the non-cleft side, there was also a significant increase only in the UCL group (1.9mm, p=0.004).

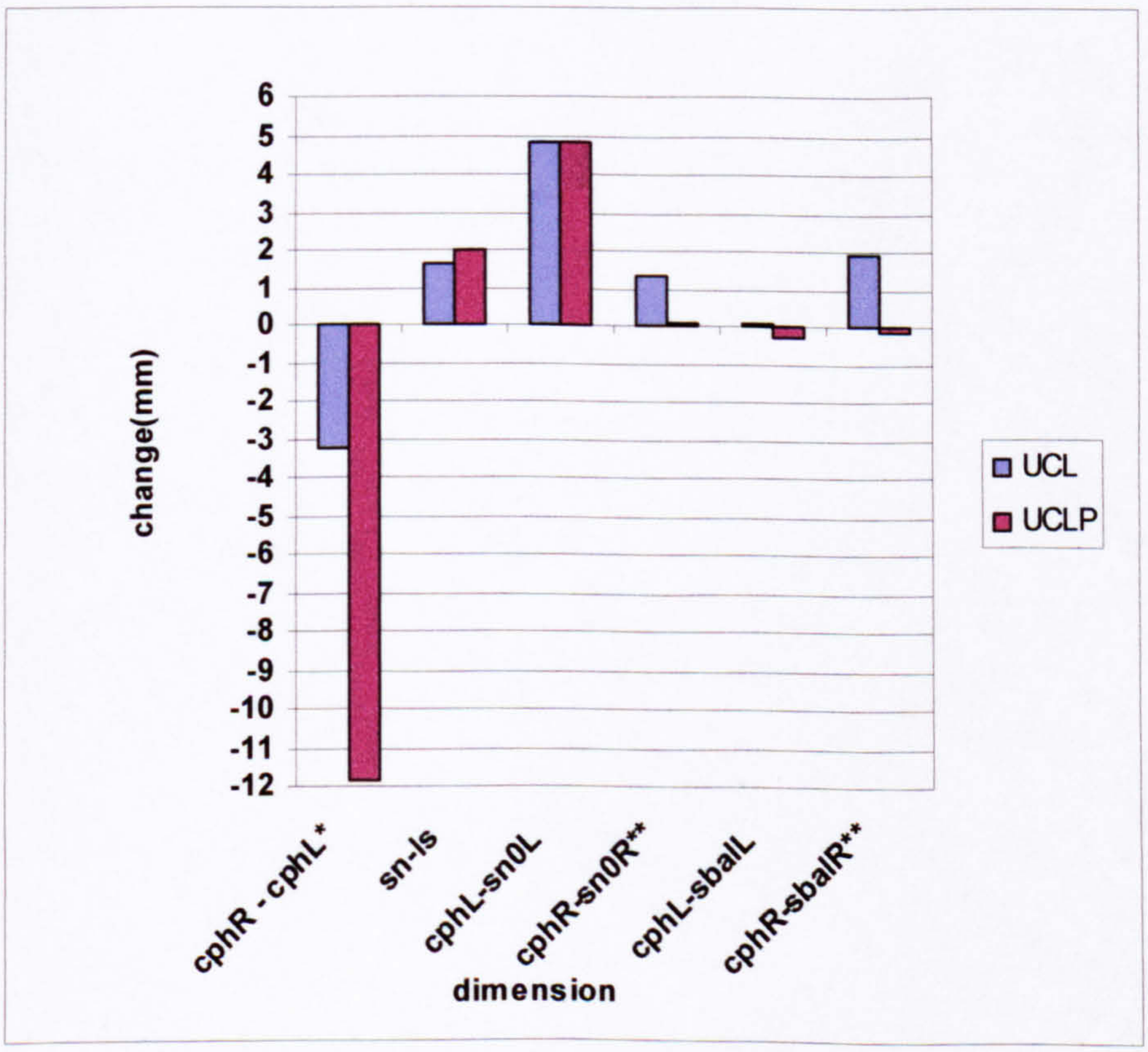


Figure 4.15 ***Philtrum dimension median changes with primary surgery, in UCL and UCLP. (*significant change UCL & UCLP; *significant change in UCL only)***

Table 4.34 Philtrum dimension changes with primary lip/nose surgery (UCL & UCLP combined)

Philtrum Dimensions						
Measurement	**Distance/Angle**		**Median Actual Change (mm)**	**p-value**	**Mean % change**	**Sdev Mean %**
Cupid's Bow Width		**cphR - cphL**	**-6.2**	**0.000****	**-31.1**	**30.9**
Medial length		**sn-ls**	**1.5**	**0.003***	**20.4**	**23.8**
Paramedial philtrum length	**cleft side**	**cph0R-sn0L**	**4.8**	**0.000****	**103.5**	**78.9**
	non-cleft side	cphR-sn0R	0.6	0.046	5.6	16
Philtral point to alar base	cleft side	cphL-sbalL	0.0	0.989	0.4	9.9
	non-cleft side	**cphR-sbalR**	**1.1**	**0.008***	**13.4**	**21.7**

*Significant ($p<0.01$)** highly significant ($p<0.001$)

Table 4.35 Differences between UCL and UCLP in philtrum dimension changes with lip / nose surgery

Philtrum Dimensions			UCL	UCLP	Mann-Whitney	
Measurement	**Distance**		**Median change (mm)**	**Median change (mm)**	**99% CI**	**p-value**
Cupid's Bow		**cphR-cphL**	**-3.3**	**-11.8**	**1.6, 13.3**	**0.003***
Medial length		sn-ls	1.6	2.0	-1.9, 2.7	0.86
Paramedial Philtrum length	cleft side	cph0R-sn0L	4.8	4.8	-2.5, 2.6	0.89
	non-cleft side	**cphL-sn0L**	**1.3**	**0.1**	**0.1, 3.6**	**0.007***
Philtral point to alar base	cleft side	cphL-sbalL	0.1	-0.3	-1.1, 1.4	0.73
	non-cleft side	cphR-sbalR	1.9	-0.2	-0.9, 3.0	0.13

*Significant ($p<0.01$)

After surgery, cleft and non-cleft side philtrum dimensions were compared, for each individual (Table in Appendix 7).

The discrepancy between the repaired and non-cleft side philtral point to alar base dimension in UCL infants was 1.1mm (p=0.008). In UCLP infants this discrepancy was 1.6mm (p=0.003) i.e. the repaired side was shorter in both cleft groups. However, the paramedial philtrum height from cph-sn0 on the repaired and non-cleft sides were not significantly different in either group (Fig 4.16)

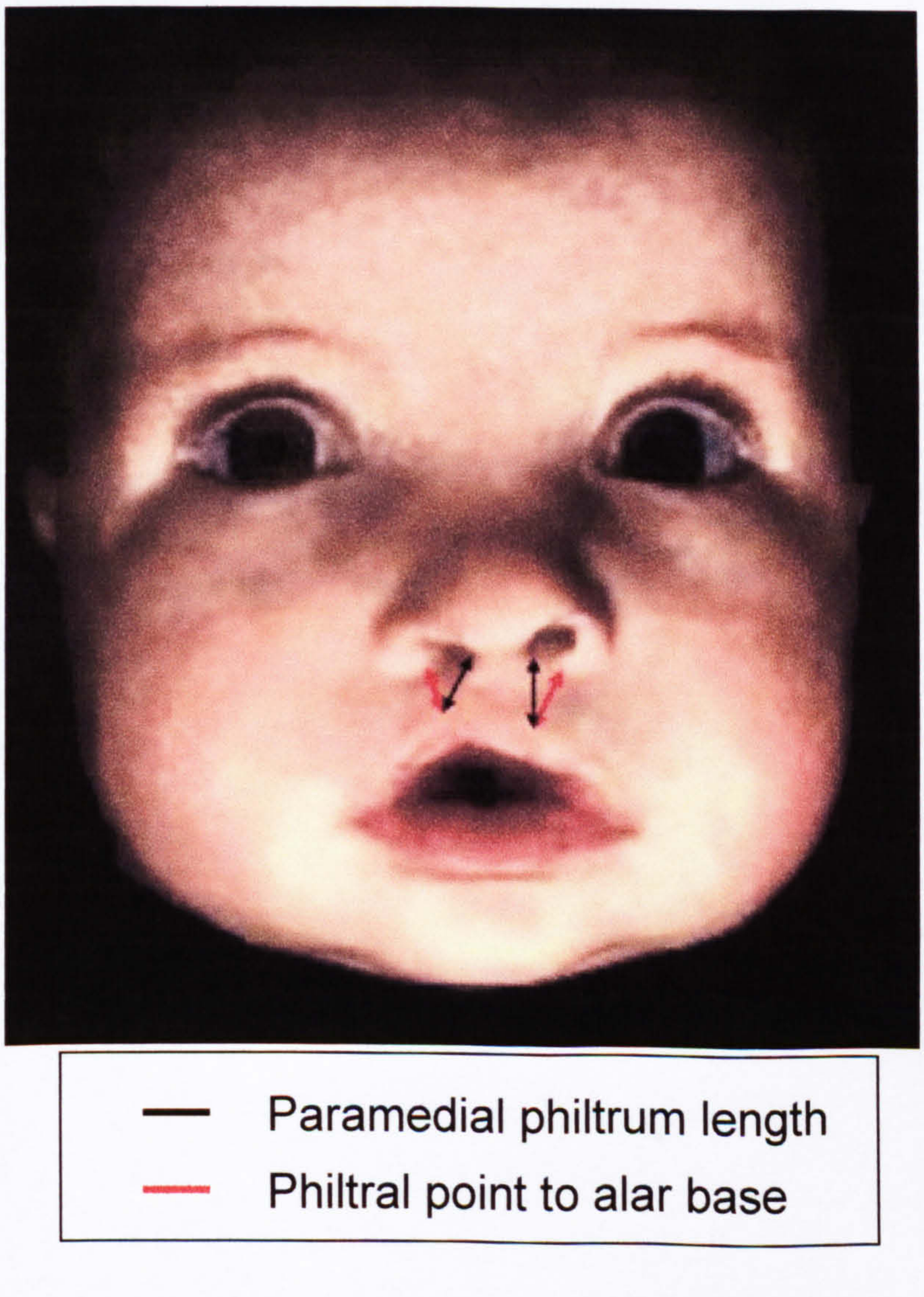


Figure 4.16 ***Cleft and non-cleft Philtrum dimensions, after lip/nose surgery***

4.5.1.6.2 Mouth Dimensions

Table 4.36 shows the magnitude of change in mouth dimensions with primary surgical repair in both cleft groups.

Mouth width did not significantly alter with surgery. Lower Vermillion width did not significantly increase, but lower lip length increased by 7.4% (0.7mm). Table 4.37 shows that there were no significant differences between cleft groups in mouth dimension changes

Table 4.36 Mouth dimension changes with primary lip/nose surgery (UCL & UCLP combined)

Mouth Dimensions					
Measurement	**Distance/Angle**	**Median Actual Change (mm or degrees)**	**p-value**	**Mean % change**	**Sdev Mean %**
Lower vermillion width	stoi-li	0.6	0.03	18.1	36.7
Lower lip length	stoi-sl	0.7	**0.005***	7.4	10.3
Mouth width	chL-chR	1.7	0.050	6.6	10.9

*Significant ($p<0.01$)

Table 4.37 Differences between UCL and UCLP in mouth dimension changes with lip/nose surgery

Mouth Dimensions		UCL	UCLP	Mann-Whitney	
Measurement	**Distance**	**Median change (mm)**	**Median change (mm)**	**99% CI**	**p-value**
Lower vermillion width	stoi-li	0.50	0.42	-1.4, 1.7	0.89
Lower lip length	stoi-sl	0.85	0.12	-1.0, 1.61	0.33
Mouth width	chL-chR	2.1	-0.1	-0.8, 6.7	0.06

4.5.1.7 Face height

Fig 4.17 & Table 4.38 (overleaf) show the magnitude of changes in face height dimensions during the period encompassing primary lip/nose repair in both cleft groups. Table 4.39 shows that the magnitude of change in total face height and upper face height was similar in UCL and UCLP. Total face height increased by 12.6% (7mm) in this interval. Upper face height increased by 7.4% (1.9mm) (Fig 4.17).

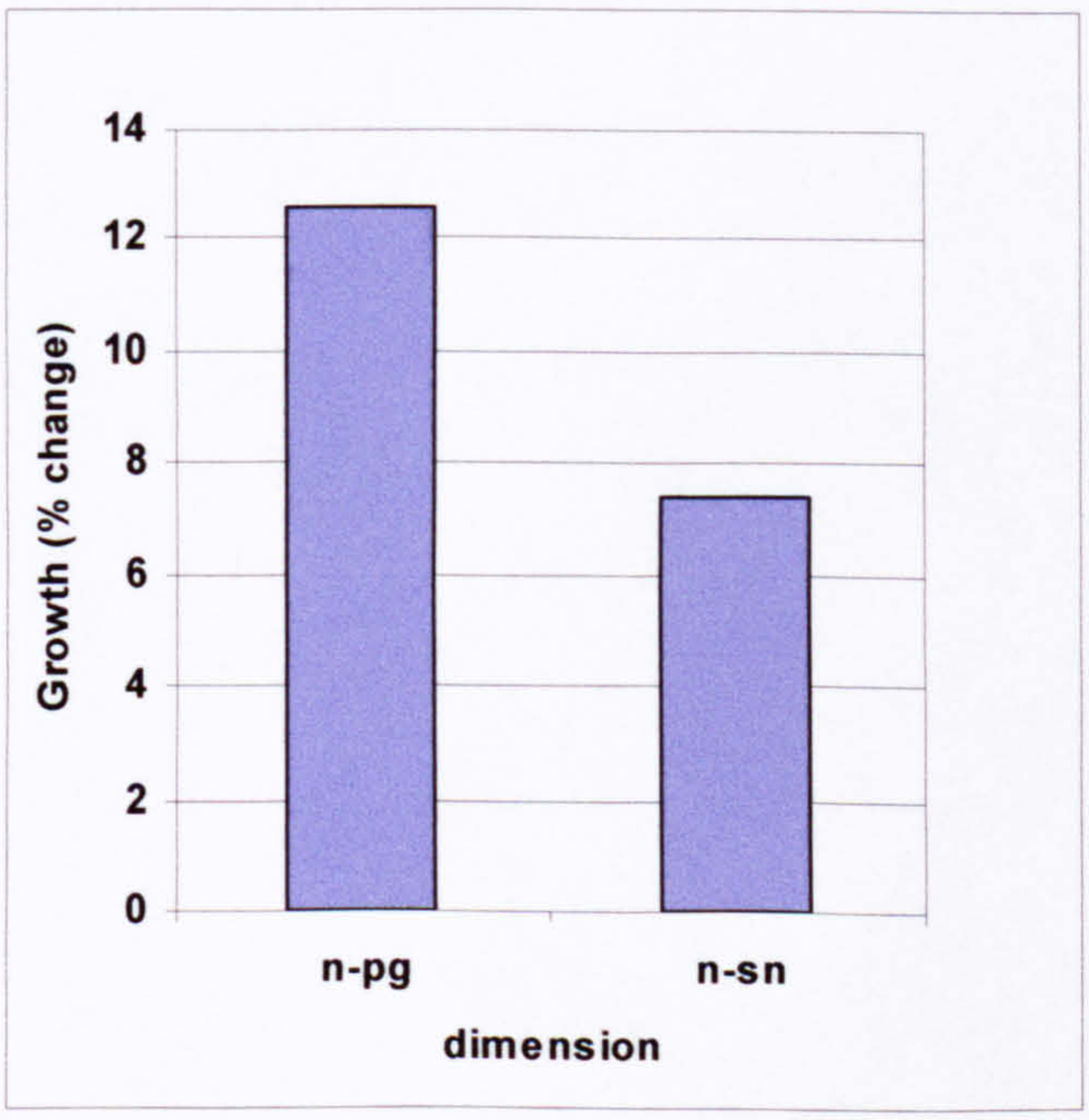


Figure 4.17 ***Percentage growth (%) in face height during period of lip/nose repair***

Table 4.38 Face height changes with primary lip / nose surgery (UCL & UCLP combined)

Face Height Dimensions					
Measurement	**Distance/Angle**	**Median Actual Change (mm)**	**p-value**	**Mean % change**	**Sdev Mean %**
Total Face height	n-pg	6.9	**0.000****	12.6	8.8
Upper face height	n-sn	1.9	**0.001***	7.4	8.7

*Significant (p<0.01)** highly significant (p<0.001)

Table 4.39 Differences between UCL and UCLP in face height changes with lip/nose surgery

Face Height Dimensions		UCL	UCLP	Mann-Whitney	
Measurement	**Distance**	**Median change (mm)**	**Median change (mm)**	**99% CI**	**p-value**
Total Face height	n-pg	6.2	6.9	-6.6, 4.9	0.74
Upper face height	n-sn	1.5	2.1	-3.5, 2.5	0.69

4.5.2 Summary of facial changes with primary lip/nose repair

Upper face Dimensions
5-6% growth occurred in all upper face dimensions except the inner canthus to nasion distance on the cleft and non-cleft sides.

Horizontal Nose Dimensions
Alar base width was reduced in both cleft groups, but to a greater extent in UCLP. Anatomic nose width was not significantly altered in either cleft group. Soft nose width was unaltered in either cleft group. Horizontal orientation of the nasal tip relative to base of the nose improved in UCLP, with reduction of the nasal tip horizontal displacement angle, but not significantly in UCL.

Vertical Nose Dimensions
Nose length was unaltered after surgery and the degree of protrusion of nasal tip (tip-base length) was increased. The vertical prominence of the nasal tip was slightly reduced (2.4%)

Alar Wing
Cleft side alar wing length was unchanged whilst non-cleft side alar wing length was increased. Cleft side alar wing angle was reduced in both cleft groups, but this was greater in UCLP. Non-cleft side alar wing angle was increased in both cleft groups by the same amount.

Columella
Cleft side columella height increased by 0.8mm. Non-cleft side columella length did not alter. Columella width increased. Marked reduction in cleft side columella angle occurred but there was no corresponding statistically significant change on non-cleft side.

Nostrils
Nostril floor width and nostril long axis were reduced and the corresponding non-cleft dimensions unaltered in both cleft groups. Nostril width (sn0-al0i) altered only in the UCLP group. The cleft side nostril width decreased and the non-cleft side width increased.

Nasolabial Dimensions
The distance from the alar base to mouth commisure on cleft and non-cleft sides increased. Nasolabial angle and the degree of protrusion of upper lip relative to nasal base were unaltered. Nose:mouth width ratio was reduced.

Philtrum
Cupid's Bow width was reduced in both cleft groups, but this was greater in UCLP. Philtrum medial length increased. Cleft side paramedial philtrum length increased, but cleft side distance from philtral point to alar base was unchanged in both groups. Non-cleft side paramedial length and philtral point to alar base were increased only in UCL.

Mouth Dimensions
Lower lip length increased but lower vermillion width did not alter. Mouth width was unaltered.

Face Height
Total face height increased by 12.6% and upper face height increased by 7.4%.

4.5.3 Post-surgical Facial soft tissue changes

4.5.3.1 Differences in Facial Dimensions in UCL and UCLP infants at age 1 year and age 2 years

In this section, data relates to cross sectional measurements of facial dimensions in UCL and UCLP children at age 1 year and age 2 years. Complete data are shown in Appendix 8 and Appendix 9. Facial dimensions were compared by cleft group and the significance of any differences were tested by Mann-Whitney tests ($p<0.01$).

There were no significant differences in median facial dimensions between cleft groups at age 1 year, except in anatomic nose width and upper face height (Fig 4.18). For UCLP children, these dimensions were increased, relative to UCL infants (2.2mm and 1.8mm respectively).

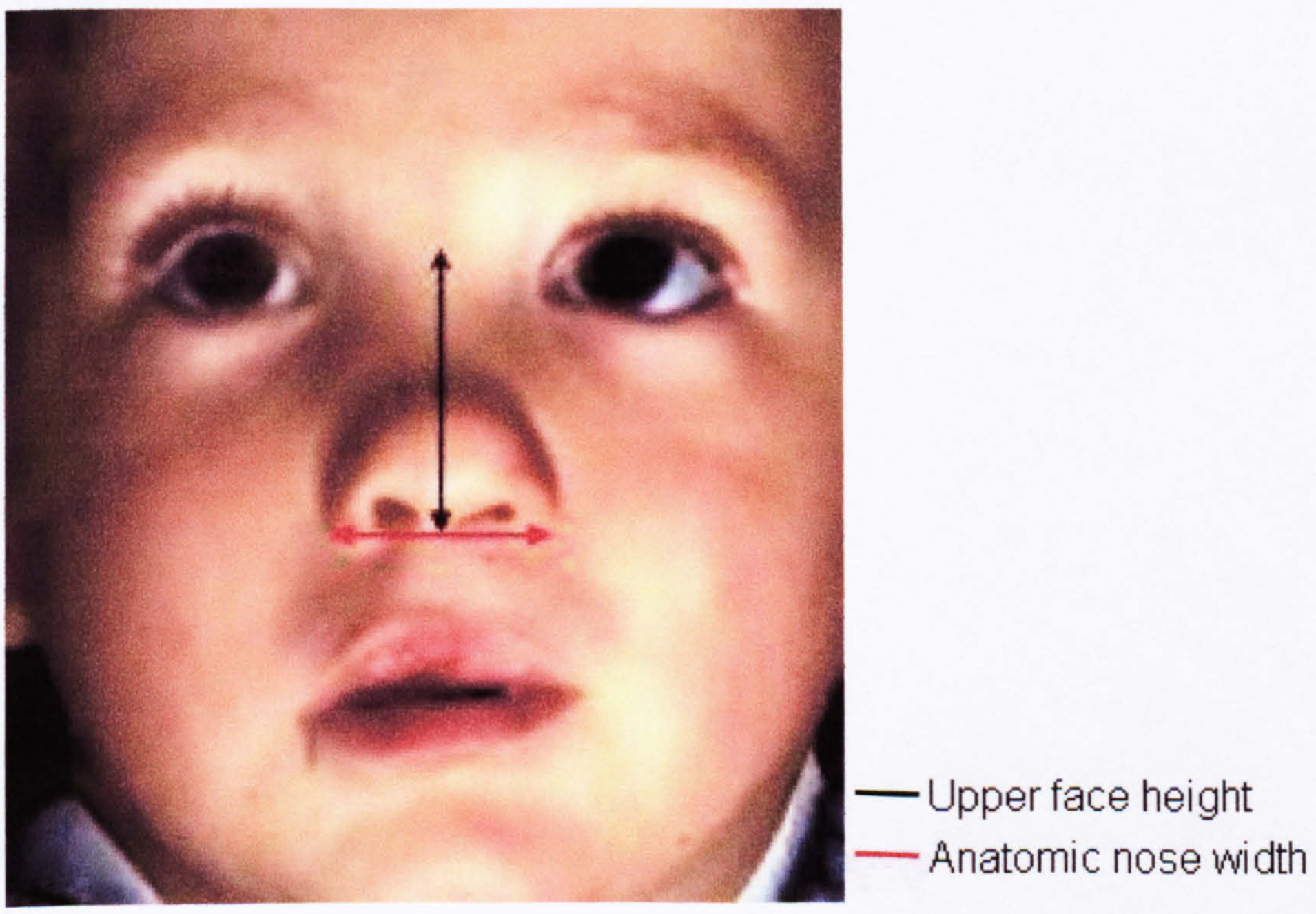


Figure 4.18 1-year-old UCLP face illustrating increased dimensions, compared to UCL

Appendix 9 shows 2-year-old facial dimensions in UCLP and UCL children. At age 2 years, no significant differences in median facial dimensions could be demonstrated between cleft groups.

4.5.4 Differences in the magnitude of post-surgical changes in Facial Dimensions and total change over 2 years in UCL and UCLP children

This section relates to differences in the magnitude of longitudinal facial changes with growth after lip/nose surgery and total change up to age 2 years. Changes in facial dimensions were compared by cleft group to ascertain if they grew differently. A similar pattern and amount of change occurred in facial dimensions with growth after primary lip/nose repair (post-1y, 1y-2y and overall post-2y), in both cleft groups.

However, when compared to the pre-op baseline, significant differences in the magnitude of total change in year one and total change over 2 years were demonstrated between cleft groups (pre-1y and pre-2y).

4.5.4.1 Cleft group differences in total change with surgery and growth in the first year (pre-1y)

Cleft groups differed significantly in the total amount of change experienced with surgery and growth in ten facial dimensions in the first year (Table 4.40, Page 201).

Nine of these differences were in the nasal area (alar base width, anatomic nose width, cleft side alar wing length and angle, cleft side columella angle, all cleft side nostril dimensions and non-cleft side nostril width). The tenth difference was in Cupid's bow width.

Greater changes occurred in some nasal dimensions and Cupid's bow width in UCLP children in the first year, and were consistent with greater soft tissue disruption prior to surgery (Figs 4.19 & 4.20). One non-cleft dimension (nostril width) was significantly increased from the pre-op baseline in the UCLP group alone. This was an effect of surgery in this group, which persisted to age 1 year.

UCL children experienced an overall gain in anatomic nose width and cleft side alar wing length, compared to negligible change in UCLP children in the same first year period (Fig 4.21). However, this was due to a combination of the effects of surgery (reduction) and growth (increase) in the UCLP group, resulting in no apparent net change in the first year.

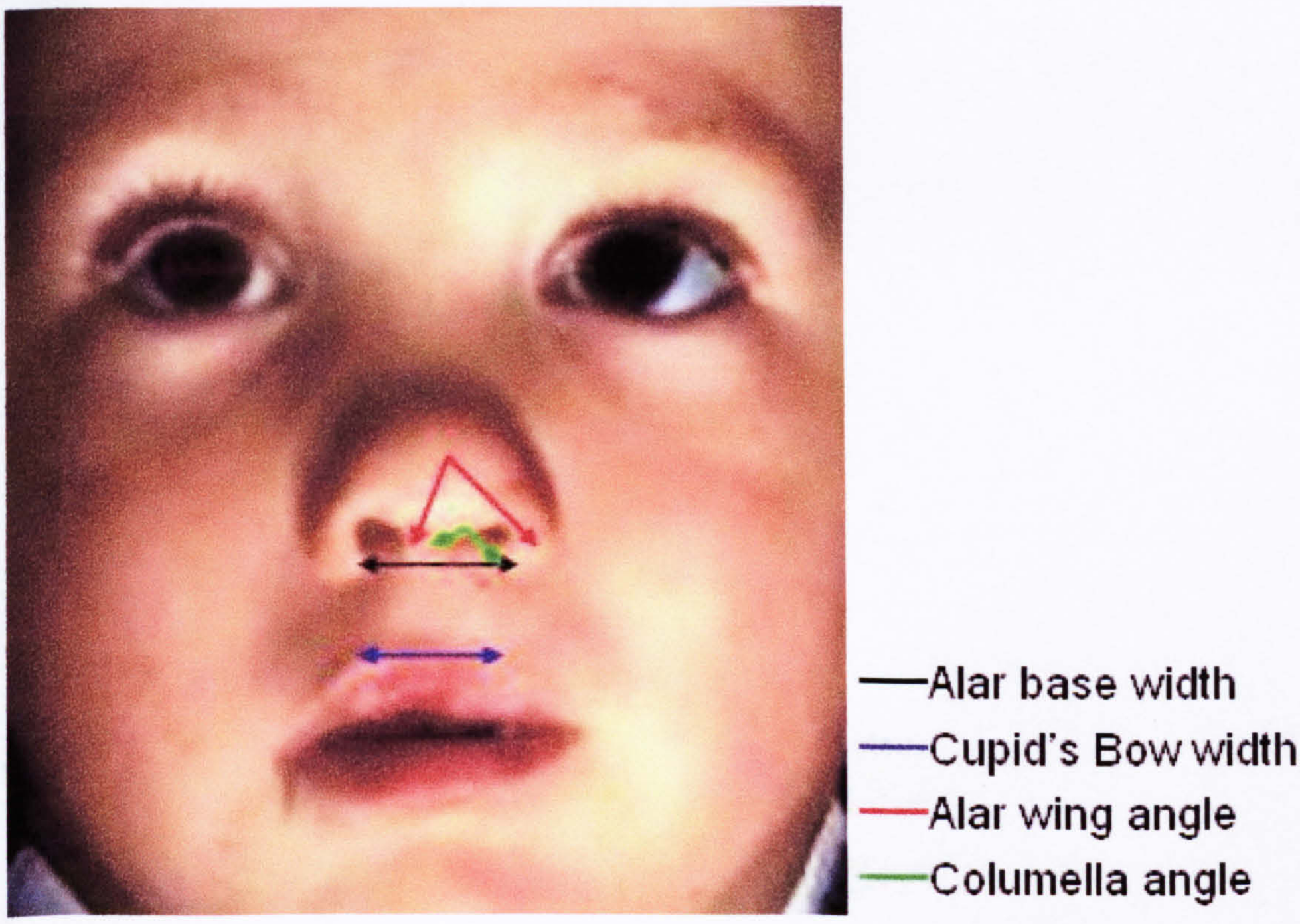


Figure 4.19 Dimensions in which UCLP children experienced significantly greater reduction pre-op to age 1 year, compared to UCL children

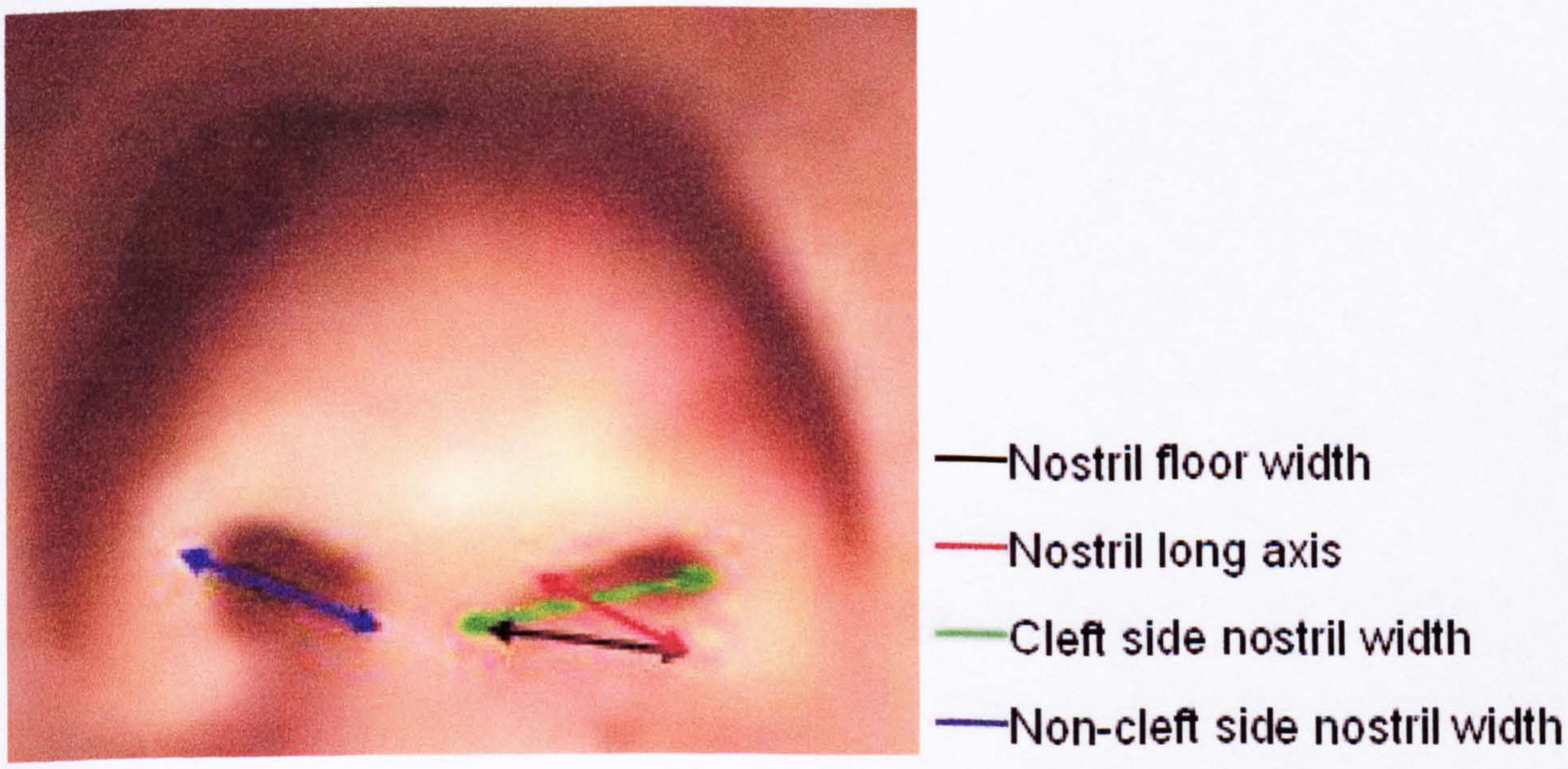


Figure 4.20 Nostril dimensions where significantly greater change was demonstrated in UCLP compared to UCL, in first year.

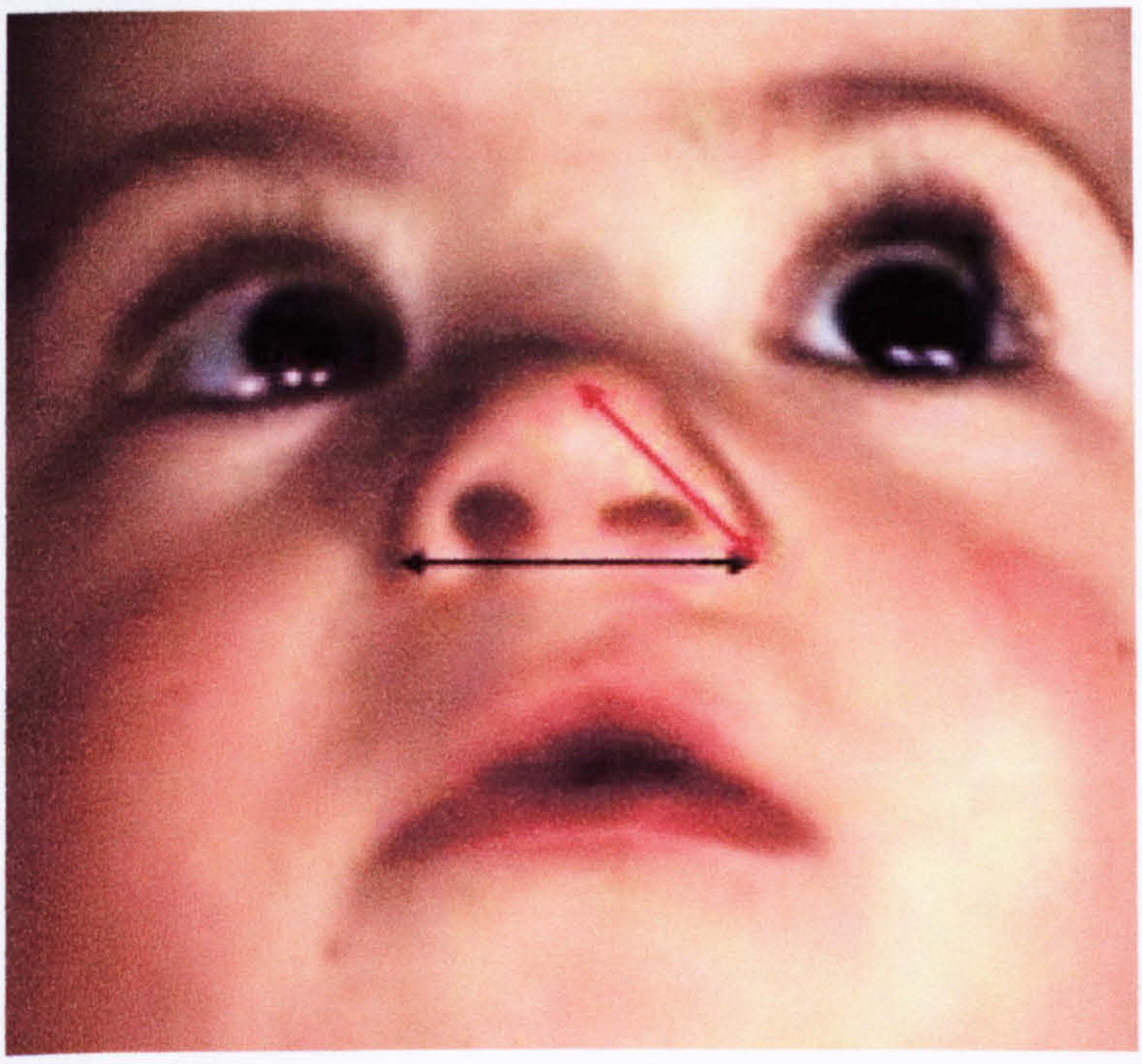


Figure 4.21 Dimensions in which UCL experienced a slight gain in length compared to negligible change in UCLP, over the first year

4.5.4.2 Cleft group differences in magnitude of total change in facial dimensions over 2 years

The total amount of change from pre-op baseline to age 2 years reflects net improvement with surgery and subsequent growth over 2 years in repaired UCL and UCLP children. Only the overall change in alar base, cleft-side nostril floor and nostril long axis dimensions demonstrated significant cleft group differences. In each case, UCLP children experienced changes of greater magnitude, reflecting the greater initial disruption by the cleft and the improvement following repair, and growth. The amount of growth in these dimensions after surgery was small and so the effect of the greater reduction achieved by surgery in the UCLP group, compared to the UCL group, persisted at age 2 years (Fig 4.22 overleaf).

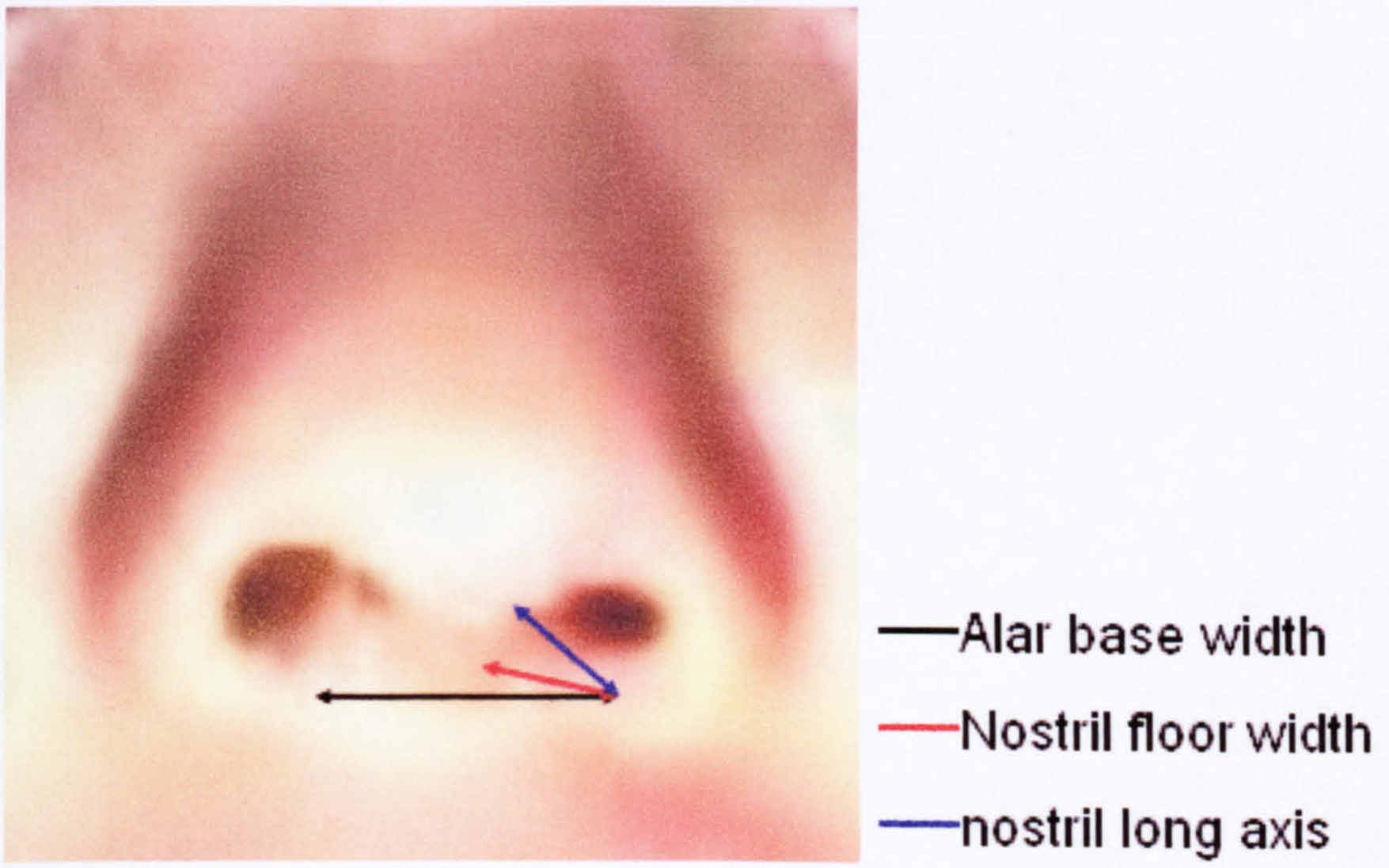


Figure 4.22 Dimensions where UCLP children demonstrated greater change (reduction) over 2 years, compared to UCL children

4.5.5 Summary of cleft group differences in changes in facial dimensions in year one and total change over two years.

The facial soft tissues of UCL and UCLP children did not grow differently after surgical repair.

UCL and UCLP children differed in the amount of change with surgery and growth experienced in the first year and in total change over 2 years. Most of these differences could be explained by the greater surgical correction required in these dimensions in UCLP children and the effects of surgical improvement.

Table 4.40 Changes in dimension from pre-op baseline to age 1 year and age 2 years - Significant median differences between UCL and UCLP children

Dimensions			preop-1y				preop-2y			
			UCL (n=12)	UCLP (n=13)	Mann-Whitney		UCL (n=8)	UCLP (n=11)	Mann-Whitney	
Measurement		side	Median Change (mm)	Median Change (mm)	99% CI	p-value	Median Change (mm)	Median Change (mm)	99% CI	p-value
Alar base width			-0.5	-7.2	3.7, 9.9	**0.001**	0.3	-7.3	1.6, 13.2	**0.003**
Anatomic nose width			1.6	-0.5	0.7, 3.9	**0.006**	-	-	-	-
Alar Wing										
Projective alar length		cleft	1.6	-0.8	1.0, 3.9	**0.004**	-	-	-	-
Alar wing angulation		cleft	-8.8	-23.1	4.4, 19.9	**0.006**	-	-	-	-
Columella										
Columella angulation		cleft	-10.2	-44.1	13.4, 59.9	**0.002**	-	-	-	-
Nostril										
Nostril floor width		cleft	-1.0	-9.8	5.2, 10.9	**0.001**	0.7	-8.5	4.1, 11.7	**0.001**
Nostril long axis		cleft	-0.1	-3.2	1.4, 4.0	**0.007**	-0.6	-6.5	2.9, 9.9	**0.001**
Nostril width		cleft	-1.0	-7.5	4.2, 9.0	**0.000**				
		non-cleft	0.7	2.2	-2.1, -0.4	**0.006**	-	-	-	-
Philtrum										
Cupid's Bow			-2.7	-6.7	1.7, 8.9	**0.006**	-	-	-	-

Significance level (p>0.01)

4.5.6 Facial Growth by region over 2 years

Changes in facial dimensions and angles over time from primary lip/nose surgery to age 2 years were compared by cleft type. Although some differences were identified in the magnitude or pattern of growth between UCL and UCLP children in after primary surgery, these were attributable to surgical repair. In this section, to further examine the effects post-surgery over time and for ease of interpretation, changes are presented for both cleft groups combined. Significant results are highlighted in **bold** and the level of significance indicated by *.

4.5.6.1 Upper Face and Eyes

Figure 4.23 (overleaf) illustrates the percentage growth in the upper face and eyes in the period after primary lip/nose surgery, and over the entire 2 year period. Table 4.41 (page 204) shows actual median changes in dimension for each time interval, for both cleft groups combined.

Significant growth changes were demonstrated in the upper face in the first 2 years. The width of the upper face (biocular width), rapidly increased by about 6mm up to 1 year of age, then slowed to 1.6mm between the ages of 1 and 2 years, giving a total width increase in the upper part of the face of 7.6mm, by age 2 years.

Inter-canthal growth (enL-enR) was more uniform. A small but significant increase was noted during the period of surgical lip/nose repair (Table 4.41). which continued to age two, resulting in growth in inter-canthal width of 7% (2mm) over 2 years. Cleft side and non-cleft side eye widths (ex-en) increased by 2.6-3mm up to age two. Most of this growth took place in the first year.

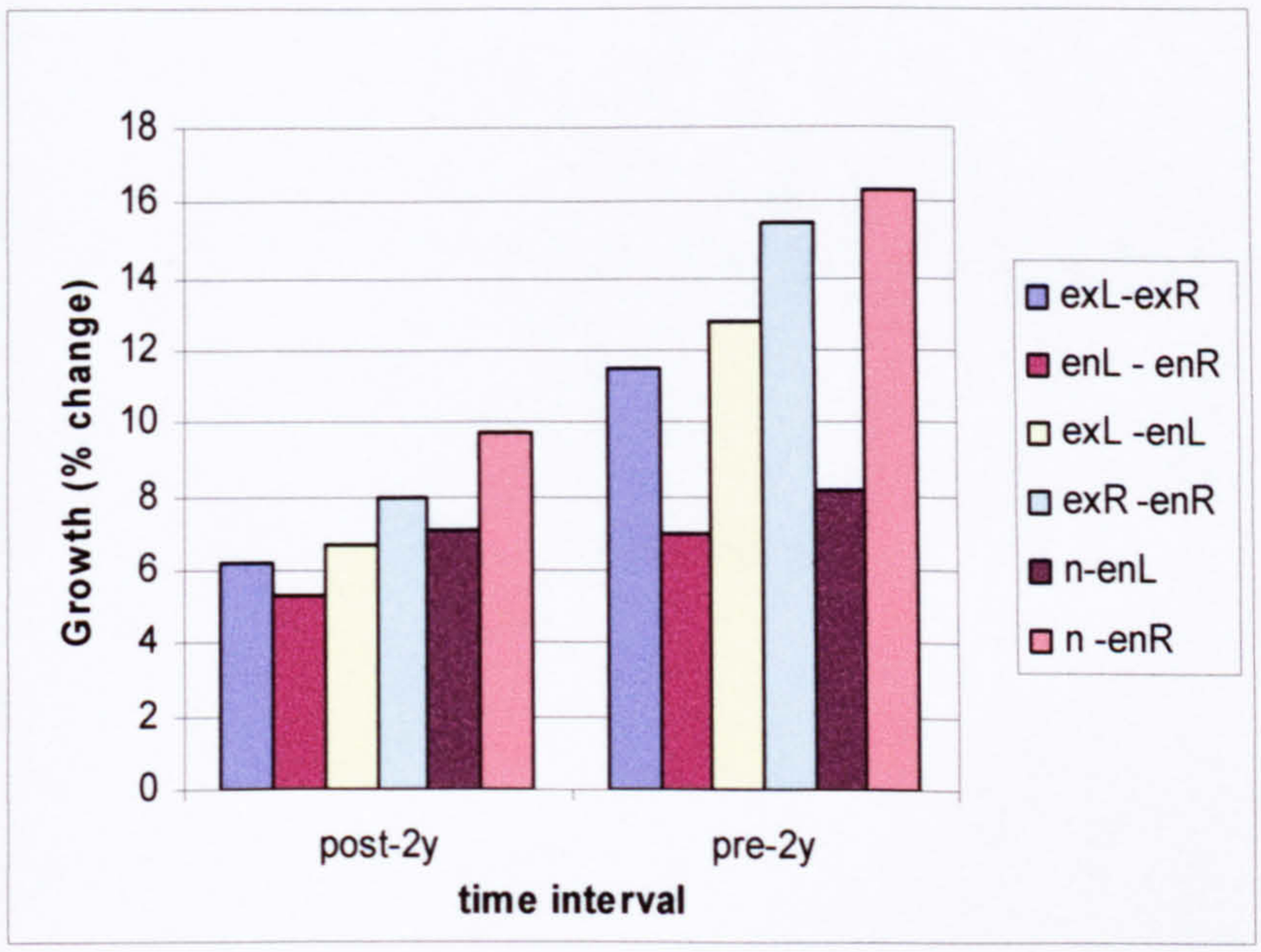


Figure 4.23 Growth (% change) of upper face & eye dimensions after primary lip/nose surgery (post-2y) and over entire 2 year period (pre-2y)

A small, but significant increase in the distance from soft tissue nasion to the inner-canthus of the eye on both sides of the face occurred over time. This increase was not symmetrical, however. On the non-cleft side, a median increase of 2.6mm occurred from over 2 years, whilst on the cleft side, this dimension increased by 1.6mm ($p=0.042$). Although the difference tested by Wilcoxon's signed ranks test failed to reach statistical significance at the 99% level, there was a trend towards discrepancy in growth rates of the cleft and non-cleft sides of the upper face during the first 2 years of life.

Table 4.41 Upper face & Eye dimension changes with time in UCL and UCLP (combined)

Upper Face & Eyes		post-1y		1y-2y		pre-1y		pre-2y		post-2y	
Measurement		**Median Change (mm)**	**p-value**	**Median Change (mm)**	**p-value**	**Median Change (mm)**	**p-value**	**Median Change (mm)**	**p-value**	**Median Change (mm)**	**p-value**
Biocular width		2.3	0.000**	1.6	0.000**	5.9	0.000**	7.6	0.000**	4.5	0.000**
Intercanthal width		0.5	0.05	0.5	0.032	1.5	0.000**	2.0	0.002*	1.1	0.002*
Ocular width	cleft	0.8	0.000**	0.5	0.005*	2.0	0.000**	2.6	0.000**	1.4	0.000**
	non-cleft	1.0	0.000**	0.6	0.002*	2.4	0.000**	3.1	0.000**	1.7	0.000**
Endocanthion to nasion	cleft	0.4	0.029	0.8	0.000**	0.8	0.000**	1.6	0.005*	1.2	0.001*
	non-cleft	0.4	0.041	1.2	0.000**	1.1	0.006*	2.6	0.001*	1.7	0.000**

*Significant ($p<0.01$)** highly significant ($p<0.001$)

4.5.6.2 Nose

4.5.6.2.1 Horizontal dimensions

Table 4.42 shows post-surgical change and total change in horizontal nasal dimensions up to age 2 years in both cleft groups combined.

A significant median gain in alar base width of 2.2mm was noted after surgery to age 2 years. A similar amount of post-surgical growth occurred in anatomic nose width (2.4mm). Although there was no change with surgery, soft nose width grew by 3.6mm to age 2 years. Horizontal displacement of the nasal tip continued to reduce with growth up to 2 years. Post-surgical growth in all horizontal nose dimensions was of similar magnitude in UCL and UCLP children (Fig 4.24).

4.5.6.2.2 Vertical Dimensions

Table 4.42 shows post-surgical changes and total change in vertical nasal dimensions up to age 2 years in both cleft groups combined.

Nose dorsum length increased in total by 3.7mm in UCL and UCLP children over 2 years. However, the nose did not start to grow in length until the age of 1 year. Protrusion of the tip of the nose increased mostly in the first year and grew by 2.8mm by the age of 2 years. The vertical prominence of the tip of the nose, relative to nasion and the base of the columella did not change with growth after surgery.

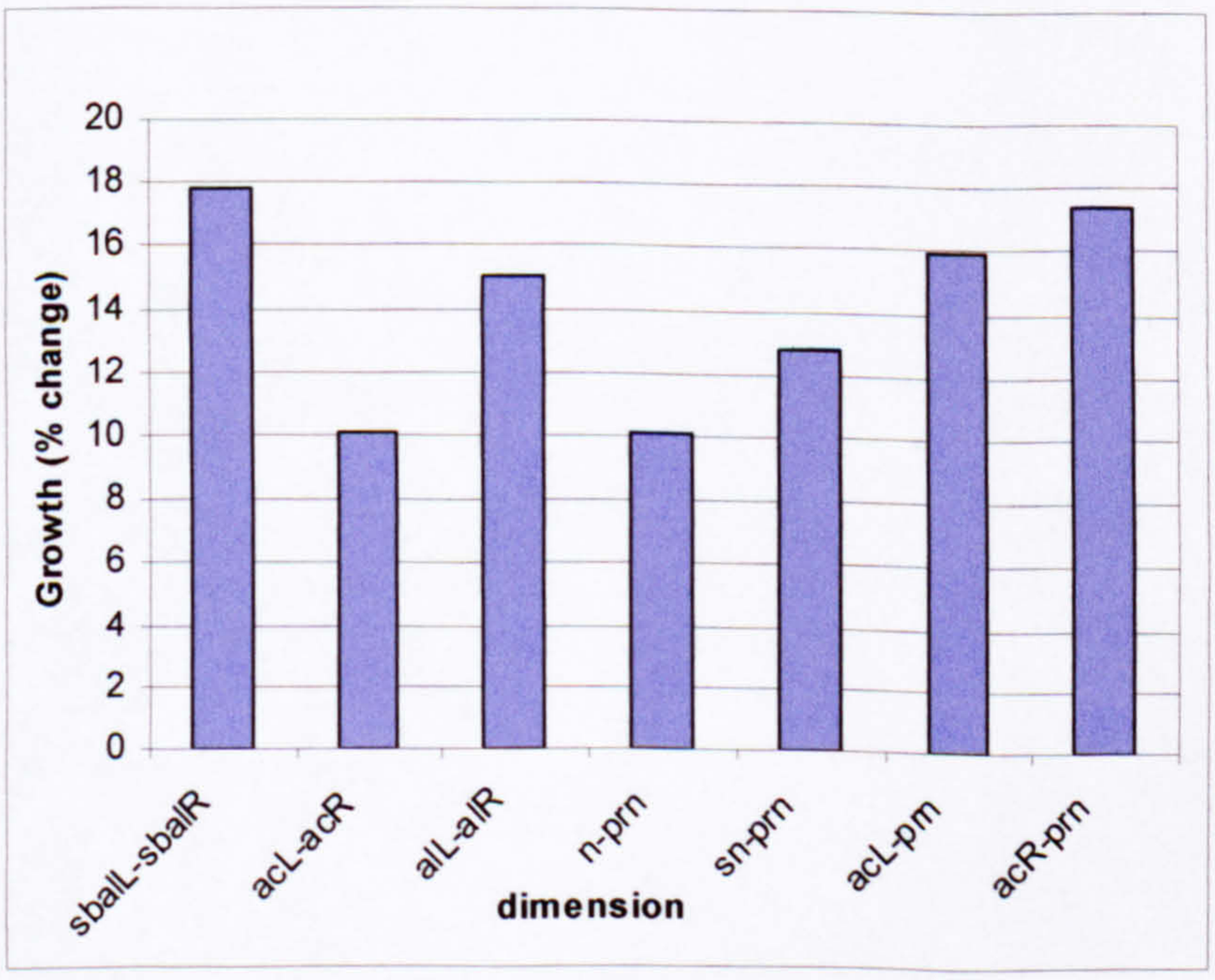


Figure 4.24 Nasal dimensions in which significant post-surgical growth up to age 2 years occurred, in UCL and UCLP children. (% change illustrated).

Table 4.42 Nose dimension changes with time in UCL and UCLP (combined)

Nose Dimensions		post-1y		1y-2y		pre-1y		pre-2y		post-2y	
Measurement		**Median Change (mm)**	**p-value**	**Median Change (mm)**	**p-value**	**Median Change (mm)**	**p-value**	**Median Change (mm)**	**p-value**	**Median Change (mm)**	**p-value**
Horizontal											
Alar base width		0.4	0.484	1.1	0.069	-4.1	**0.000****	-3.3	0.029	2.2	**0.005***
Anatomic nose width		1.0	**0.001***	0.9	0.03	0.6	0.27	1.5	0.088	2.4	**0.001***
Soft nose width		1.5	**0.001***	1.7	**0.000****	1.4	**0.001***	3.0	**0.002***	3.6	**0.000****
Nasal tip horizontal displacement (angle)		-3.6	**0.008***	-3.5	**0.000****	-7.8	**0.000****	-11.3	**0.001***	-6.2	0.011
Vertical											
Nose dorsum length		0.4	0.338	2.2	**0.000****	1.8	**0.003***	3.7	**0.000****	2.3	**0.003***
Nasal tip-base		1.0	**0.000****	0.4	0.027	2.2	**0.000****	2.8	**0.000****	1.4	**0.000****
Nasal tip angulation		1.4	0.084	-1.1	0.135	-2.1	0.029	-2.2	0.156	1.3	0.098
Alar Wing											
Projective alar length	cleft	1.8	**0.000****	1.0	**0.002***	0.6	0.247	2.0	**0.008***	2.9	**0.000****
	non-cleft	1.6	**0.000****	1.0	**0.003***	2.8	**0.000****	4.2	**0.000****	3.0	**0.000****
Alar wing angulation	cleft	-1.5	0.338	0.4	0.846	-15.8	**0.000****	-17.4	**0.000****	-0.5	0.776
	non-cleft	-1.1	0.384	-3.6	**0.004***	6.8	**0.000****	4.7	**0.002***	-2.9	0.065

*Significant ($p<0.01$)** highly significant ($p<0.001$)

4.5.6.2.3 Alar Dimensions

Table 4.43 (overleaf) shows post-surgical change and total change in alar wing dimensions up to age 2 years for both cleft groups combined.

After primary lip / nose repair, a similar amount of growth (approx 3mm) occurred in cleft side and non-cleft side alar wing length up to age 2 years. Alar wing angle on the cleft side did not change with growth following initial reduction with surgery. On the non-cleft side however, there was a small relapse in alar wing angle (-3.6°) between the age of 1 to 2 years. A small net increase in non-cleft side alar wing angle (4.7) degrees was demonstrated by 2 years of age.

4.5.6.2.4 Columella Dimensions

Table 4.43 shows post-surgical change and total change in columella and nostril dimensions up to age 2 years in both cleft groups combined.

Following a small but significant increase in columella thickness pre-postoperatively, no further changes were detected up to 2 years. No further changes in columella height occurred after surgery. In common with the cleft alar wing angle, cleft side and non-cleft side columella angle did not change significantly following initial improvement with surgery.

4.5.6.2.5 Nostril Dimensions

Only a small amount of growth was noted in certain nostril dimensions after surgery (post– 2y) (Table 4.43).

Over the first 2 years of infancy there was a median reduction in cleft side nostril floor width of 8.5mm in UCLP, compared to a net gain in UCL of 0.7mm (Table 4.40). After surgical repair, the median nostril floor width in both cleft groups grew by 1.8mm on the cleft side and 1.4mm on the non-cleft side. Non-cleft side nostril long axis continued to increase in length by an amount similar to that gained with surgery (1.3mm), up to age 2 years. On the cleft side, however a similar magnitude of change failed to reach statistical significance ($p=0.042$). Post-operative growth in cleft side nostril width averaged 1.5 mm. On the non-cleft side, there was no significant growth in nostril width dimension after surgery.

Table 4.43 Nose dimension changes with time (continued) in UCL and UCLP (combined)

Nose Dimensions		post-1y		1y-2y		pre-1y		pre-2y		post-2y	
Measurement		**Median Change (mm)**	**p-value**	**Median Change (mm)**	**p-value**	**Median Change (mm)**	**p-value**	**Median Change (mm)**	**p-value**	**Median Change (mm)**	**p-value**
Columella											
Columella height	cleft	0.1	0.637	0.0	0.82	0.9	**0.000****	0.8	0.042	0.1	0.67
	non-cleft	0.0	0.959	-0.1	0.673	0.6	0.036	0.3	0.449	-0.1	0.74
Columella thickness		-0.3	0.106	0.5	0.346	0.9	**0.000****	1.2	**0.008***	0.2	0.705
Columella angulation	cleft	6.7	0.166	-4.1	0.559	-30.7	**0.000****	-34.5	0.011	5.3	0.508
	non-cleft	-1.0	0.808	-0.6	0.976	8.1	**0.009***	9.1	0.029	0.4	1.0
Nostril											
Nostril floor width	cleft	0.9	0.036	0.6	0.163	-5.5	**0.000****	-5.3	**0.002***	1.8	**0.006***
	non-cleft	0.5	0.029	0.4	0.055	-0.1	0.638	0.8	**0.007***	1.4	**0.002***
Nostril long axis	cleft	0.6	0.038	0.5	0.074	-1.4	**0.003***	-1.0	0.065	1.3	0.042
	non-cleft	0.4	0.021	0.5	0.119	-0.1	0.687	0.3	0.394	1.3	**0.002***
Nostril width	cleft	0.5	0.126	0.6	0.098	-4.4	**0.000****	-3.6	**0.001***	1.5	**0.002***
	non-cleft	0.3	0.126	0.0	0.974	1.5	**0.000****	1.7	**0.001***	0.3	0.281

*Significant ($p<0.01$) ** highly significant ($p<0.001$)

4.5.6.3 Nasolabial Dimensions

Table 4.44 (page 198) shows post-surgical change and total change in nasolabial and philtrum dimensions up to age 2 years in both cleft groups combined.

In the first year, the distance between the corner of the mouth and the alar base on the cleft side increased by almost 5mm. There was no further significant increase in year 2. On the non-cleft side, this dimension increased by 3.5mm to 1 year, with again, no significant change up to age 2 years. Following initial improvement primary surgical repair, there was no further change in nose: mouth width ratio, up to age 2 years. No significant change in nasolabial angle was demonstrated over 2 years. Similarly, no change took place in the degree of upper lip protrusion relative to the base of the nose over time.

4.5.6.3.1 Philtrum

There was no significant post-op growth in philtral width up to age 2 years (Table 4.44). A change of similar magnitude to that achieved by surgery (1.5mm) occurred in philtrum medial length up to age 1 year, but no further increase in medial philtrum length was detected up to age 2 years. Total increase in philtrum medial length in the first year was almost 3mm, but no continued growth occurred up to age 2years. Paramedial philtrum length on the cleft side increased by a small amount after surgery, but there was no further change after the age of 1 year. On the non-cleft side, no significant growth occurred. Total change in paramedial philtrum length on the cleft side was 6.1mm, compared to 1.6mm on the non-cleft side. The distance between the philtral point and the alar base on the cleft side was unaltered by surgery, but an increase of 2mm occurred after lip/nose repair to age 1 year. However, no further growth occurred thereafter. Similarly, the non-cleft side increased by 2mm up to age 1 year, but. no significant change occurred thereafter, as on the cleft side.

4.5.6.3.2 Mouth

Table 4.45 (page 200) shows post-surgical change and total change up to age 2 years in both cleft groups combined.

A total increase in mouth width of approximately 4 mm occurred by age two years, with the major part of this change happening in the first year. Lower vermillion width increased by 2.1mm over 2 years and the major part of this growth occurred from age 1 year onwards (1.4mm). Lower lip length increased by a similar amount (2.2mm) over 2 years, but the increase was more uniform (Fig 4.25).

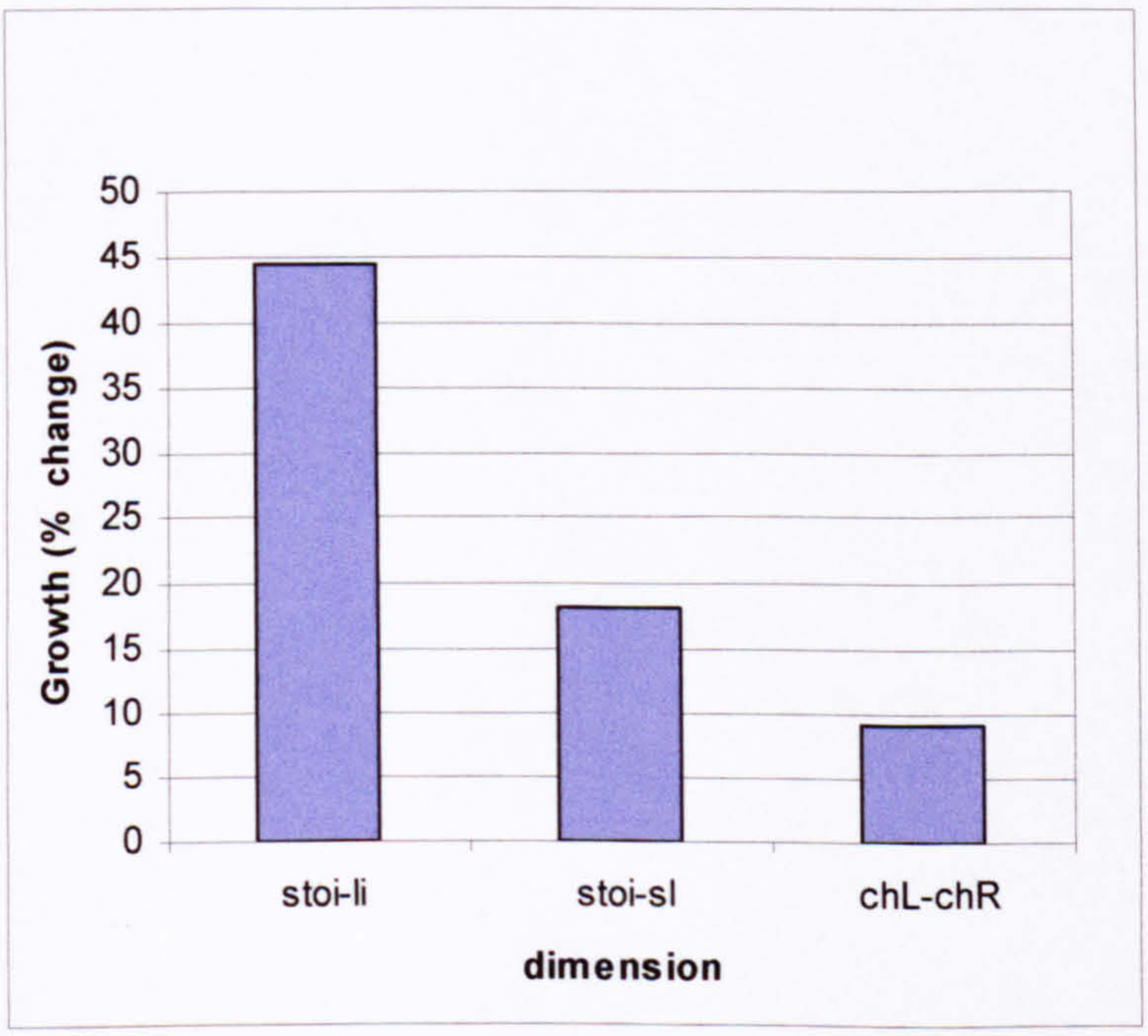


Figure 4.25 Post-surgical growth in mouth dimensions to age 2 years in UCL & UCLP

Table 4.44 Nasolabial dimension & philtrum changes with time in UCL and UCLP (combined)

Nasolabial Dimensions		post-1y		1y-2y		pre-1y		pre-2y		post-2y	
Measurement		**Median Change (mm)**	**p-value**	**Median Change (mm)**	**p-value**	**Median Change (mm)**	**p-value**	**Median Change (mm)**	**p-value**	**Median Change (mm)**	**p-value**
Alar base to corner of the mouth	cleft	1.4	0.023	0.9	0.153	4.9	**0.000****	5.4	**0.000****	1.4	0.029
	non-cleft	0.3	0.786	0.9	0.056	3.4	**0.000****	4.1	**0.000****	0.5	0.32
Nose/mouth width ratio		0.0	0.466	0.0	0.101	-0.1	**0.000****	-0.2	**0.001***	-0.1	0.023
Nasolabial angle		-2.2	0.175	-2.7	0.035	0.5	0.809	-2.3	0.421	-4.5	0.065
Protrusion of upper lip, relative to nasal base		0.5	0.523	0.2	0.559	0.5	0.179	1.2	0.037	0.5	0.156
Philtrum											
Cupid's Bow		0.6	0.113	-0.8	0.051	-4.3	**0.001***	-6.3	**0.000****	-0.6	0.636
Medial length		1.3	**0.000****	0.6	0.098	2.9	**0.000****	2.7	**0.001***	1.6	**0.003***
Paramedial philtrum length	cleft	1.4	**0.003**	0.1	0.704	6.5	**0.000****	6.1	**0.000****	1.4	0.026
	non-cleft	0.9	0.018	0.3	0.368	1.6	**0.001***	1.6	**0.008***	0.8	0.067
Philtral point to alar base	cleft	2.1	**0.000****	0.6	0.173	2.0	**0.000****	2.3	**0.001***	2.1	**0.001***
	non-cleft	1.1	**0.002***	0.4	0.242	2.4	**0.000****	2.3	**0.011**	1.1	0.014

*Significant ($p<0.01$) ** highly significant ($p<0.001$

4.5.6.4 Face height

Table 4.46 (overleaf) shows post-surgical growth and total growth in face height and upper face height up to age 2 years in both cleft groups.

Upper face height increased by 5mm up to age 2 years (3mm in the first year, and a further 2mm increase in the second year). Total face height increased by 13.5mm over 2 years (a 9mm increase in the first year, followed by a 4mm increase in the second year). Total change over 2 years is illustrated in Fig 4.26 below.

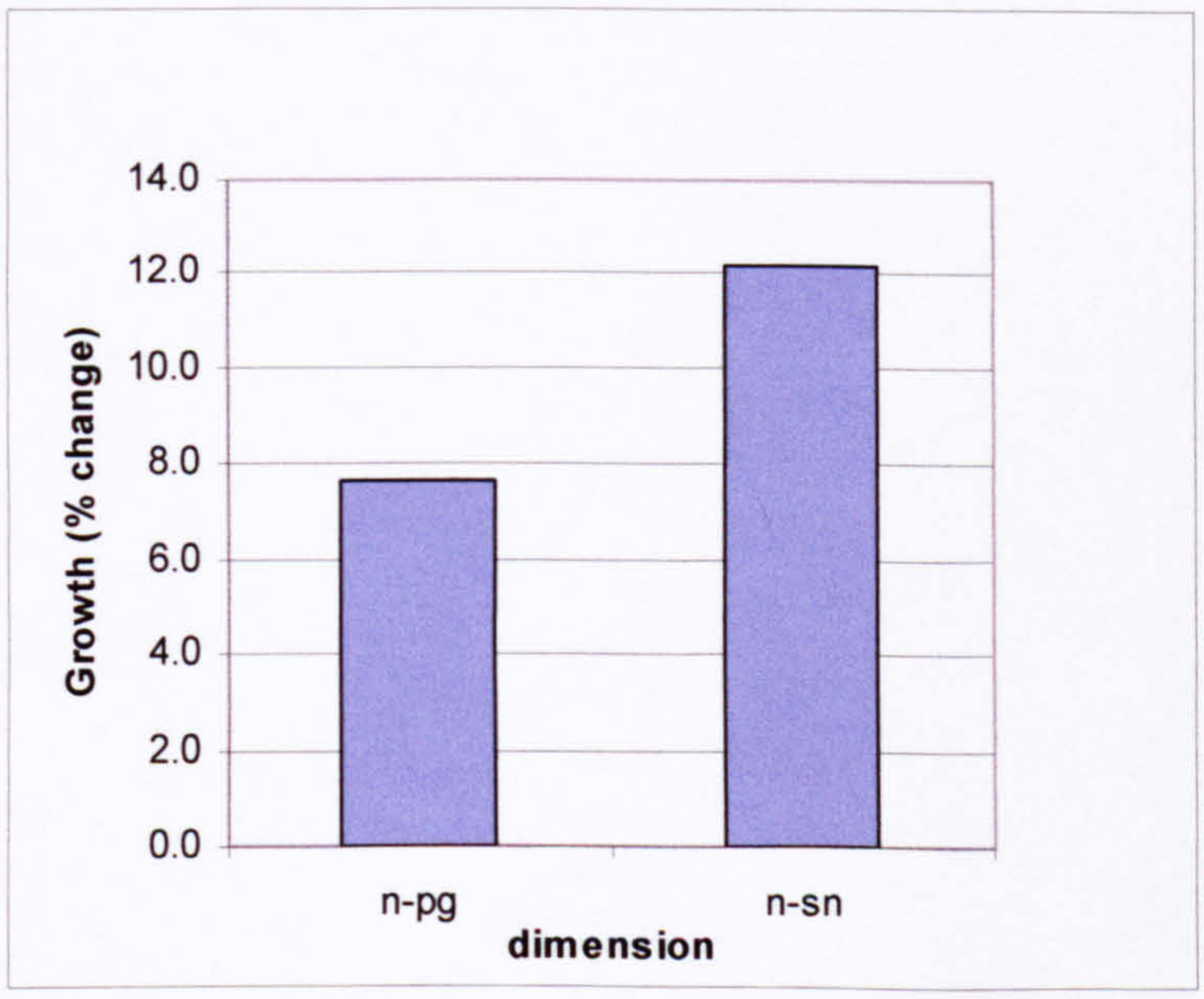


Figure 4.26 ***Post-surgical growth in face height to age 2 years in UCL and UCLP***

Table 4.45 Mouth dimension changes with time in UCL and UCLP (combined)

Mouth	post-1y		1y-2y		pre-1y		pre-2y		post-2y	
Measurement	Median Change (mm)	p-value	Median Change (mm)	p-value	Median Change (mm)	p-value	Median Change (mm)	p-value	Median Change (mm)	p-value
Lower vermillion width	0.3	0.420	1.4	0.001	0.6	0.023	2.1	0.000**	1.7	0.000**
lower lip length	0.1	0.030	0.9	0.008*	1.3	0.000**	2.2	0.000**	1.9	0.000**
mouth width	2.3	0.001*	0.2	0.871	4.1	0.000**	4.3	0.001*	2.9	0.005*

*Significant ($p<0.01$) ** highly significant ($p<0.001$)

Table 4.46 Face height dimension changes with time in UCL and UCLP (combined)

Face height Dimensions	post-1y		1y-2y		pre-1y		pre-2y		post-2y	
Measurement	Median Change (mm)	p-value	Median Change (mm)	p-value	Median Change (mm)	p-value	Median Change (mm)	p-value	Median Change (mm)	p-value
Total Face height	1.8	0.011	3.9	0.000**	8.9	0.000**	13.5	0.000**	4.8	0.001*
Upper face height	1.2	0.001*	2.2	0.000**	3.1	0.000**	5.1	0.000**	3.2	0.001*

*Significant ($p<0.01$) ** highly significant ($p<0.001$)

4.5.7 Summary of Facial soft tissue growth after lip / nose repair

Upper Face Growth
Growth continued in all dimensions. Biocular width (upper face width) and eye widths increased rapidly in the first year and more slowly in the second year of life. Inter-canthal growth was more uniform and of smaller magnitude. The amount of growth in nasion to endocanthion dimension appeared greater on the non-cleft side, but this failed to reach statistical significance.

Nose Growth
Horizontal Growth
Alar base width, anatomic nose width and soft nose width increased with growth.
Horizontal nasal tip displacement angle continued to reduce with post-op growth.

Vertical Growth
Nose dorsum length did not grow until age 1 year. Protrusion of the tip of the nose continued to increase with growth. Nasal tip angle did not change with growth, despite initial small reduction (2.7 degrees) with surgery

Alar wing Growth
Growth continued in the alar wing length on cleft and non-cleft sides after surgery. No continued reduction in cleft side alar wing angle after surgery, however, a small relapse in non-cleft side alar wing angle occurred from age 1-2 years. Despite this, there was an overall increase from pre-op to 2 years.

Columella Growth
No further growth in width or height and no change in either cleft or non-cleft side columella angles occurred after primary surgery up to age 2 years.

Nostril Growth
Growth occurred in the floor of both cleft and non-cleft side nostrils after surgery. Slight differences occurred in the growth pattern in other nostril dimensions. On the non-cleft side, nostril long axis increased and the nostril width was static. On the cleft side, the long axis was static and the nostril width increased. Total change in nostril dimensions was greater in UCLP children and related to greater initial deformity.

(Summary continued overleaf)

Nasolabial Growth
Growth in the distance from alar base to the corner of the mouth was negligible on both sides of the face after surgical repair. Nose:mouth width ratio did not change with growth. Neither nasolabial angle, nor the degree of upper lip protrusion, altered with surgery or with post-op growth up to age 2 years.

Philtrum Growth
No growth occurred in Cupid's bow width after surgery. Philtrum medial length increased to age 1 year, but no further growth occurred up to age 2 years. Philtrum point to alar base distance increased on both sides by a small amount until 1 year of age, but no further growth occurred to age 2 years. Philtrum paramedial distance on the repaired side increased by a small amount after repair, but did not change thereafter.

Mouth Growth
Lower lip and vermillion growth was of similar magnitude over 2 years. Lower vermillion grew mostly in the 2nd year and lower lip grew more uniformly over 2 years. Mouth width increased mainly in the first year of life.

Face Height Growth
Total face height increased rapidly in the first year and more slowly in the second year. Upper face height followed a similar pattern of growth.

4.6 Relationship between Facial dimensions and Somatic dimensions in UCL and UCLP

4.6.1 Correlation between facial dimensions and body dimensions

The relationships between facial size and growth and body size and growth were investigated using the following measurements:

Table 4.47 Facial and Somatic Dimensions

Facial Dimensions	Measurement	Somatic Measurements
Upper face width (binocular width)	exR-exL	Weight (kg)
Upper face height	n-sn	Height (cm)
Total face height	n-pg	Head circumference (cm)

4.6.1.1 Prior to primary surgery

Prior to corrective surgery, upper face height, total face height and upper face (binocular) width were moderately correlated with head circumference. There was no correlation between these facial measurements and height or weight (Table 4.48).

Table 4.48 Correlation between face and body measurements prior to primary surgery

Correlation	Weight		Height		Head circumference	
	Pearson Correlation coeff	P value	Pearson Correlation coeff	P value	Pearson Correlation coeff	P value
Total face height (n-pg)	0.37	0.051	0.28	0.16	**0.56**	**0.003**
Upper face height (n-sn)	0.23	0.232	0.36	0.057	**0.52**	**0.007**
Biocular width (ex-ex)	0.37	0.05	0.36	0.06	**0.53**	**0.005**

(Significance level $p<0.05$)

4.6.1.2 2 Years of Age

At age 2 years, upper face (biocular) width correlated moderately with head circumference and moderately with weight. There was no correlation between upper face height and weight, height or head circumference. Similarly, there was no correlation between total face height and body measurements at age 2 years (Table 4.49)

Table 4.49 Correlation between face and body measurements at age 2 years

Correlation	Weight		Height		Head circumference	
	Pearson Correlation coeff	P value	Pearson Correlation coeff	P value	Pearson Correlation coeff	P value
Total face height (n-pg)	0.14	0.482	0.22	0.250	0.15	0.439
Upper face height (n-sn)	0.06	0.775	0.06	0.749	-0.02	0.910
Biocular width (ex-ex)	**0.60**	**0.001**	0.43	0.020	**0.42**	**0.026**

(Significance level $p<0.05$)

4.6.2 Correlation between facial growth and body growth up to age 2 years.

Significant correlations between body parameters and facial dimensions are reported in the relevant table below and highlighted in **bold** type.

4.6.2.1 Changes in Total Face height (n-pg) over time

No correlation was found between somatic changes and total face height changes from age 3 months (pre lip repair) to 2 years, in either cleft group.

4.6.2.2 Changes in Upper Face height (n-sn) over time

Table 4.50 shows significant correlation between upper face height growth and body/head growth over time for both cleft groups combined.

An overall moderate to strong correlation was found between upper face height growth and increase in head circumference in the first 2 years of life. No corresponding relationship could be demonstrated with height or weight. This relationship was not detected in the

intervening time intervals i.e. pre-postop; 1y-2y; preop-1y. In the post-op to 2 years period, there was a moderate correlation between changes in upper face height and systemic height gain.

Table 4.50 Correlation between Upper Face height growth and body growth, by time interval

Time Interval	Weight		Height		Head circumference	
	Pearson Correlation coeff	P value	Pearson Correlation coeff	P value	Pearson Correlation coeff	P value
Pre-op to 2y	-0.21	0.448	0.17	0.554	**0.67**	**0.009**
Post op – 2y	0.13	0.620	**0.64**	**0.005**	0.29	0.239

(Significance level p<0.05)

4.6.2.3 Changes in Upper face (Biocular) width (Ex-Ex) over time

Table 4.51 shows the time intervals in which significant correlation was found between growth in upper face (binocular) width and body / head growth, for both cleft groups combined.

A moderate to strong correlation (0.66) was found between change in biocular width and weight gain in the overall period up to 2 years of age. There were no correlations with changes in height or head circumference.

Strong correlations were detected between height gain and change in biocular width up to the age of 1 year. No relationship was found between upper face width and increase in head circumference, or weight gain over the same interval.

Table 4.51 Correlation between upper face width growth and body growth, by time interval

Time Interval	Weight		Height		Head circumference	
	Pearson Correlation coeff	P value	Pearson Correlation coeff	P value	Pearson Correlation coeff	P value
Preop-postop	0.04	0.851	**0.70**	**0.001**	0.16	0.512
Preop-1y	0.35	0.147	**0.76**	**0.000**	0.52	0.029
Pre-op to 2y	**0.66**	**0.008**	0.50	0.07	0.21	0.471

(Significance level p<0.05)

4.7 Facial Asymmetry

Asymmetry Scores were calculated for configurations of landmarks representing the face (Table 4.52), and the nasolabial area (Table 4.53). Global Face and Nasolabial Asymmetry Scores were decomposed to show the distribution and quantify the relative contribution of component facial regions and features to overall asymmetry. Differences in Asymmetry Scores between UCL, UCLP and controls over time were analysed using mixed-effects models (Pinheiro & Bates, 2000; Bock & Bowman, 2005).Numbers of subjects included in the analyses are presented in Table 4.54.Significance was tested at the 95% level ($p<0.05$).

Results of the Asymmetry investigations are presented in two parts:

1 Distribution of asymmetry across the face and nasolabial area prior to primary repair, after lip/nose repair, at 1 year and at 2 years.

2 Changes in asymmetry in the entire face, upper face region and individual nasolabial features with primary surgery and growth over 2 years.

Table 4.52 Landmarks representing Global facial asymmetry and component regions

Facial Region	Landmarks
Global face	exR enR n enL exR acL alL al0oL prn al0oR al0iR al0iL hnR hnL alR acR sbalR sn sbalL sn0R cR cL sn0L chR cphR ls <cph>L(preop) cphL(postop) chL
Upper face	exR enR n enL exR
Nasal Rim	acL alL al0oL prn al0oR alR acR
Nasal base & columella	sbalR sn sbalL sn0R cR cL sn0L
Upper vermillion shape	chR cphR ls <cph>L(preop) cphL(postop) chL

Table 4.53 Landmarks representing Nasolabial area and component features

Nasolabial Features	Landmarks
Nasolabial Area	acL alL al0oL prn al0oR alR acR sbalR sn sbalL sn0R cphR ls cph0R(pre-op) cphL(post-op) sn0L chR chL n
Nasal Rim	acL alL al0oL prn al0oR alR acR
Nasal base	sbalR sn sbalL
Philtrum	sn0R cphR ls cph0R(pre-op) cphL(post-op) sn0L

Table 4.54 Numbers of cleft and non-cleft subjects included in analysis

Group	Time point			
	preop	postop	1 year	2years
UCL	17	16	16	11
UCLP	15	12	18	21
Control	83	93	91	92

4.7.1 Distribution of Asymmetry

A square-root transformation was applied to all mean Asymmetry Scores to reduce skewness. This new scale allowed graphical display of the differences in mean Asymmetry Scores between groups and different facial regions (Figs 4.27 - 4.30).

4.7.1.1 Facial Asymmetry before primary lip / nose surgery

Fig 4.27 shows the relative contribution of facial regions to facial asymmetry prior to primary lip/nose surgery in UCL and UCLP infants, and in non-cleft infants.

Significant asymmetry was noted in global facial asymmetry and in each facial region, in UCL and UCLP groups, relative to non-cleft controls, before surgery. The lip region contributed most strongly to overall facial asymmetry, followed by the nasal base and columella region. The upper face region displayed the least asymmetry, but this was significantly elevated for both cleft groups, compared to controls. Furthermore, the degree of upper face, nasal base and columella and lip asymmetry was greater in the UCLP group than in the UCL group, but nasal rim asymmetry was similar.

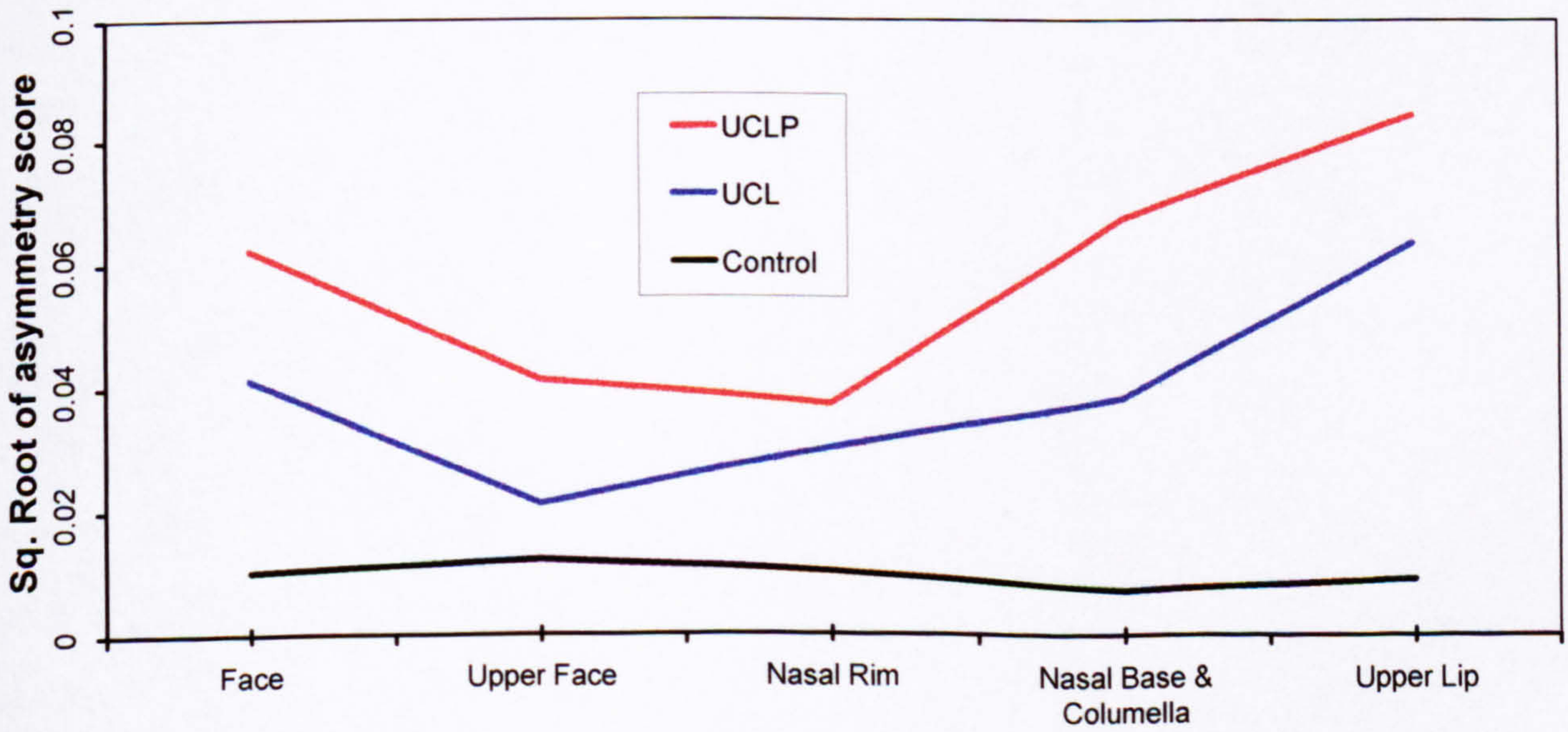


Figure 4.27 Residual Facial asymmetry distribution by facial region, prior to surgery

4.7.1.2 Residual Facial Asymmetry after lip/nose surgery

Fig 4.28 shows the relative contribution of facial regions to residual facial asymmetry after primary lip/nose surgery in UCL and UCLP infants and in non-cleft infants.

After surgery, upper face region asymmetry in the UCL group was close to that of the non-cleft group; however, significant asymmetry in this region remained in the UCLP group. Significant residual asymmetry was displayed in all other regions in both cleft groups compared to the non-cleft baseline. Residual lip region asymmetry dominated in the UCL group after surgery, but no single facial region contributed more strongly than any other to the residual asymmetry seen in the UCLP group.

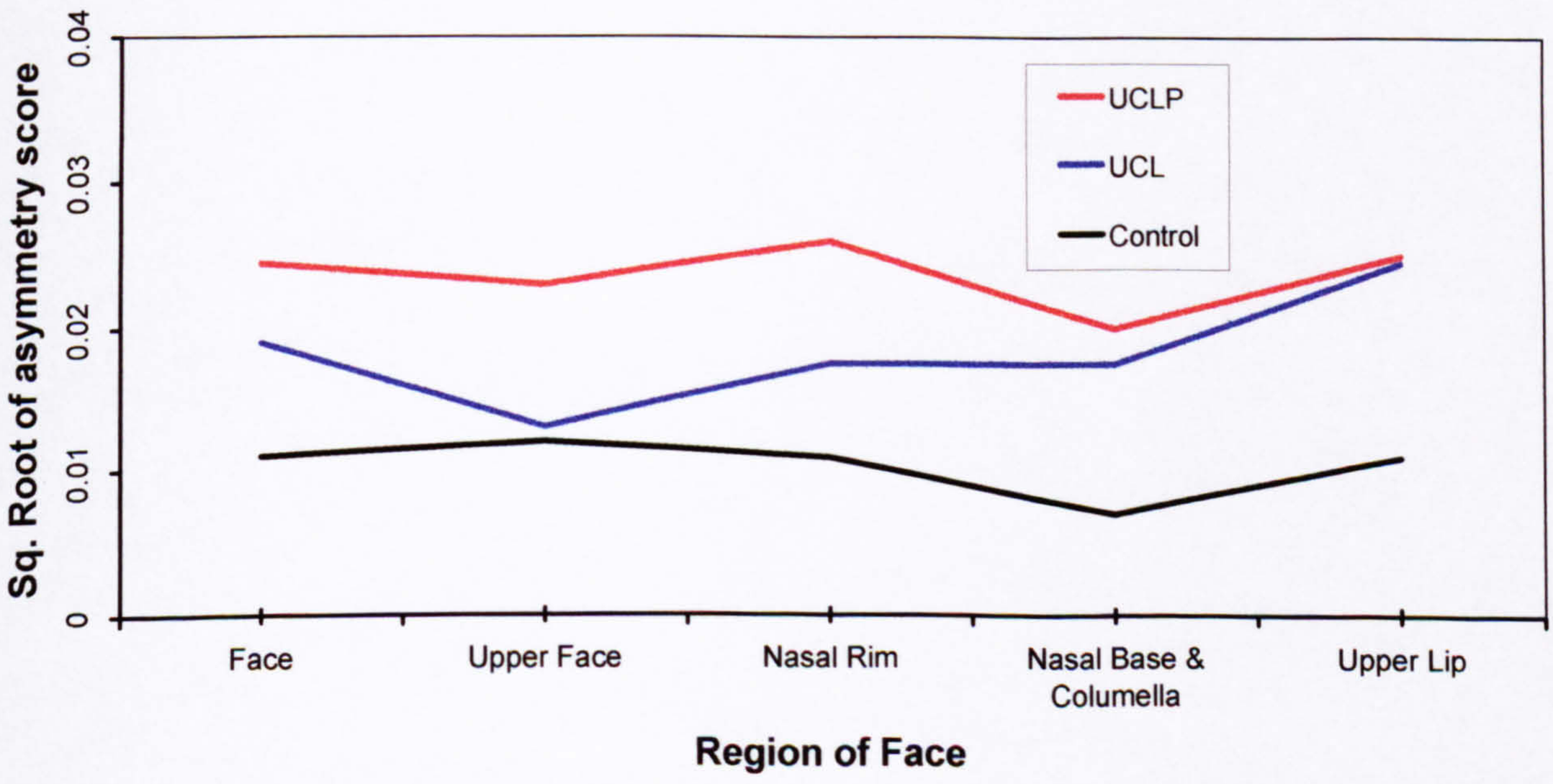


Figure 4.28 Residual Facial asymmetry distibution by facial region, after primary lip/nose surgery

4.7.1.3 Residual Facial Asymmetry at age 1 year

Fig 4.29 shows the relative contribution of facial regions to residual facial asymmetry at age 1 year, in UCL, UCLP and non-cleft children.

At age 1 year, upper face asymmetry in the UCL group was similar to baseline, but remained elevated in the UCLP group. However, the upper face was least asymmetric in both cleft groups. Lip region asymmetry was the strongest contributor to residual facial asymmetry in the UCL group, but there were no significant differences in the residual asymmetry in nasal and lip regions in the UCLP group.

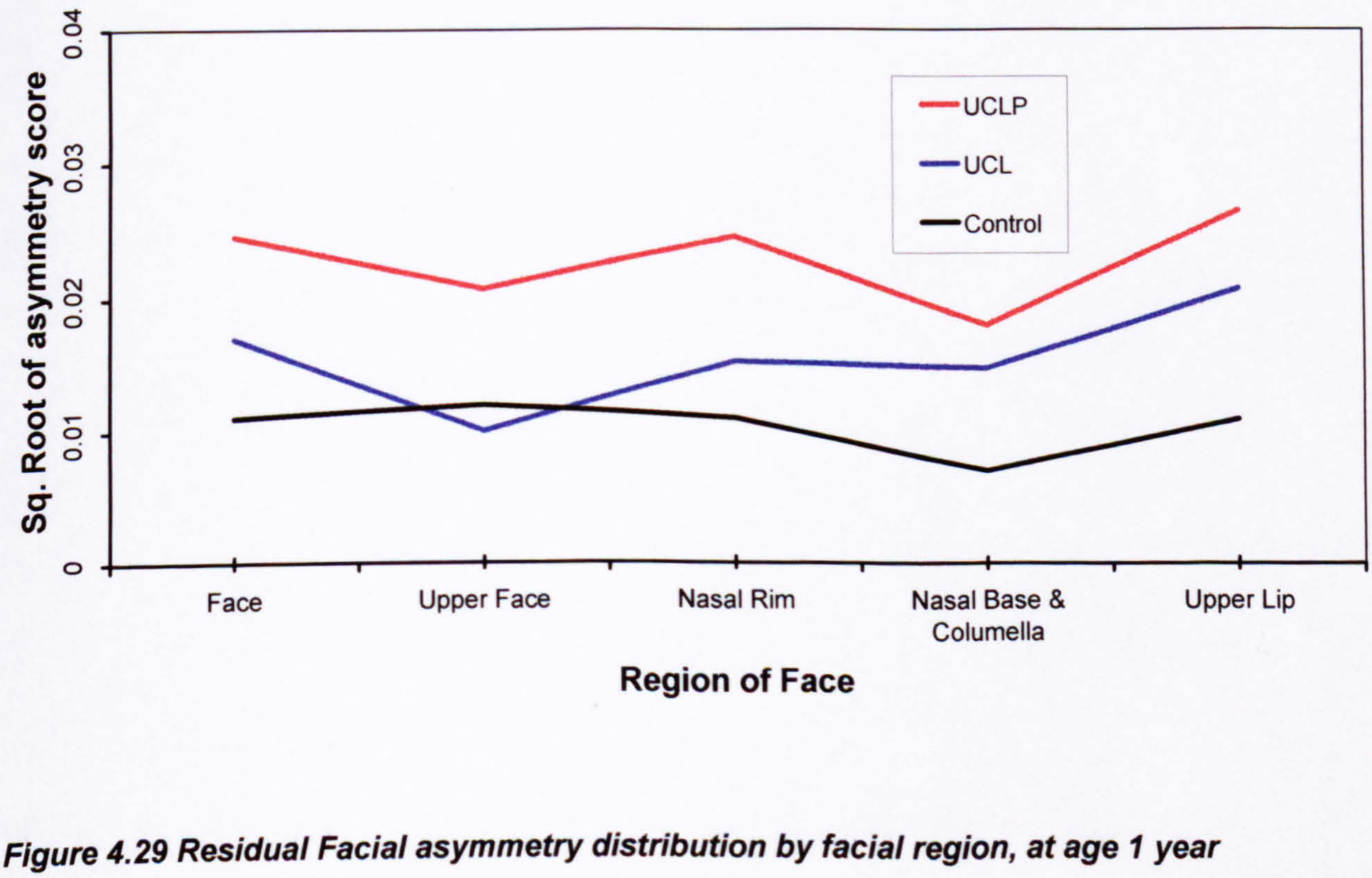


Figure 4.29 Residual Facial asymmetry distribution by facial region, at age 1 year

4.7.1.4 Residual Facial Asymmetry at age 2 years

Fig 4.30 shows the relative contribution of facial regions to residual facial asymmetry at age 2 years, in UCL, UCLP and non-cleft children.

The upper face contributed least to global facial asymmetry in UCL subjects at age 2 years. Upper face asymmetry remained significantly elevated in UCLP, compared to UCL and control children. No significant differences were found in the degree of residual asymmetry in nasal and lip regions and no single facial region dominated global facial asymmetry in either cleft group.

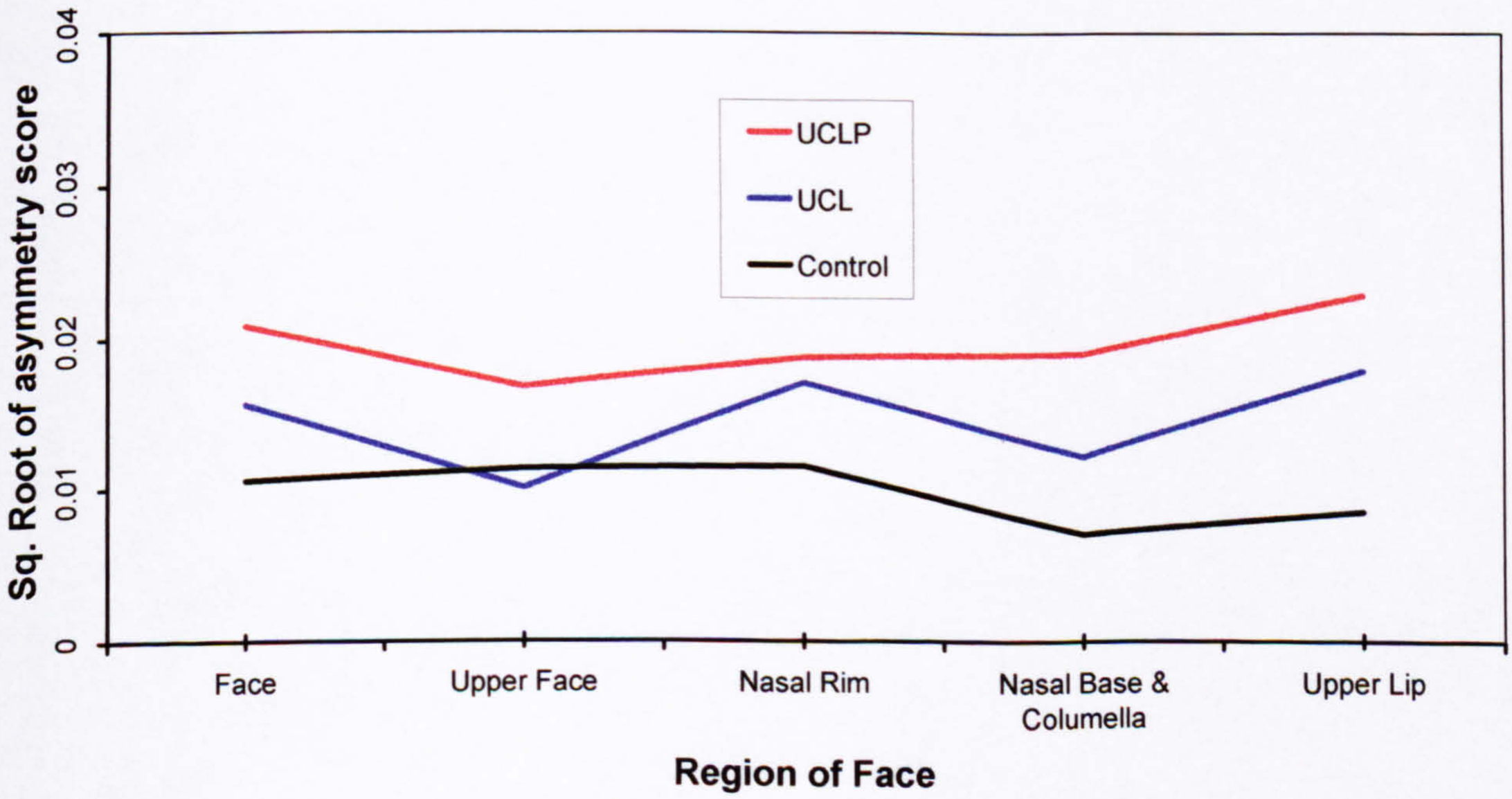


Figure 4.30 Residual Facial asymmetry distribution by facial region, at age 2 years

4.7.2 Nasolabial Asymmetry Distribution

A square-root transformation was applied to all mean Asymmetry Scores to reduce skewness. This new scale allowed graphical display of the differences in mean Asymmetry Scores between groups and different nasolabial features (Figs 4.31 - 4.34).

4.7.2.1 Nasolabial Asymmetry before primary lip/nose surgery

Fig 4.31 shows relative contribution of specific nose and lip features to nasolabial asymmetry, prior to surgical repair in UCL and UCLP infants, and in non-cleft infants.

Prior to repair, the most asymmetric part of the nasolabial area was the philtrum, followed by the nasal base and then the nasal rim in UCL and in UCLP infants. All features in both cleft groups were significantly more asymmetric than in controls ($p<0.001$). In the UCLP group the philtrum and nasal base made a greater relative contribution to nasolabial asymmetry than in the UCL group. Nasal base and philtrum were significantly more asymmetric in UCLP than in UCL infants. The nasal rim contributed least to nasolabial asymmetry and was of the similar magnitude in UCL and UCLP infants before primary repair.

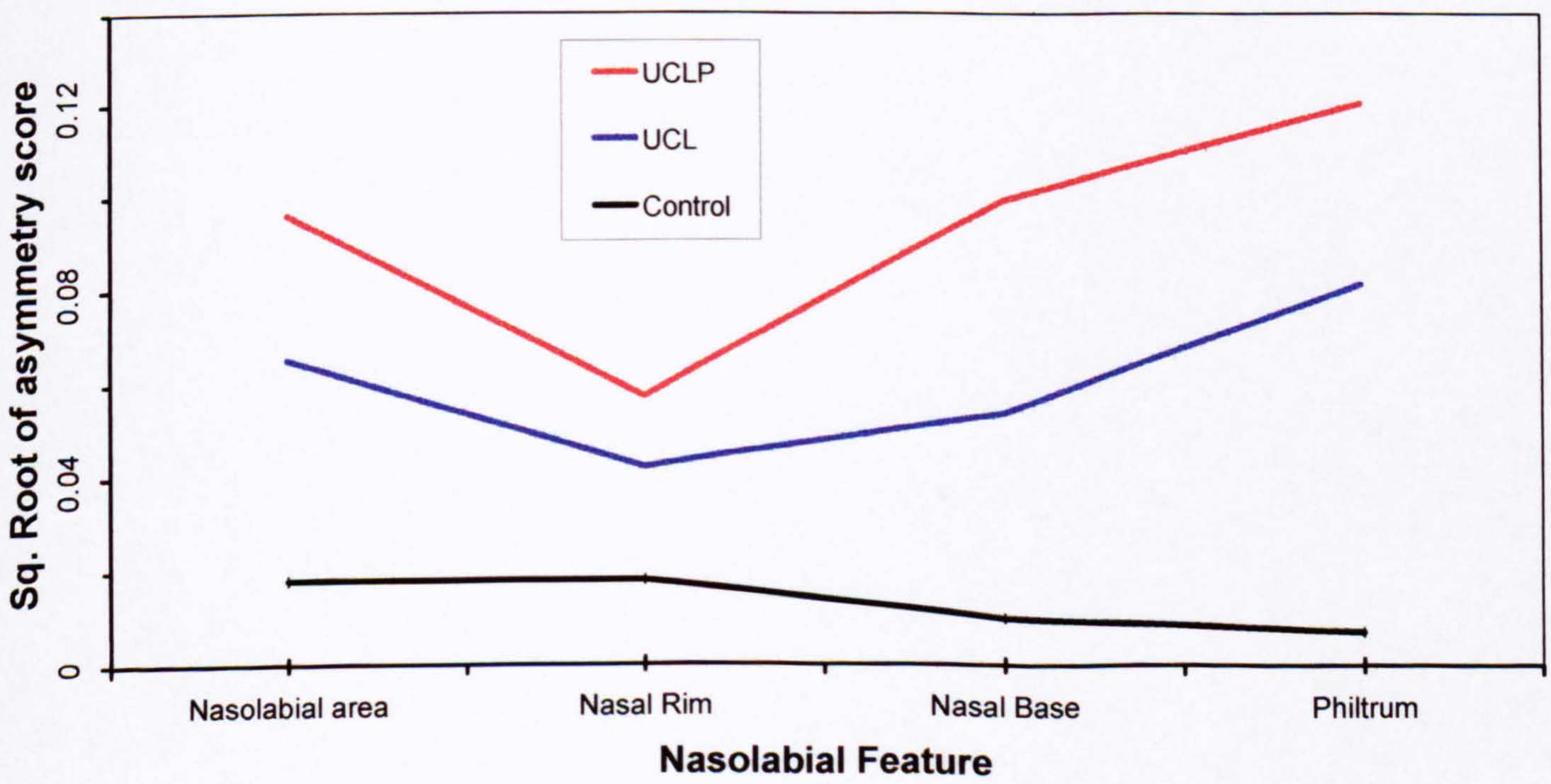


Figure 4.31 Nasolabial asymmetry distribution prior to surgery

4.7.2.2 Residual Nasolabial Asymmetry after lip / nose repair

Fig 4.32 shows relative contribution of specific nose and lip features to nasolabial asymmetry, after surgical repair in UCL and UCLP infants, and in non-cleft infants.

In the UCLP group, residual asymmetry was evident in the nasal rim, nasal base and philtrum, relative to controls, after lip/nose repair. No one dominant feature contributed more to overall nasolabial asymmetry. Residual nasal base and philtrum asymmetry were of similar magnitude to that of UCL infants, despite a greater degree of asymmetry in UCLP infants before surgery. Residual nasal rim asymmetry in the UCLP group was significantly higher than in the UCL group ($p=0.037$), despite a similar degree of asymmetry before surgery.

In the UCL group, the pattern of residual asymmetry differed from the UCLP group, in that residual nasal rim asymmetry was closer to control baseline (albeit still significantly higher). Nasal base and philtrum asymmetry were of similar magnitude and although the nasal rim appeared to be less asymmetric, relative to overall nasolabial asymmetry, this was not statistically significance ($p=0.101$).

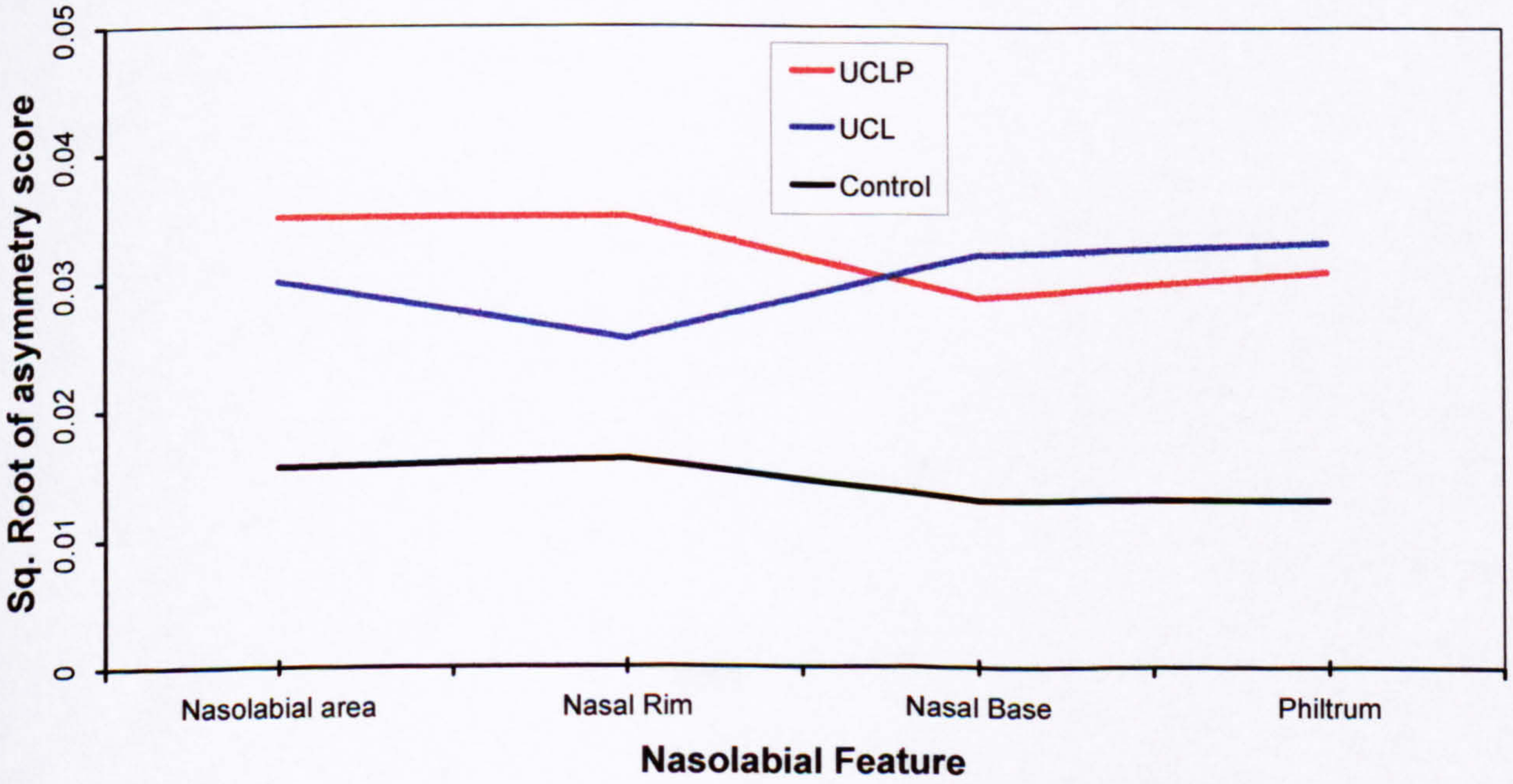


Figure 4.32 Residual Nasolabial asymmetry distribution, after lip/nose repair

4.7.2.3 Nasolabial Asymmetry at age 1 year

Fig 4.33 shows relative contribution of specific nose and lip features to nasolabial asymmetry at age 1 year in UCL, UCLP and non-cleft children.

Significant residual asymmetry was found in all nasolabial features in both UCL and UCLP children, relative to the control baseline at the age of 1 year. The pattern of distribution of residual nasolabial asymmetry was similar in both cleft groups i.e. neither group displayed a dominance of one feature relative to the others (UCLP p=0.062; UCL p=0.062). Residual nasal rim asymmetry was appeared elevated in UCLP children relative to UCL children, but the difference was not significant (p=0.136). Residual nasal base and philtrum asymmetry were of similar magnitude in both cleft groups at age 1 year.

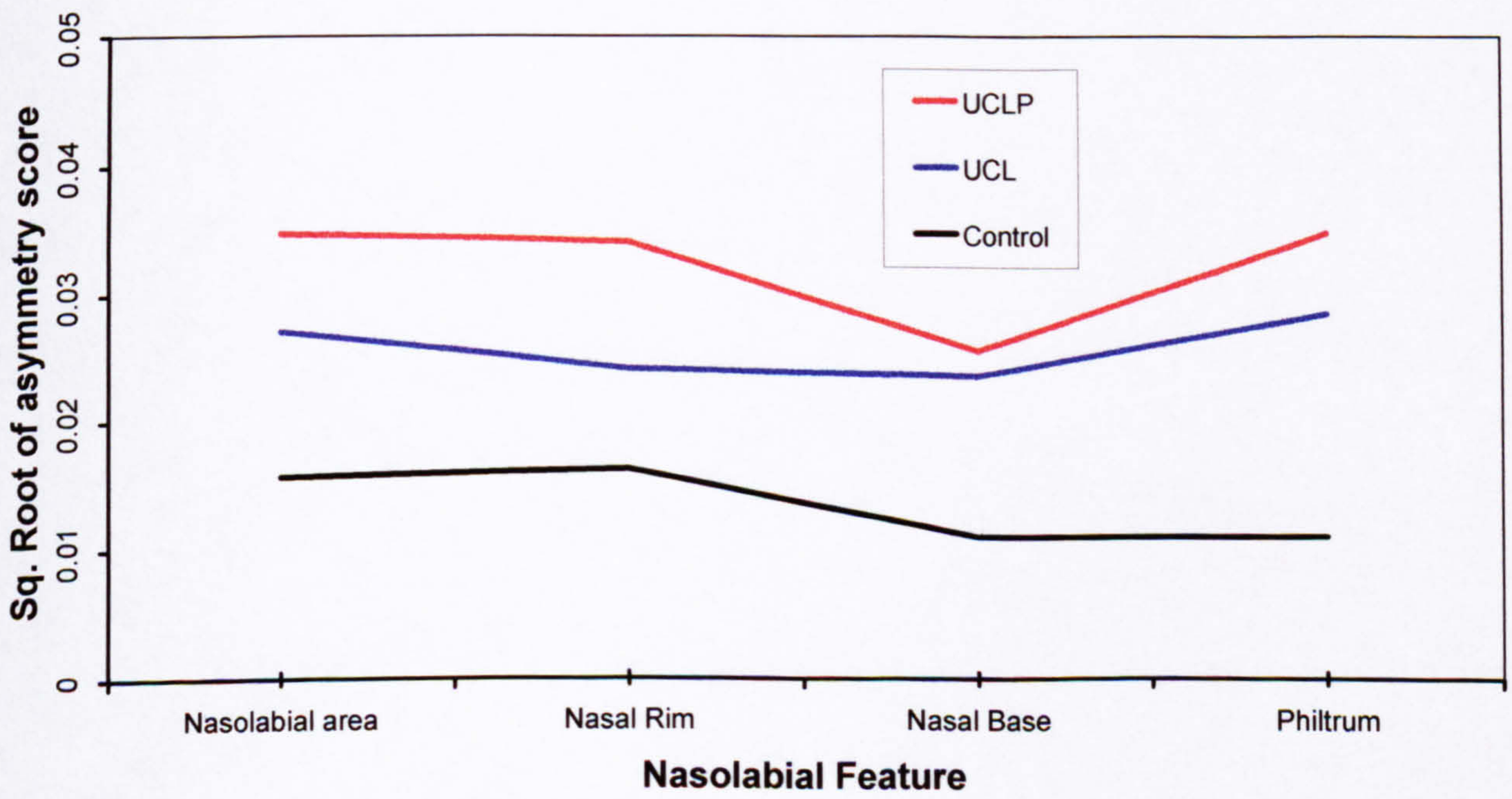


Figure 4.33 Residual Nasolabial asymmetry distribution at age 1 year

4.7.2.4 Nasolabial Asymmetry Distribution at age 2 years

Fig 4.34 shows relative contribution of specific nose and lip features to nasolabial asymmetry at age 2 years in UCL, UCLP and non-cleft children.

Significant residual asymmetry was found in all nasolabial features in both UCL and UCLP children, relative to the control baseline at the age of 2 years. The distribution of residual asymmetry across nasolabial features was uniform for both cleft groups.

There was significant difference in the degree of residual nasal base asymmetry between cleft groups at 2 years. This was significantly greater in the UCLP group than in the UCL group ($p=0.042$). In contrast, there was no difference in the degree of residual philtrum asymmetry ($p=0.101$) or residual nasal rim asymmetry ($p=0.877$) between cleft groups.

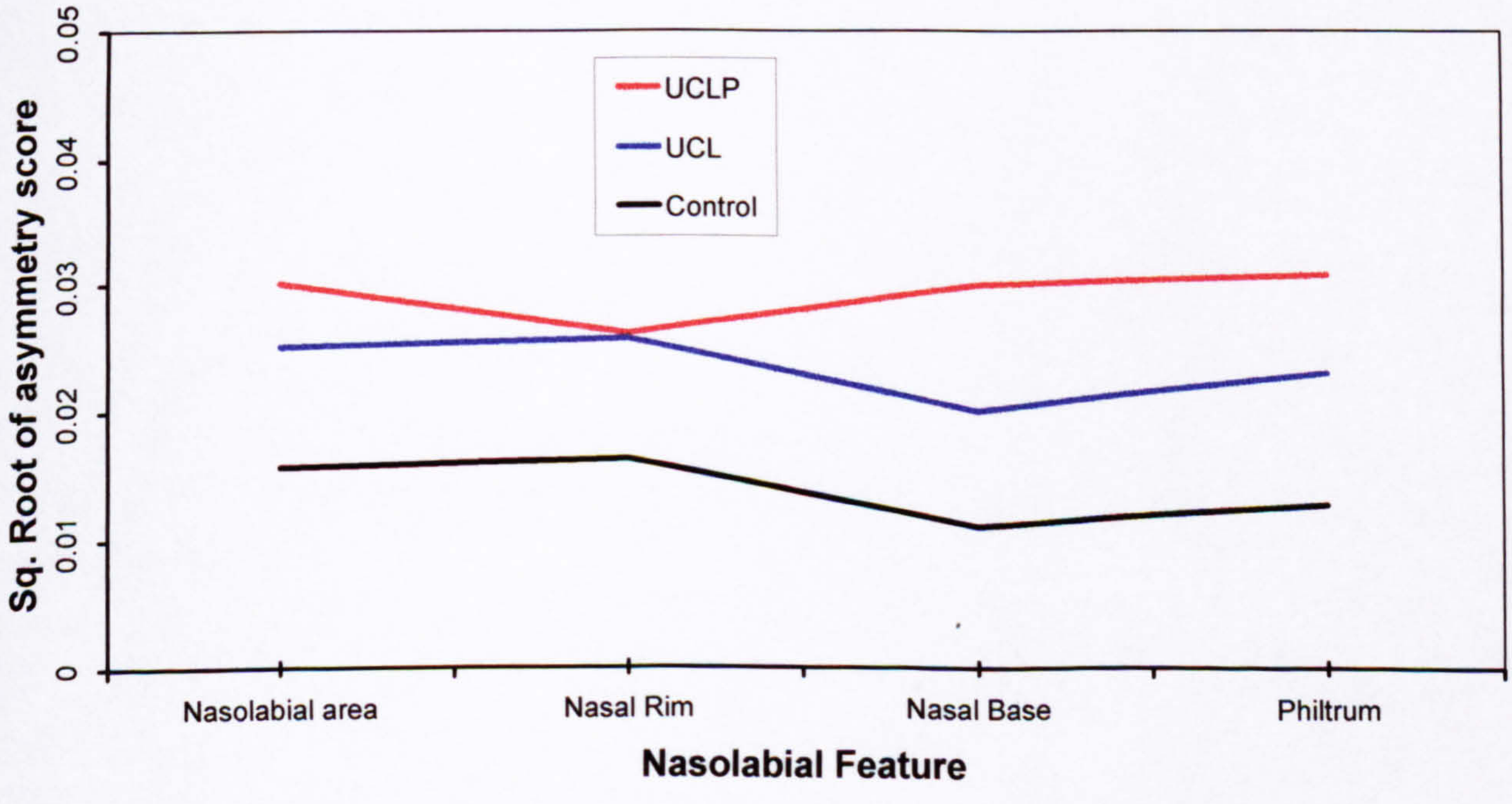


Figure 4.34 Residual Nasolabial asymmetry distribution at age 2 years

4.7.3 Summary of Asymmetry Distribution

Prior to surgery

Facial asymmetry was dominated by lip region asymmetry in both cleft groups. Least contribution to facial asymmetry was made by the upper face in UCL infants and by the upper face and nasal rim in UCLP infants. Nasolabial asymmetry was greatest in the philtrum and least in the nasal rim in both cleft groups.

After nose / lip repair

Residual lip region asymmetry dominated facial asymmetry in UCL infants, whilst no dominant region was identified in UCLP infants. Residual nasolabial asymmetry was distributed evenly between philtrum, nasal base and nasal rim in both cleft groups. However, nasal rim asymmetry was significantly smaller in the UCL group.

At age 1 year

In UCL children, residual lip region asymmetry contributed most and upper face least to overall facial asymmetry. Nasolabial asymmetry was evenly distributed across philtrum, nasal rim and nasal base. In UCLP children, no single feature dominated facial or nasolabial asymmetry.

At age 2 years

Upper face asymmetry contributed least, but neither the lip nor nasal region dominated facial asymmetry in either cleft group. Similarly, residual nasolabial asymmetry was evenly distributed across the philtrum, nasal base and nasal rim. The degree of residual upper face asymmetry and nasal base asymmetry were the only discriminating features between cleft types at 2 years:

4.7.4 Changes in Asymmetry with surgery and growth over 2 years

A square-root transformation was applied to all mean Asymmetry Scores to reduce skewness and allow graphical display of the changes in mean global facial Asymmetry Score over time.

4.7.4.1 Global facial asymmetry changes

Fig 4.35 shows global facial asymmetry changes after lip/nose repair and with growth over time to age 2 years.

Improvement in facial asymmetry was demonstrated in both cleft groups after surgery to repair the cleft lip and nose. The significant differences between UCL and UCLP shown in global facial asymmetry prior to surgery ($p=0.001$), were not detectable at age 2 years. Negligible change in global facial symmetry was noted after surgery with growth up to 2 years of age.

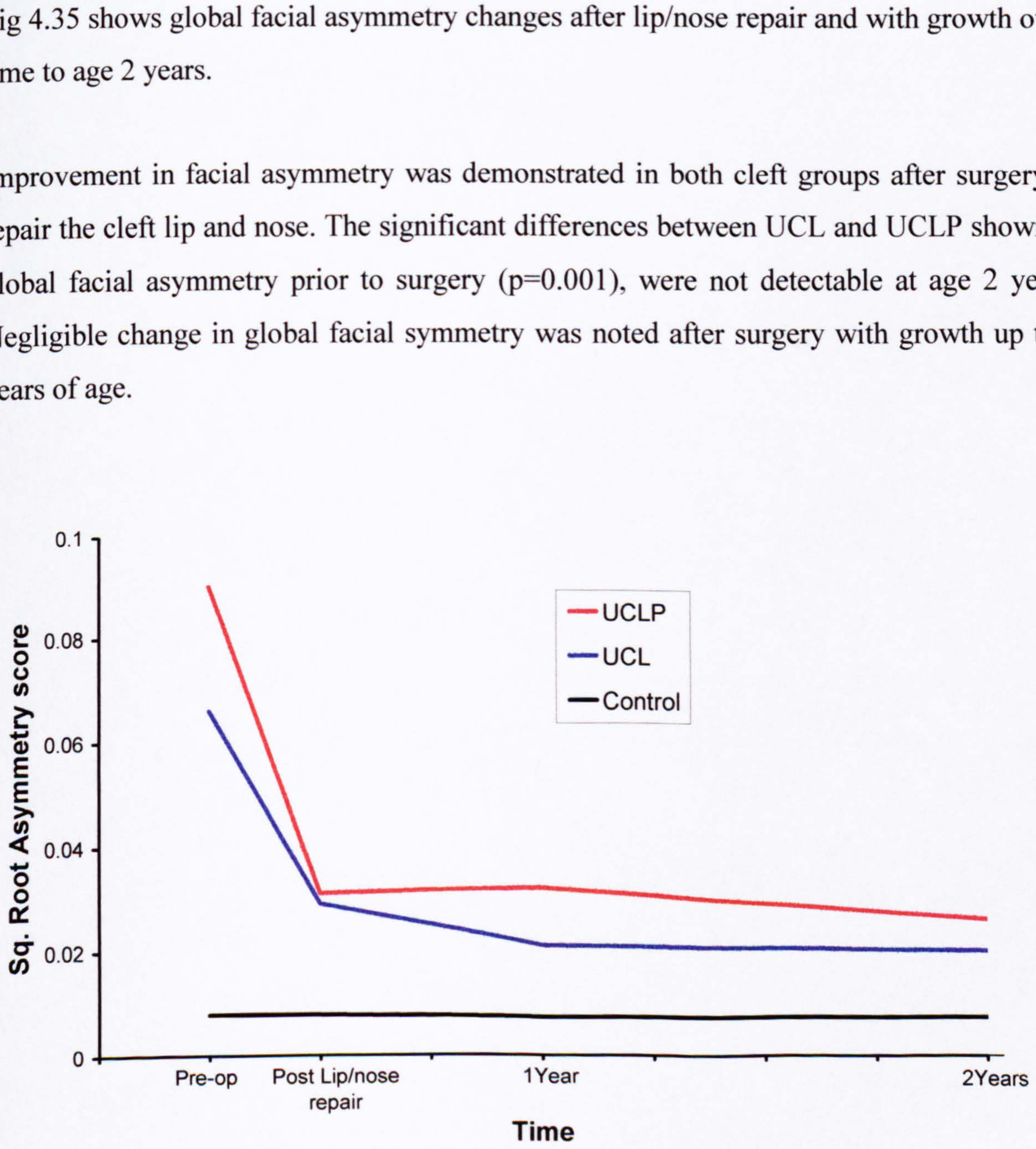


Figure 4.35 Changes in global facial asymmetry over 2 years

4.7.4.2 Changes in Facial Feature asymmetry with time

A square-root transformation was applied to all mean Asymmetry Scores to reduce skewness and allow graphical display of the changes in mean Asymmetry Scores in individual facial features over time (Figs 4.36 - 4.40).

4.7.4.2.1 Upper Face

Figs 4.36 and Fig 4.37 overleaf demonstrate the effect of including the highly asymmetric lip landmarks when configurations were aligned in order to generate Asymmetry Scores.

Upper face asymmetry improved dramatically with nasolabial repair (Fig 4.36), but there was negligible improvement thereafter. Both UCLP and UCL groups had asymmetry scores above baseline when all landmarks were used in the matching process.

Asymmetry in the upper face in the UCL group was much closer to that of controls when lip landmarks were omitted from the configuration alignment process (Fig 4.37). This demonstrates the effect of including very asymmetric regions (i.e. lips) in the overall matching process for large configurations, which can result in asymmetry of other parts of the face appearing artificially inflated.

A greater degree of asymmetry was still evident in the upper face of the UCLP group, which persisted, but continued to reduce, after lip/nose repair ($p=0.008$). In contrast, upper face asymmetry in UCL was similar to controls after primary lip/nose repair.

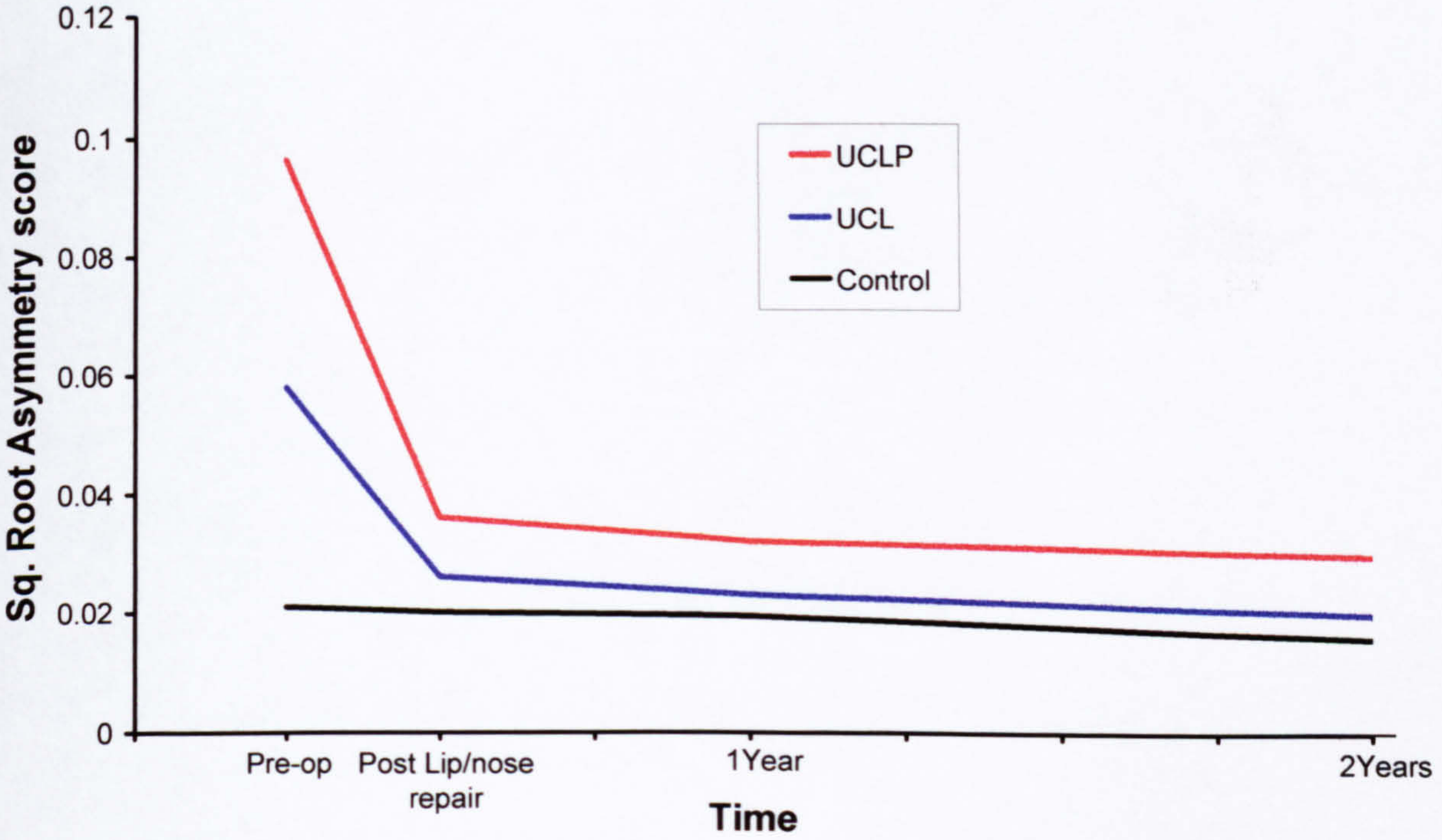


Figure 4.36 Changes in Upper face asymmetry over time

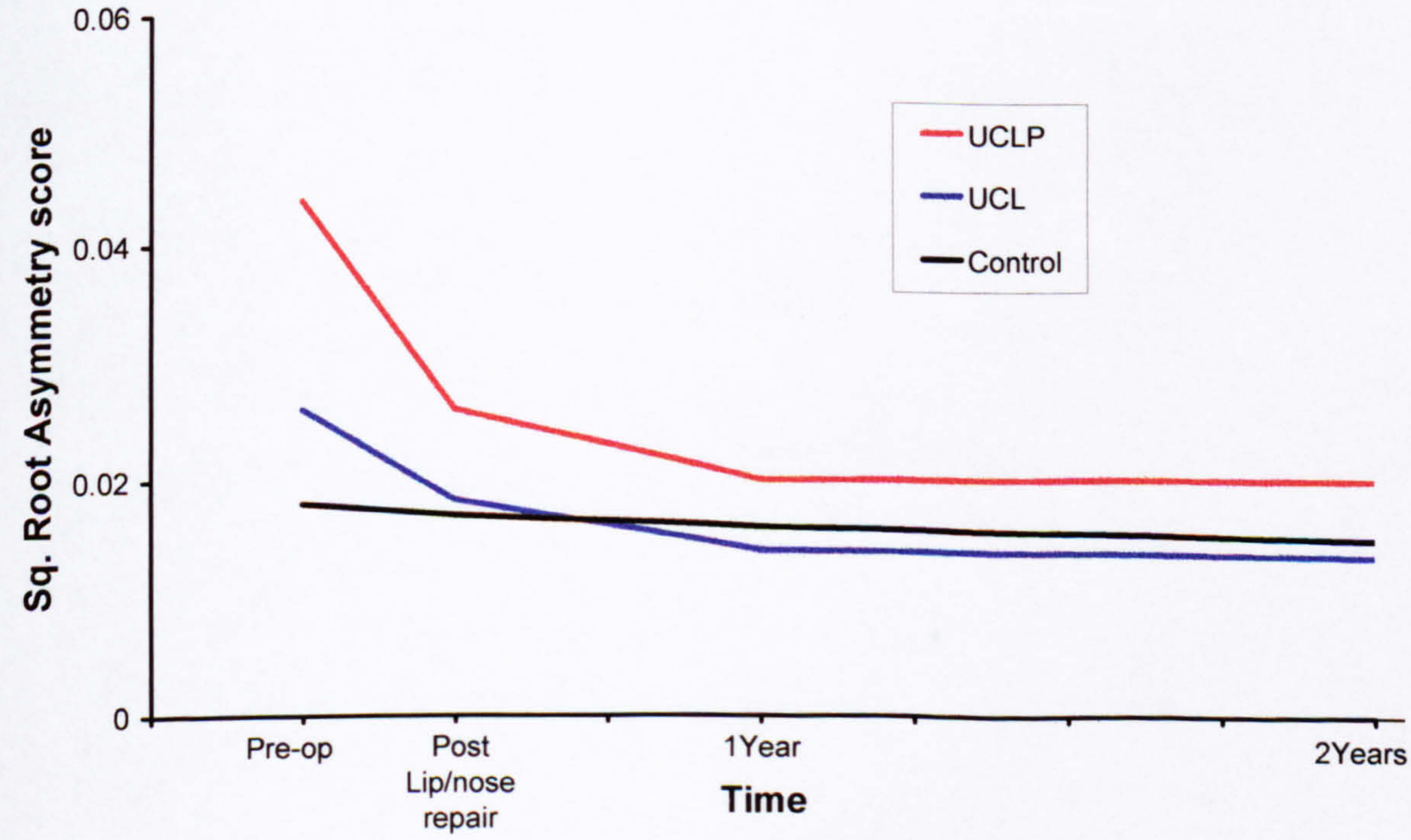


Figure 4.37 Changes in Upper face asymmetry – lip landmarks excluded from matching process

4.7.4.2.2 Nasal Rim

Fig 4.38 shows changes in nasal rim asymmetry with primary repair and over time to age 2 years.

Nasal rim asymmetry improved in both UCL and UCLP groups with lip / nose repair ($p<0.001$). Despite a slightly elevated asymmetry immediately after surgery in the UCLP group, compared to the UCL group ($p=0.037$), negligible further improvement in asymmetry occurred in the post-op period up to 2 years of age, in either group (UCL $p=0.754$; UCLP $p=0.256$).

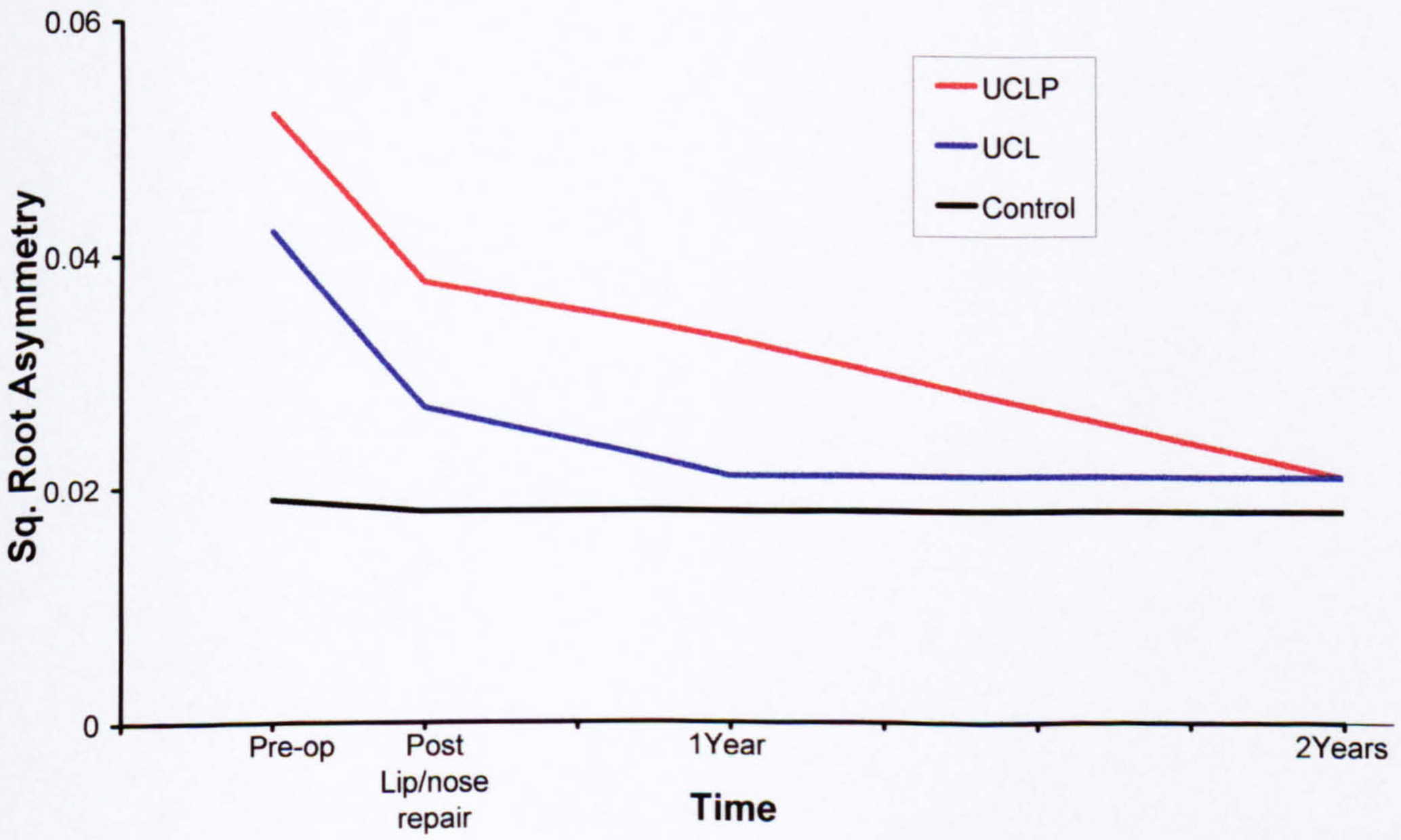


Figure 4.38 Changes in nasal rim asymmetry over time

4.7.4.2.3 Nasal Base

Fig 4.39 shows changes in nasal base asymmetry with primary repair and over time to age 2 years.

Marked nasal base asymmetry was present in both cleft groups pre-operatively. Dramatic improvement occurred with corrective surgery. This was particularly evident in the UCLP group. Negligible change occurred post lip/nose repair to 1 year, however, separation of UCLP and UCL occurred in the 1-2 year interval, such that a greater degree of residual asymmetry was seen in the nasal base in the UCLP group (p=0.042).

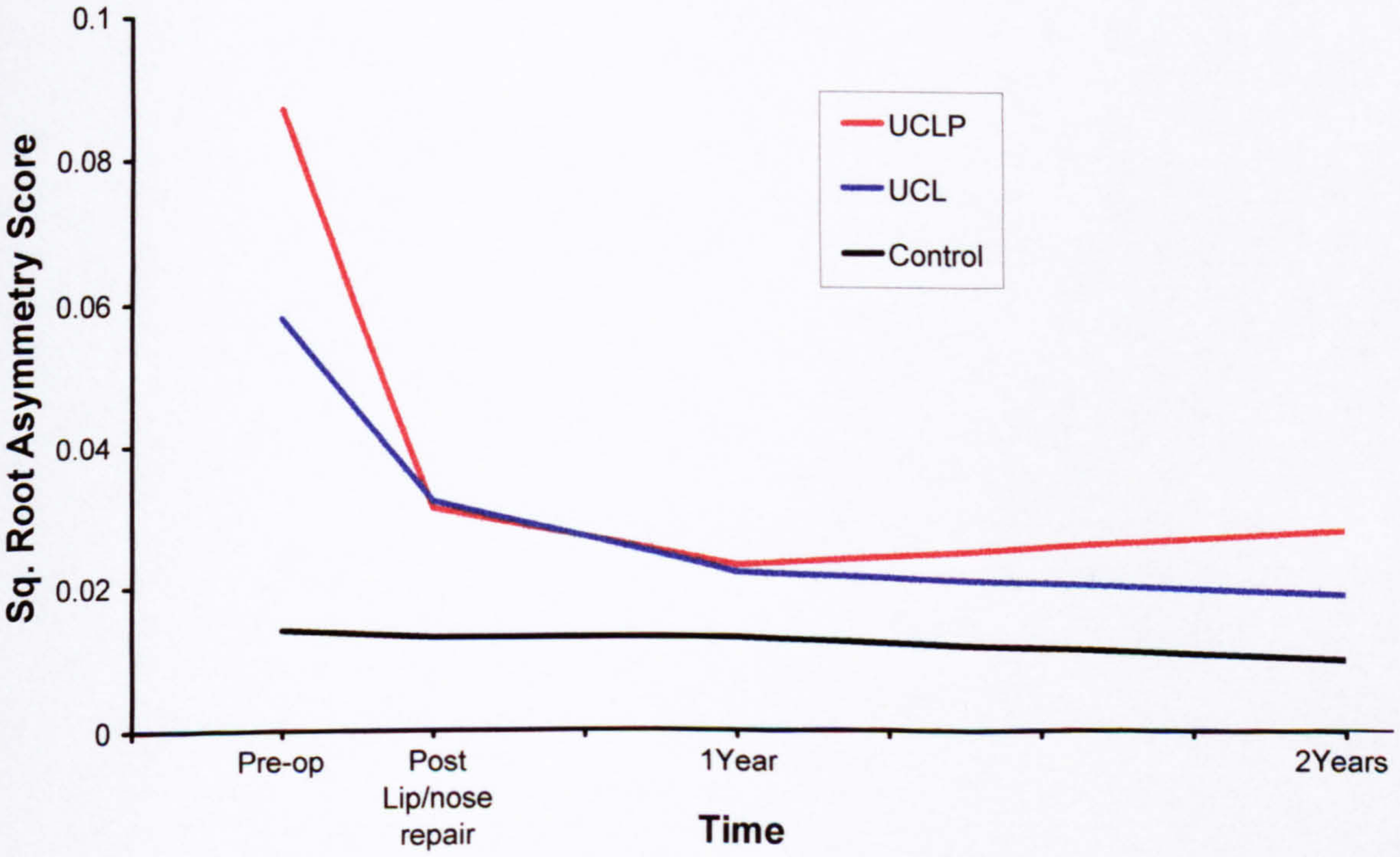


Figure 4.39 Changes in nasal base asymmetry over time

4.7.4.2.4 Philtrum

Fig 4.40 shows changes in philtrum asymmetry with primary repair and over time to age 2 years.

Marked improvement occurred in philtrum asymmetry following lip repair, but no further improvement was demonstrated up to age 2 years. UCLP and UCL groups behaved in a similar fashion compared to the non-cleft baseline. Both cleft groups had a similar degree of residual philtrum asymmetry post-op, despite a significantly greater degree of asymmetry in the UCLP group prior to surgery ($p=0.013$).

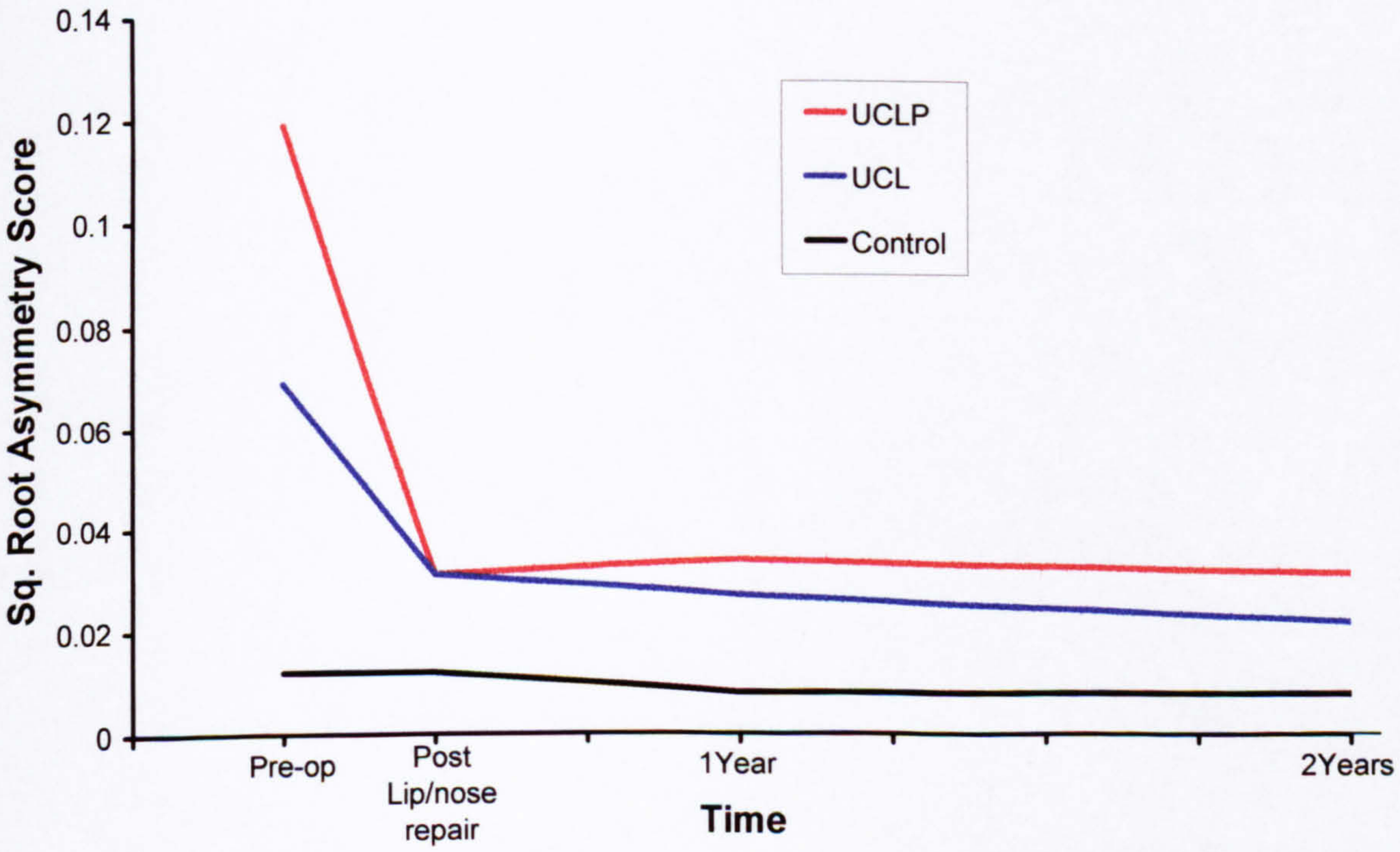


Figure 4.40 Changes in philtrum asymmetry over time

4.7.5 Summary of Asymmetry changes with surgery and growth to age 2 years.

Facial Asymmetry

Improvement in overall facial asymmetry occurred with primary lip/nose repair in UCL and UCLP, but no further changes were noted up to age 2 years in either group.

Upper face

Asymmetry in the upper face contributed least to facial asymmetry in both cleft groups and improved with primary lip/nose repair. Significant asymmetry persisted only in the UCLP group after surgery, and although this continued to improve up to age 1 year, was still evident at age 2 years.

Nasal Rim

A similar degree of nasal rim asymmetry was present in UCL and UCLP before repair, and marked improvement occurred with surgery. Correction was more successful in UCL than UCLP (asymmetry higher in UCLP post-repair). Negligible change occurred thereafter with growth to age 2 years in either group.

Nasal base

Dramatic improvement in nasal base symmetry occurred with surgery in both cleft groups. Similar level achieved in UCL and UCLP, despite a greater degree of asymmetry in UCLP prior to surgery. A slight deterioration in UCLP and continued improvement in UCL resulted in greater residual nasal base asymmetry in UCLP at age 2 years.

Philtrum

Marked improvement in philtrum asymmetry occurred with surgical repair. In common with the nasal base, a similar level of symmetry was achieved in both cleft groups, despite a greater degree of asymmetry in UCLP prior to surgery. Residual philtrum asymmetry did not change up to age 2 years.

4.8 Facial Feature Residual Shape Deformity at age 2 years

This was an exploratory study of residual shape deformity in facial features of UCL and UCLP children at age 2 years, compared to a non-cleft control 'mean'. Landmark subsets in Table 4.55 were used to define the shape of nose and lip features.

Table 4.55 Landmark subsets for Procrustes 'distance from normal' (PDFN) score at 2 years

Facial feature	Landmark Subset
Nasal Complex shape	acL alL al0oL prn al0oR alR acR sbalR sn sbalL n
Nasal Rim shape	acL alL al0oL prn al0oR alR acR
Nostril shape	sbalR al0iR hnR cR sn0R sbalL al0iL hnL cL sn0L
Columella shape	sn0R cR cL sn0L sn
Upper Lip shape	chR cphR ls cphL chL
Philtrum shape	sn0R cphR ls cphL sn0L sn

Ninety-two 2-year-old non-cleft children were used to generate a control mean shape for each nose and lip feature. The cleft sample consisted of 11 UCL and 21 UCLP two-year-old children. For each facial feature, the PDFN score was derived by calculating the distance of each cleft case to the control mean shape ('Procrustes Distance from Normal'). PDFN scores were calculated and ranked in order from best (lowest) to worst (highest), by cleft type, for each nose and lip variable. These are illustrated in Figures 4.41 to 4.44. The significance of any difference between UCL and UCLP children in median PDFN score was tested by Mann Whitney tests ($p<0.05$).

4.8.1 Nose residual deformity

The only significant difference in the magnitude of residual shape deformity between cleft types occurred in the nostrils. Nostril PDFN scores ranged from 0.14 – 0.35 (Fig 4.41) and median residual Nostril shape deformity was significantly worse in UCLP children than in UCL children ($p=0.032$). Median PDFN scores in other nasal region variables were similar in UCL and UCLP children. Nasal complex PDFN scores ranged from 0.08 to 0.27. Scores were fairly close to each other (0.08-0.19) except for one UCLP case at the upper extreme (Fig 4.42). Nasal Rim PDFN scores ranged from 0.04 to 0.19. Nasal rim had the narrowest range of scores of all the variables, except for one UCLP child at the upper extreme (Fig 4.43). Columella PDFN scores (Fig 4.44) ranged from 0.11 – 0.34. There was more

uniformity in the scores at the upper end of the scale in the columella, than in any other nasal feature.

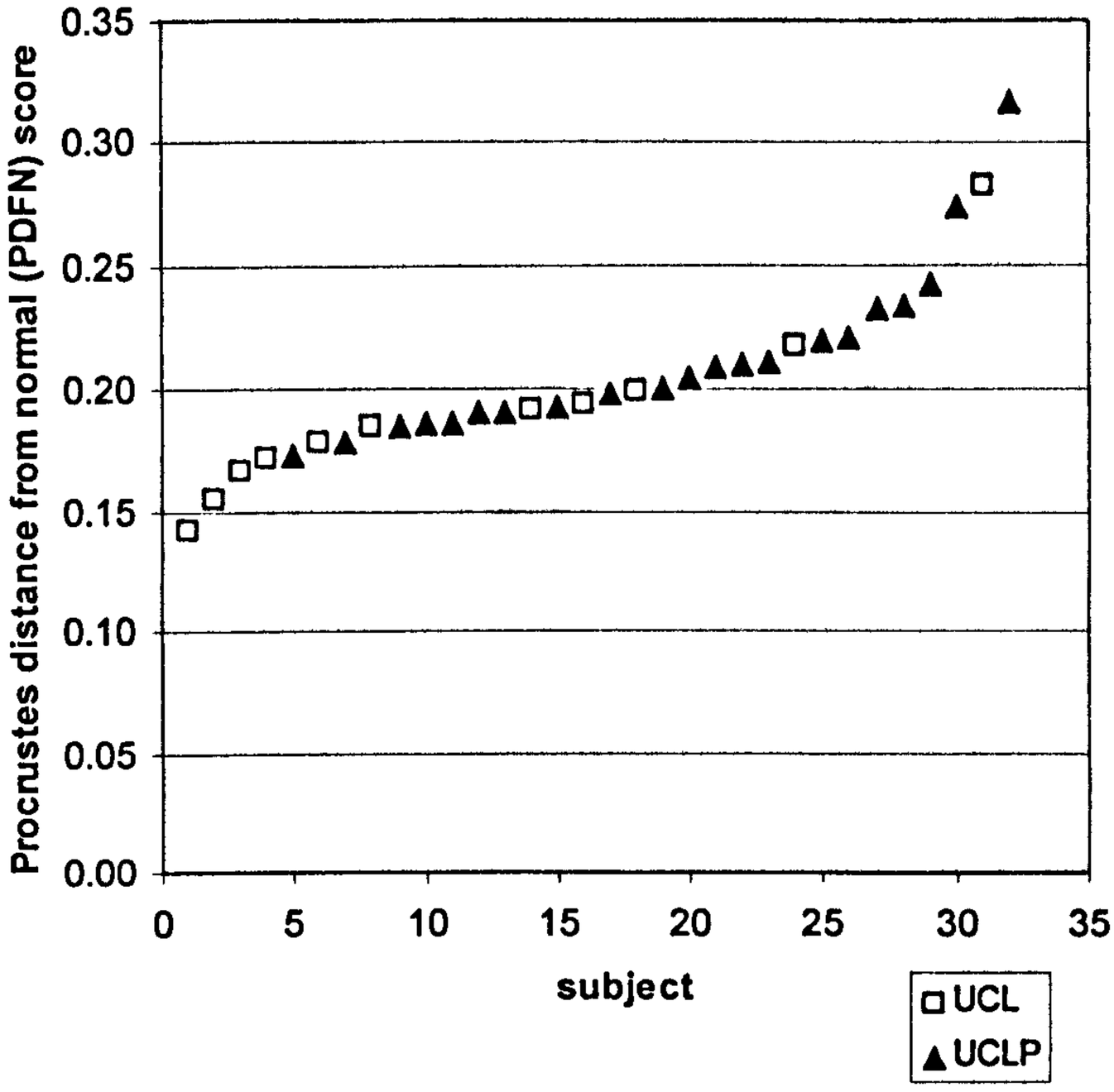


Figure 4.41 Nostrils PDFN scores for UCL and UCLP children at age 2 years

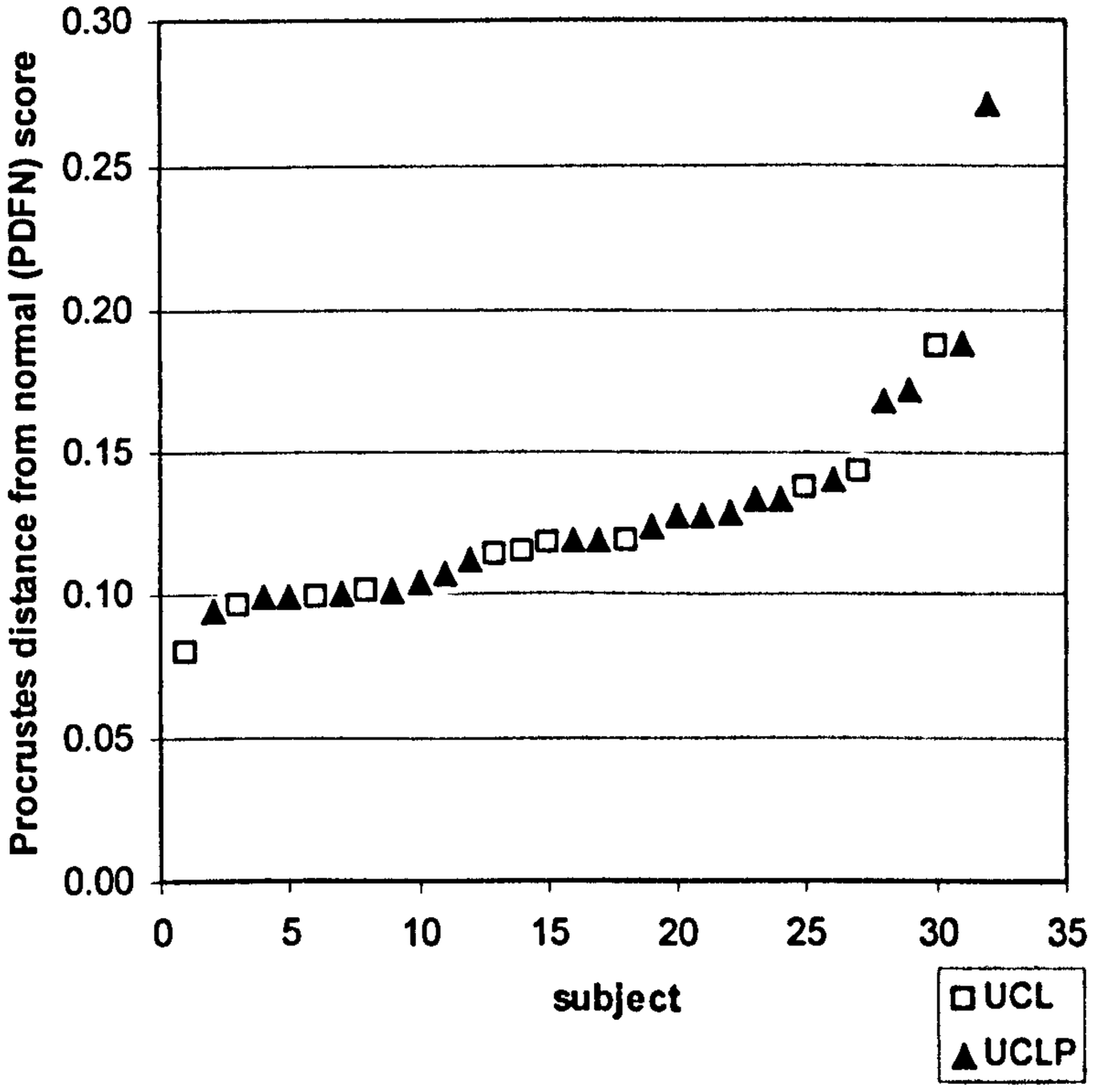


Figure 4.42 Nasal Complex PDFN scores for UCL and UCLP at age 2 years

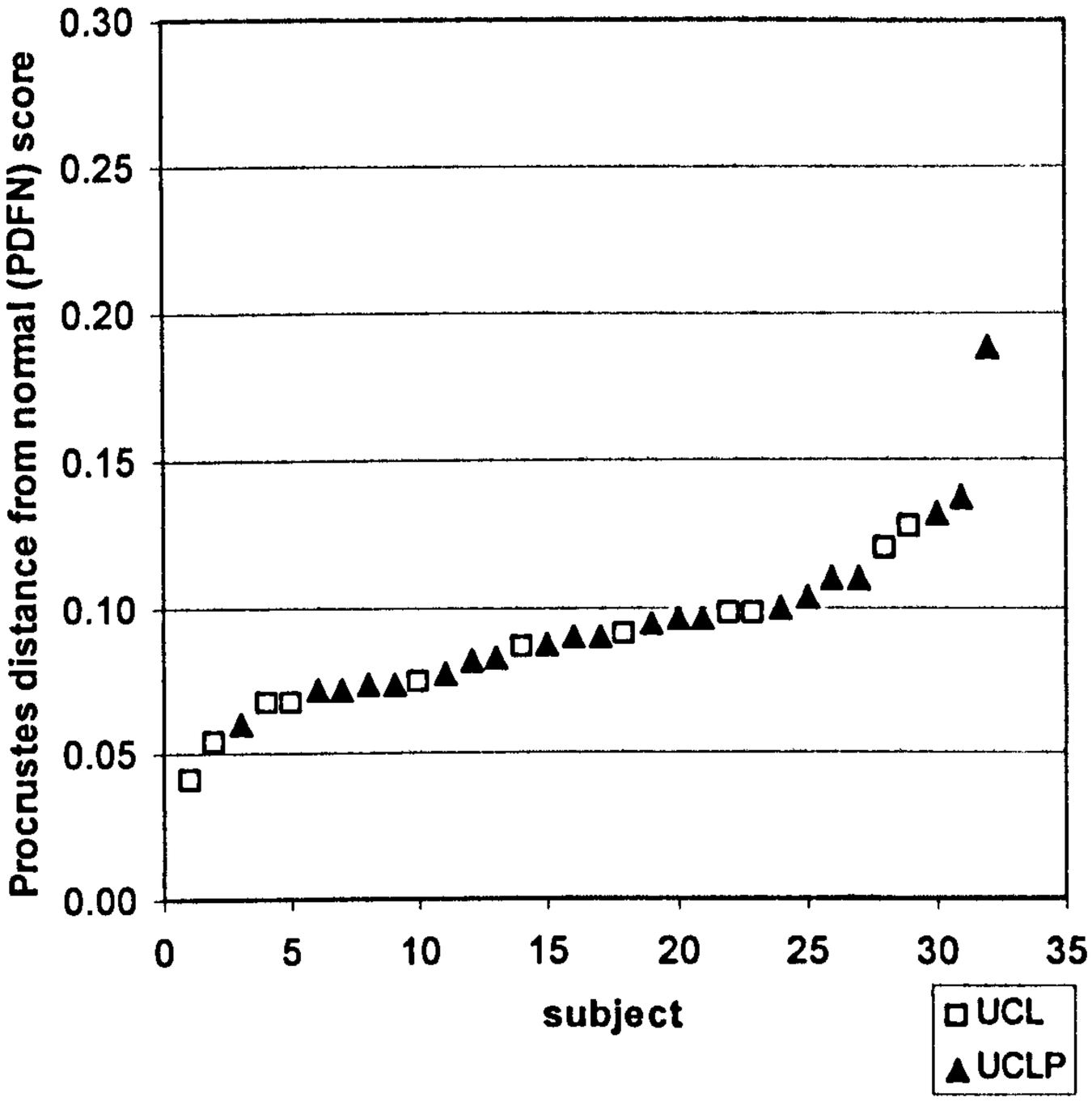


Figure 4.43 Nasal Rim PDFN scores for UCL and UCLP children at age 2 years

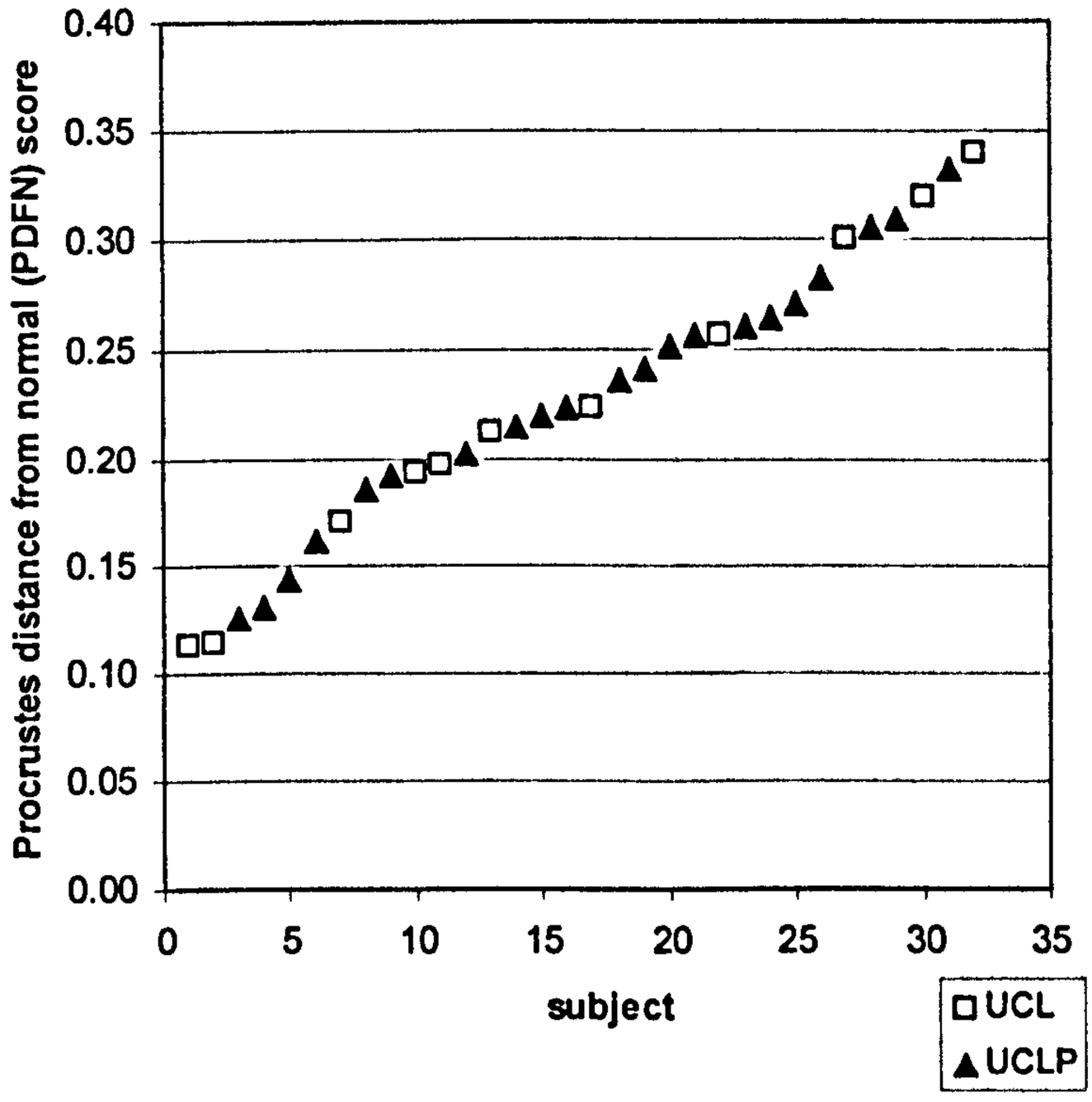


Figure 4.44 Columella PDFN scores for UCL and UCLP children at age 2 years

4.8.2 Lip and Philtrum residual deformity

Upper Lip PDFN scores ranged from 0.06 to 0.29 (Fig 4.45). Philtrum PDFN scores ranged from 0.11 to 0.41. The difference between individual scores was more distinct in the philtrum (Fig 4.46). Outcomes for UCL and UCLP children were not significantly different in respect to residual shape deformity in the lip and philtrum at age 2 years.

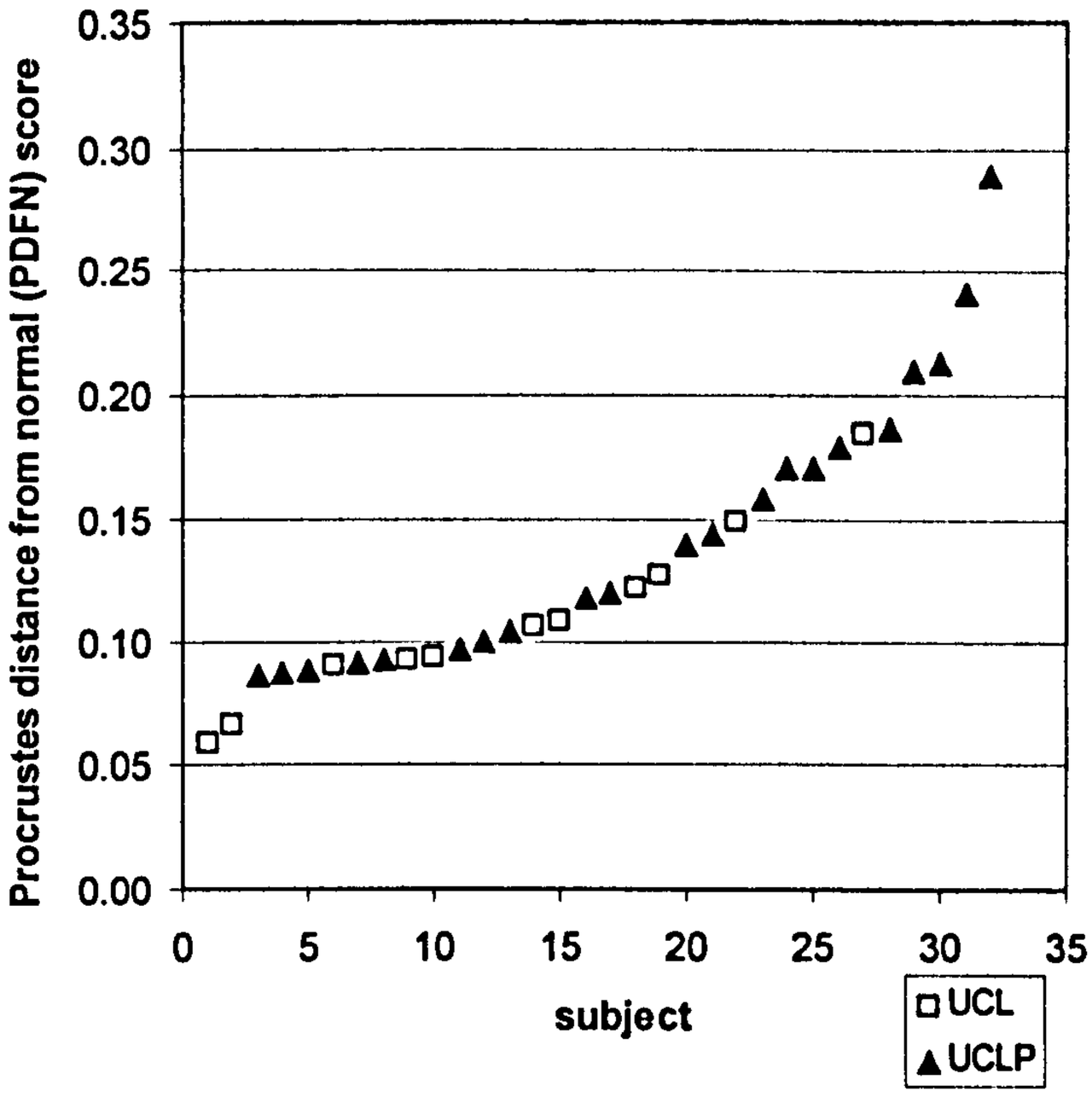


Figure 4.45 Upper Lip PDFN scores for UCL and UCLP children at age 2 years

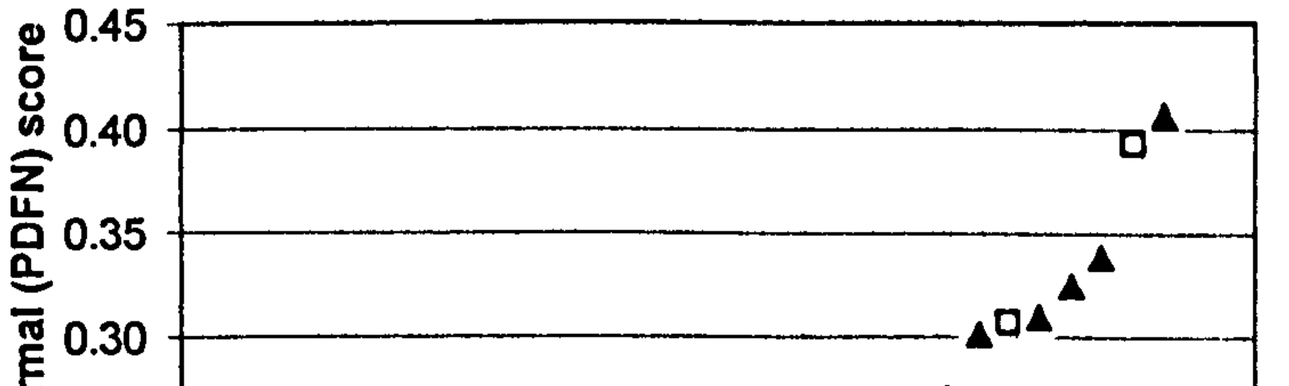


Figure 4.46 Philtrum PDFN scores for UCL and UCLP children at age 2 years

4.8.3 Summary of Residual Shape abnormality at age 2 years

There were no discernible differences in the distribution of residual shape abnormality (PDFN) Scores between UCL and UCLP children at age 2 years.

However, UCLP children had significantly greater median Nostril PDFN scores than UCL children

The amount of residual shape deformity in the nasal complex, nasal rim, columella, upper lip and philtrum was not significantly different in UCL and UCLP children at age 2 years.

4.9 Cleft Severity

4.9.1 Cleft severity Ratios

To indicate the severity of the extent of the cleft in the nose and lip, ratios were calculated from linear distances measured between equivalent pairs of 3D landmarks on the cleft and non-cleft sides of the face (Table 4.56). For each individual, if the ratio were equal to one, this would indicate no difference between cleft and non-cleft dimensions.

Table 4.56 Cleft Severity Ratios

Ratio	Distances	Definition
Nostril Floor ratio	sbalL-sn0L:sbalR-sn0R	ratio of cleft and non-cleft nostril floor widths
Cupid's Bow ratio	cphR-ls:<cph>L-ls	ratio of cleft and non-cleft side surrogate philtrum points to the centre of cupid's bow
Philtrum Height ratio	sn0R-cphR:sn0L-cph0R	ratio of non-cleft side philtrum height and philtrum height adjacent to the cleft

Data distributions approximated a normal distribution in Nostril Floor and Cupid's Bow ratio (Fig 4.47). Philtrum Height ratio data distribution was skewed to the right (Fig 4.48). As assumptions of normality could not be satisfied, a logarithmic transformation (log to base 10) was performed for philtrum height ratio. The significance of differences between UCL and UCLP groups was tested by t-test ($p<0.05$).

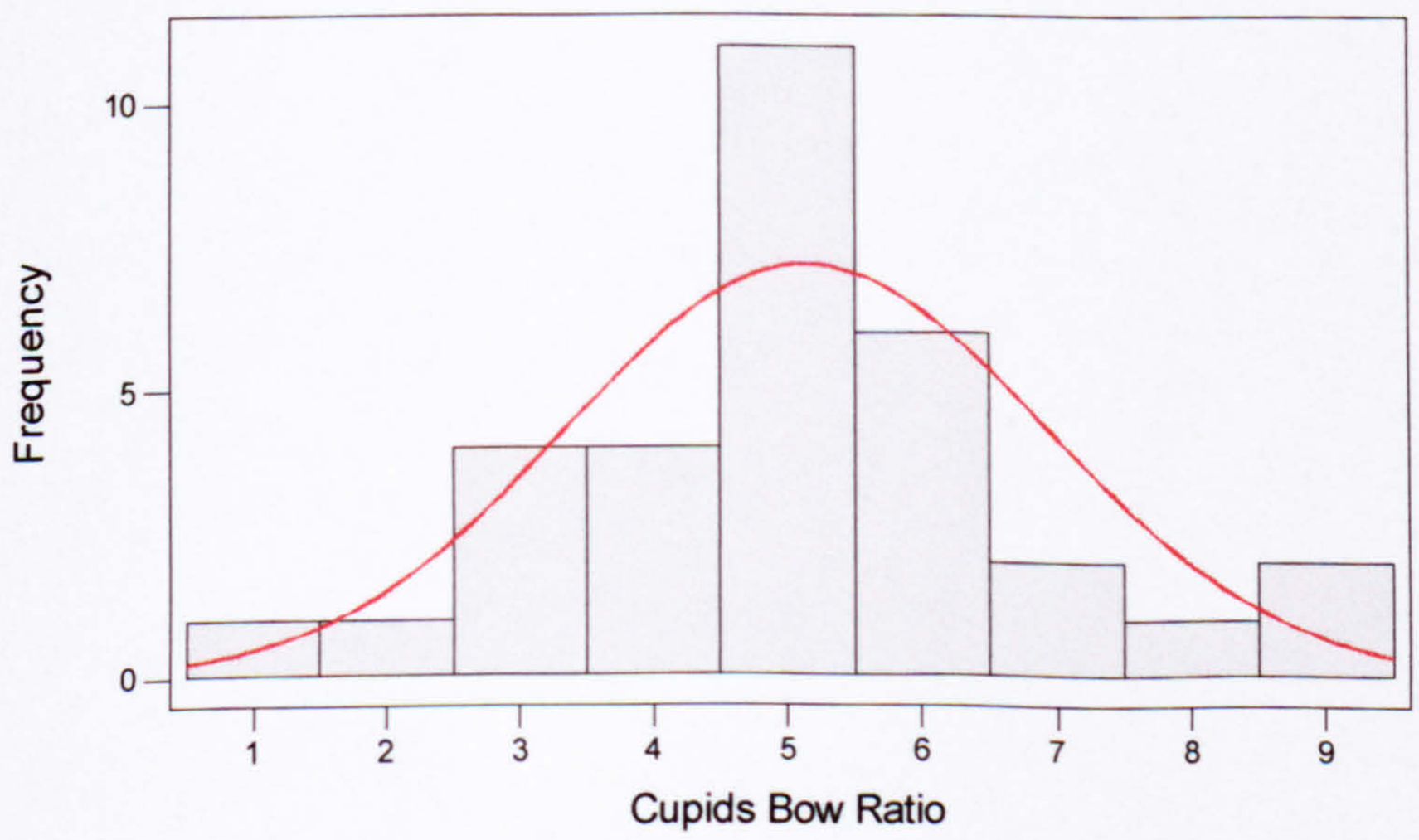


Figure 4.47 Cupid's Bow ratio histogram illustrating normal distribution

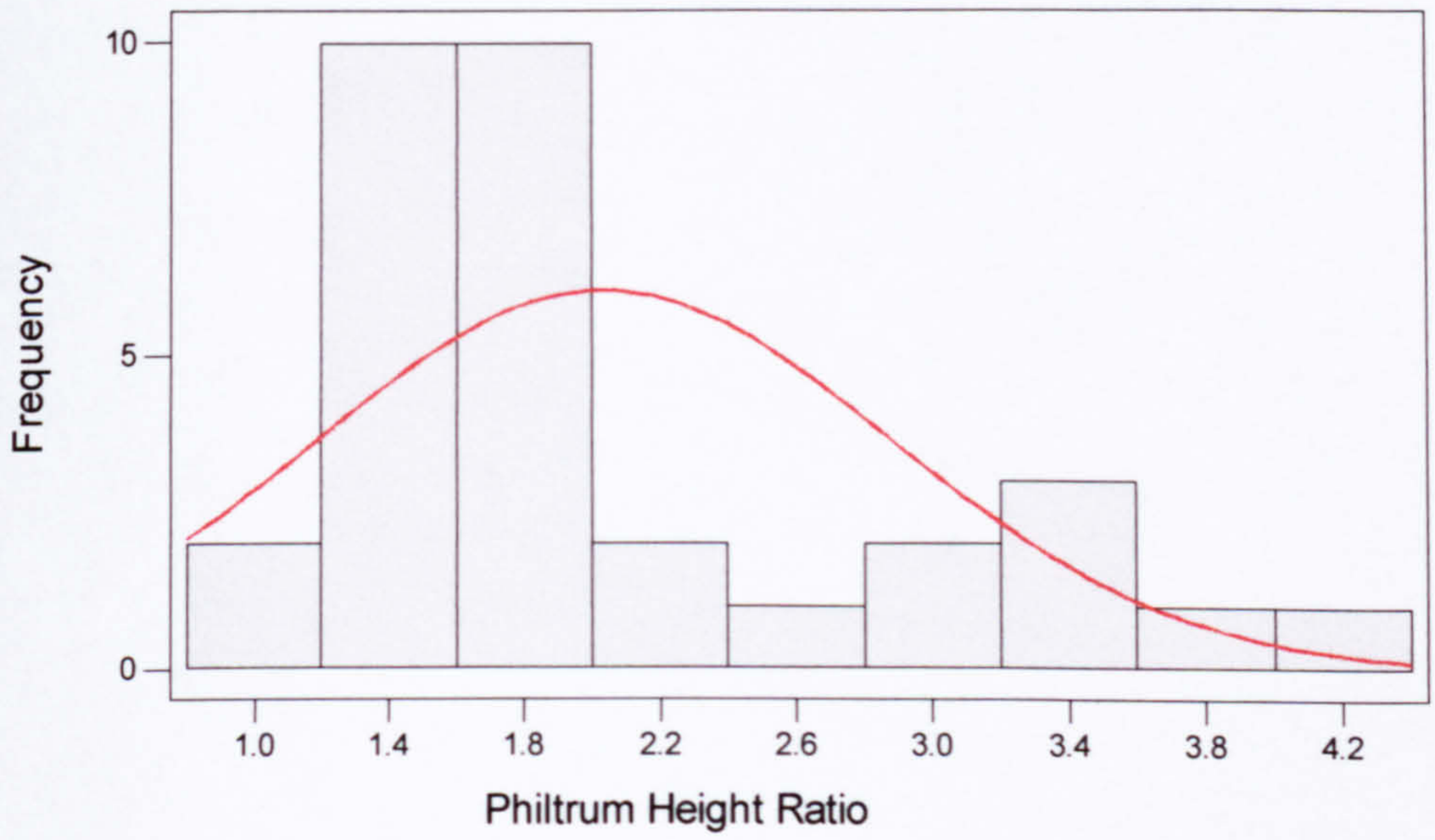


Figure 4.48 Philtrum height ratio histogram, illustrating skewed distribution

4.9.1.1 Differences in severity ratio between UCL and UCLP

Significant differences were found between UCL and UCLP in mean severity scores for Nostril Floor ratio and Philtrum Height ratio (Figs 4.49 & 4.50). Ratios were significantly greater in UCLP than UCL in both cases. UCLP philtrum height ratio was twice that of UCL. There were no differences in mean severity ratios for Cupid's Bow ratio.

Table 4.57 Differences in Severity Ratios between Cleft types

Ratio	UCL (n=17)		UCLP (n=15)		p-value
	Mean	StDev	Mean	StDev	
Cupid's Bow Ratio	4.6	1.6	5.7	1.9	0.097
Nostril Floor Ratio	1.7	1.0	3.0	0.8	**0.000**
Philtrum Height Ratio	1.5	0.1	2.45	0.2	**0.001**

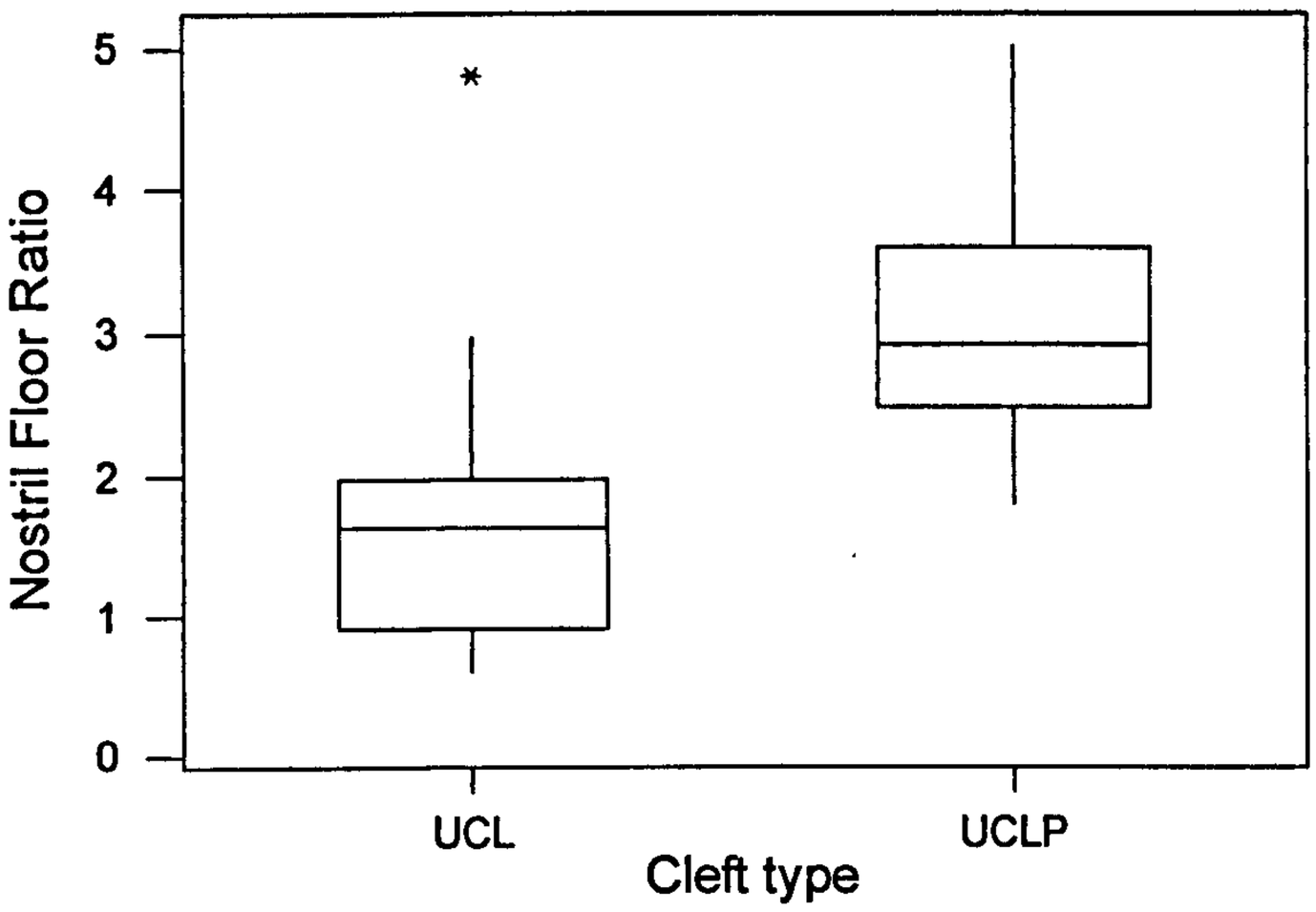


Figure 4.49 Boxplot of Nostril Floor Ratio, by cleft type

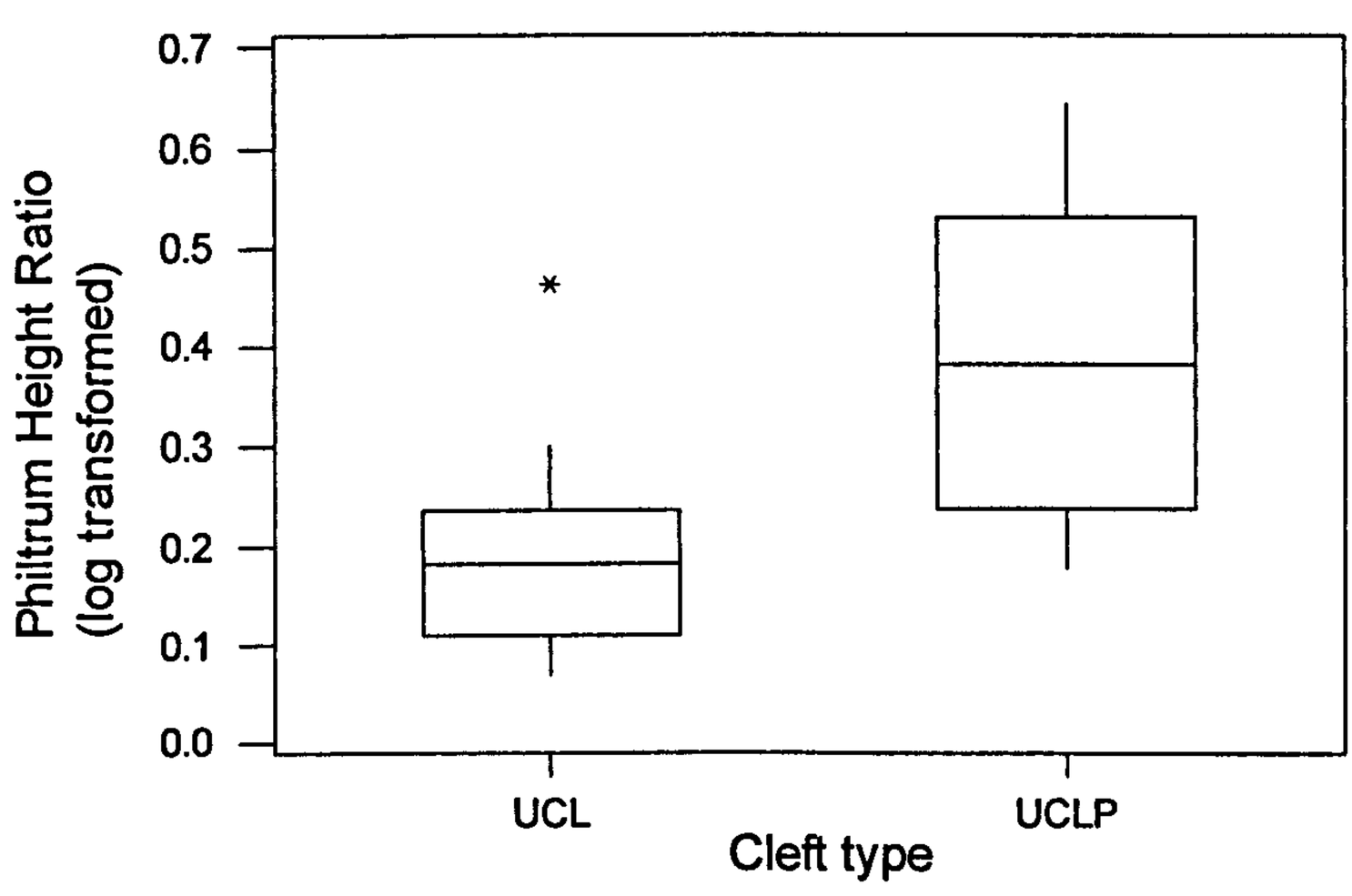


Figure 4.50 Boxplot of Philtrum Height Ratio by cleft type

4.9.1.2 Relationship between severity ratios

Table 4.58 shows significant correlation between horizontal and vertical measures of cleft severity in the form of ratios of measurements on cleft and non-cleft sides.

A moderate correlation (0.45) was found between the extent of the cleft in the nostril floor and the accompanying discrepancy in the sides of the philtrum (Fig 4.51). Although there was a tendency for Philtrum Height ratio to increase as the nostril floor ratio increased, only 20% of the variability in philtrum height ratio could be explained by this relationship. A moderate correlation (0.57) was found between horizontal measures of severity in the lip and nostril (Fig 4.52) The relationship between Cupid's Bow ratio and Nostril Floor ratio accounted for 32.5% of the variation in nostril floor ratio. There was no correlation between horizontal and vertical measures of cleft severity in the lip (Cupid's Bow ratio and Philtrum Height ratio) (Fig 4.53).

Table 4.58 Correlation between horizontal and vertical cleft severity ratios

Correlation	Philtrum Height ratio (log-transformed)		Cupid's Bow ratio	
	Pearson's correlation Coefficient	p-value	Pearson's correlation Coefficient	p-value
Nostril Floor ratio	**0.45**	**0.010**	**0.57**	**0.001**
Cupid's Bow ratio	0.07	0.726	-	-

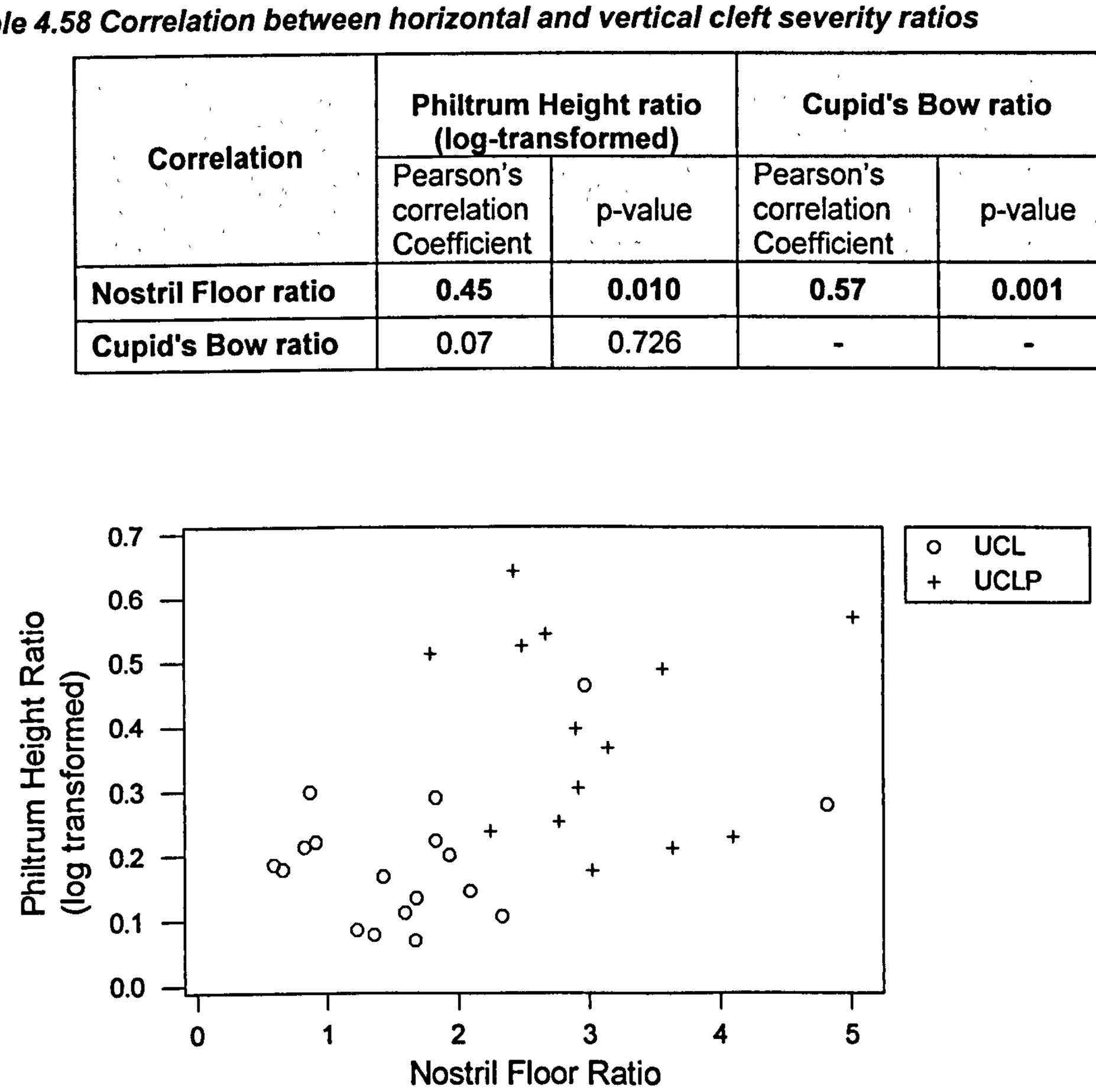


Figure 4.51Correlation between Nostril Floor ratio and Philtrum Height Ratio (log-transformed)

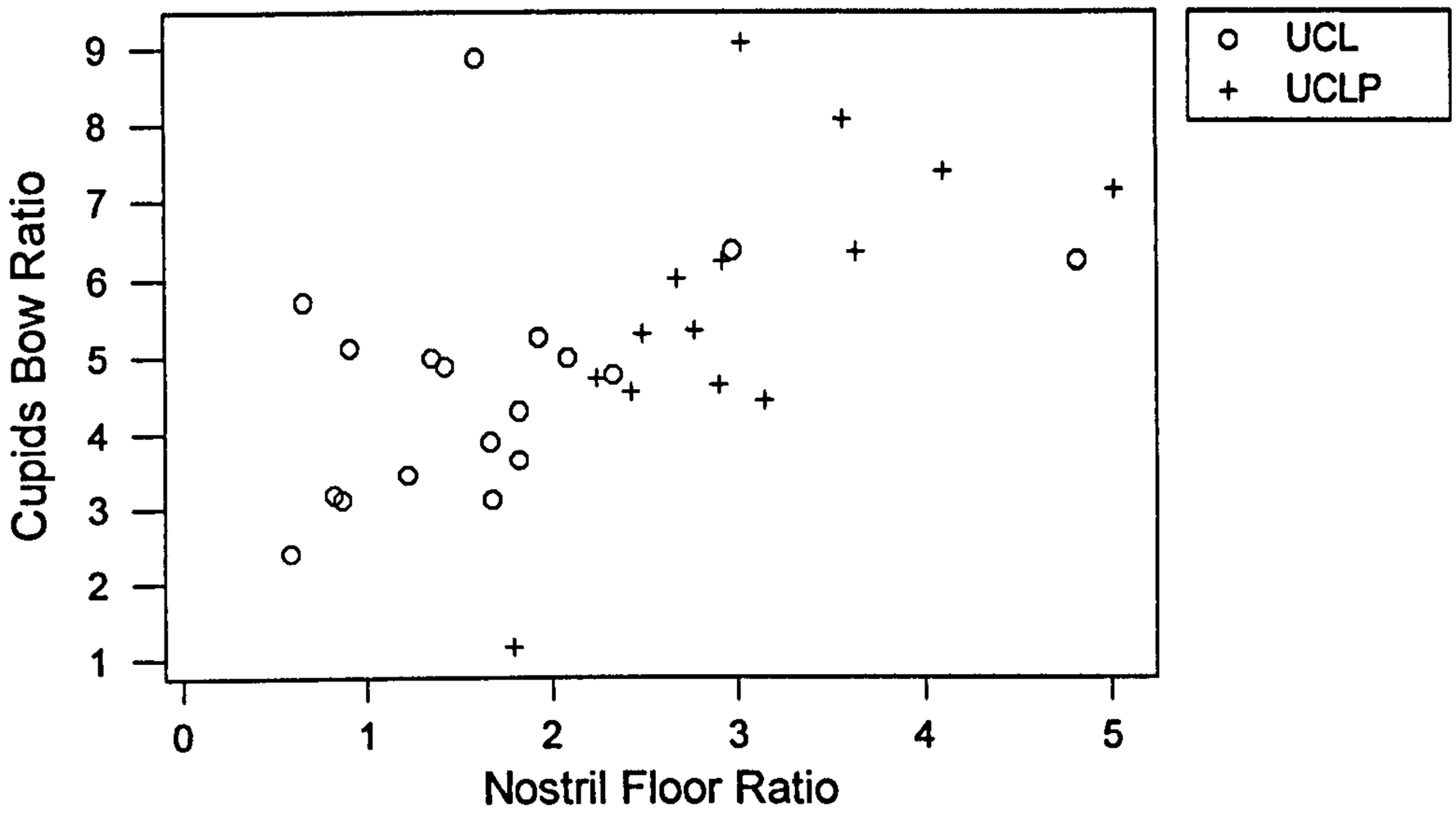


Figure 4.52 Correlation between Cupid's Bow ratio and Nostril floor ratio

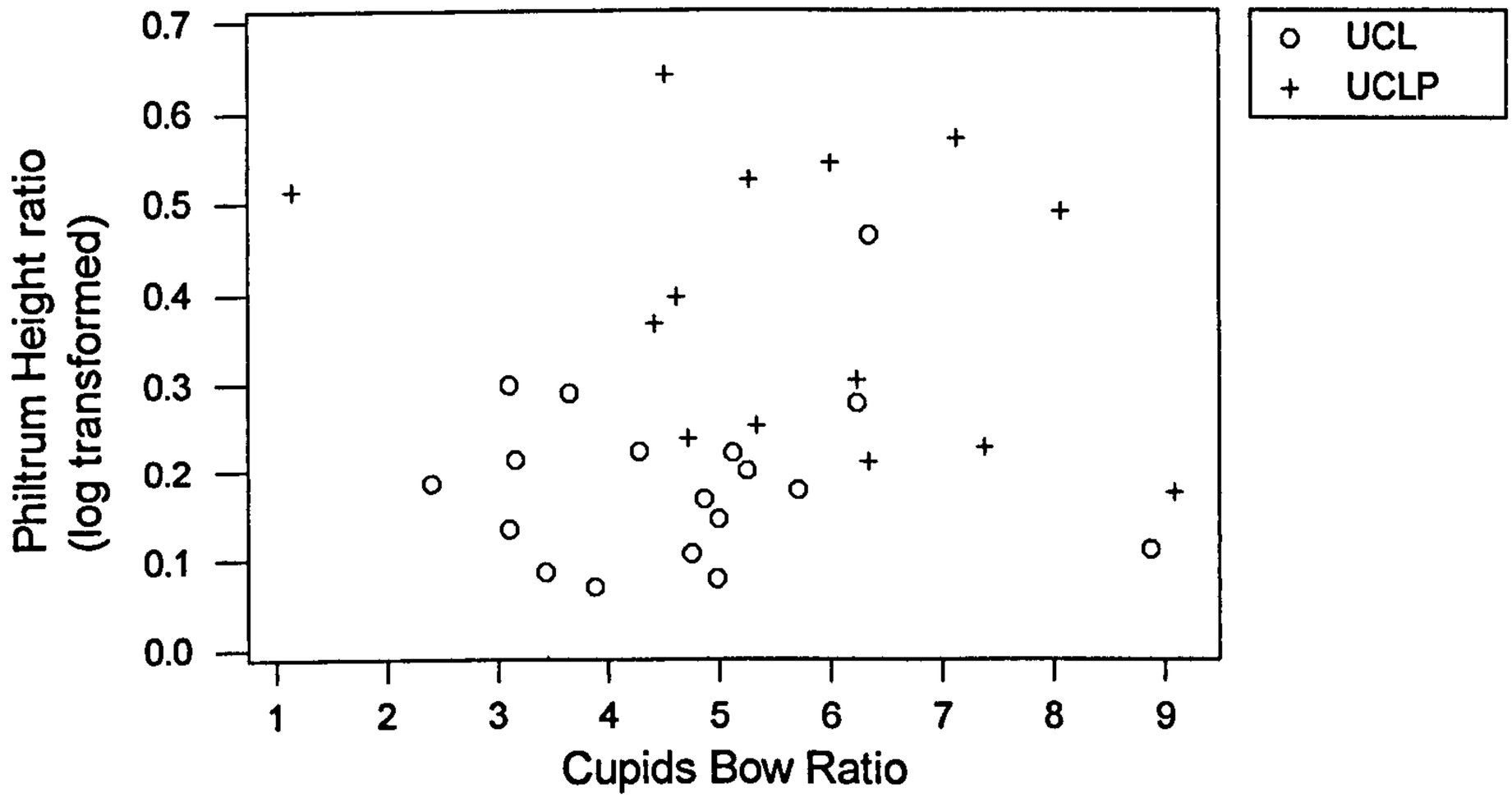


Figure 4.53 No correlation between Cupid's Bow ratio and Philtrum Height ratio

4.9.1.3 Summary of Cleft Severity ratios

Nostril Floor ratio and Philtrum Height ratio were significantly larger in UCLP than UCL infants before primary lip/nose repair.

Nostril Floor ratio was associated with the horizontal size of the cleft in the lip and the vertical discrepancy in philtrum height.

Cupid's Bow ratio could not distinguish between cleft types and was not associated with vertical discrepancy in philtrum height.

4.9.2 3D Nasal Asymmetry Severity, prior to lip/nose repair

In order to examine the relationship between different features of the nose, in terms of severity of asymmetry before surgical correction, landmark subsets were created to define nasal features (Table 4.59). Asymmetry scores were calculated, as previously described.

Table 4.59 Asymmetry score landmarks for nasal features

Nasal Feature	Landmarks for asymmetry score
Nasal Rim	acL alL al0oL prn al0oR alR acR
Nasal base	sbalR sn sbalL
Columella	sn0R cR cL sn0L sn
Nostril	sbalR al0iR hnR cR sn0R sbalL al0iL hnL cL sn0L

Asymmetry Scores for nasal variables were not normally distributed; therefore, a logarithmic transformation (log to base 10) was applied to the data for each variable. Pearson's Correlation Coefficients were calculated for the total cleft sample of 32 infants (17 UCL and 15 UCLP) to assess if there was an association between different nasal features in terms of severity of asymmetry, prior to surgery.

4.9.2.1 Relationship between Nasal Base asymmetry and Nostril asymmetry

There was a strong linear relationship between pre-operative nasal base asymmetry and nostril asymmetry (Fig 4.54, overleaf). Pearson correlation coefficient = 0.932 ($p = 0.000$). 86.8% of the variability in nostril asymmetry could be explained by its relationship with nasal base asymmetry.

4.9.2.2 Relationship between Nasal Base asymmetry and Nasal Rim asymmetry

A strong correlation was demonstrated between asymmetry of the nasal base and nasal rim asymmetry prior to primary surgery (Fig 4.55, overleaf). Pearson correlation coefficient = 0.799 ($p=0.000$). Almost two thirds (63.8%) of the variability in nasal rim asymmetry could be explained by its relationship with nasal base asymmetry.

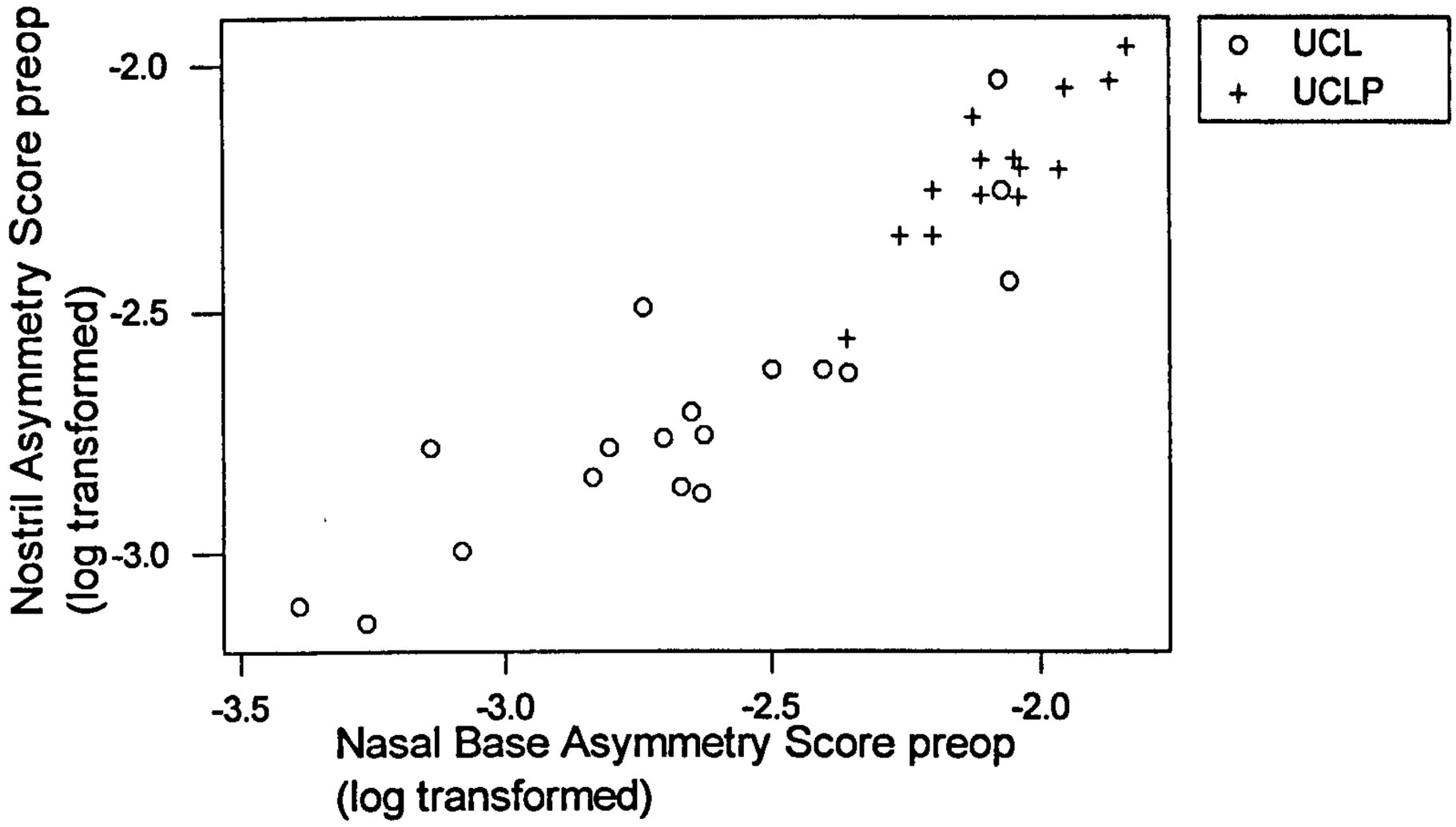


Figure 4.54 Strong correlation between nasal base asymmetry and nostril asymmetry prior to surgery (preop)

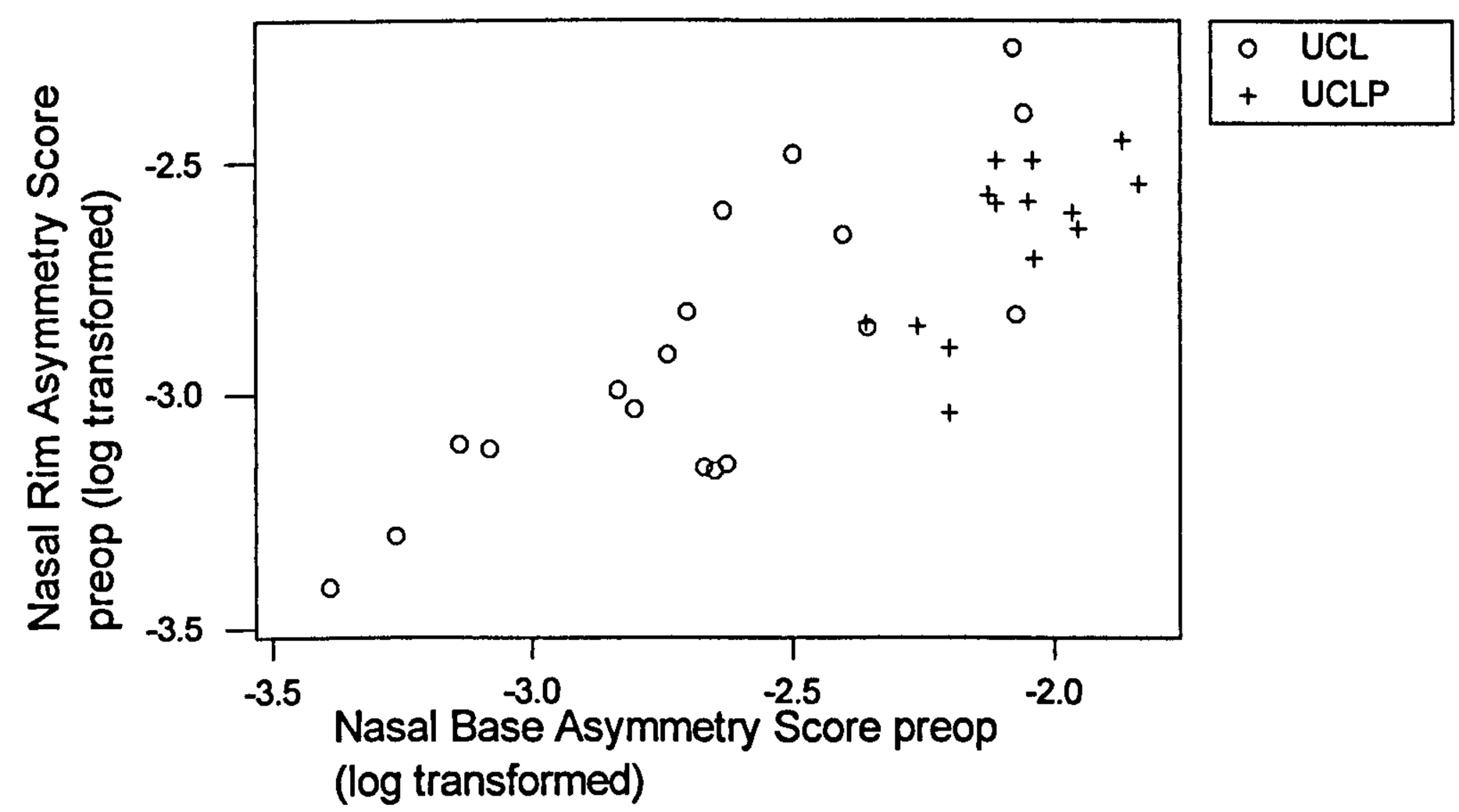


Figure 4.55 Correlation between nasal base asymmetry and nasal rim asymmetry prior to surgery (preop)

4.9.2.3 Relationship between Nasal Rim asymmetry and Nostril asymmetry

A strong correlation was found between nostril asymmetry and nasal rim asymmetry prior to surgery (Fig 4.56, overleaf). Pearson correlation coefficient = 0.752 (P-Value = 0.000). As nasal rim asymmetry increased, nostril asymmetry tended to increase; however, this relationship explained just over half (56.5%) of the variability in nostril asymmetry.

4.9.2.4 Relationship between Columella asymmetry and Nostril asymmetry

There was a strong correlation between pre-operative nostril asymmetry and columella asymmetry (Fig 4.57, overleaf). Pearson correlation coefficient = 0.907 (P-Value = 0.000). 82.3% of the variability in nostril asymmetry could be explained by its relationship with asymmetry of the columella.

4.9.2.5 Nasal base asymmetry and columella asymmetry

There was a strong correlation between columella asymmetry and nasal base asymmetry (Fig 4.58, overleaf). Pearson correlation coefficient = 0.806 (P-Value = 0.000). Two thirds (65%) of the variability in columella asymmetry could be explained by its relationship with nasal base asymmetry.

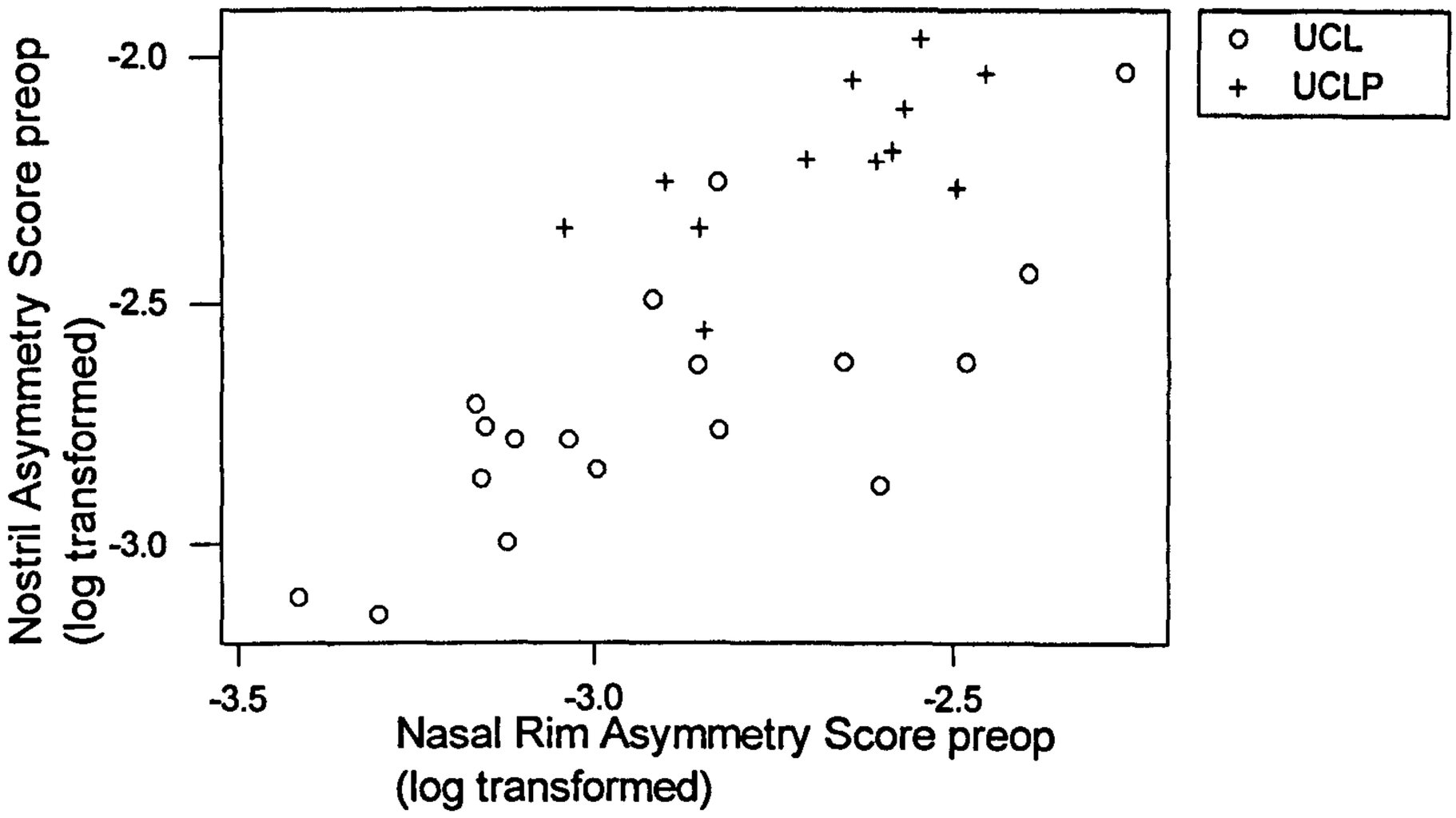


Figure 4.56 Correlation between nasal rim asymmetry and nostril asymmetry, prior to surgery (preop)

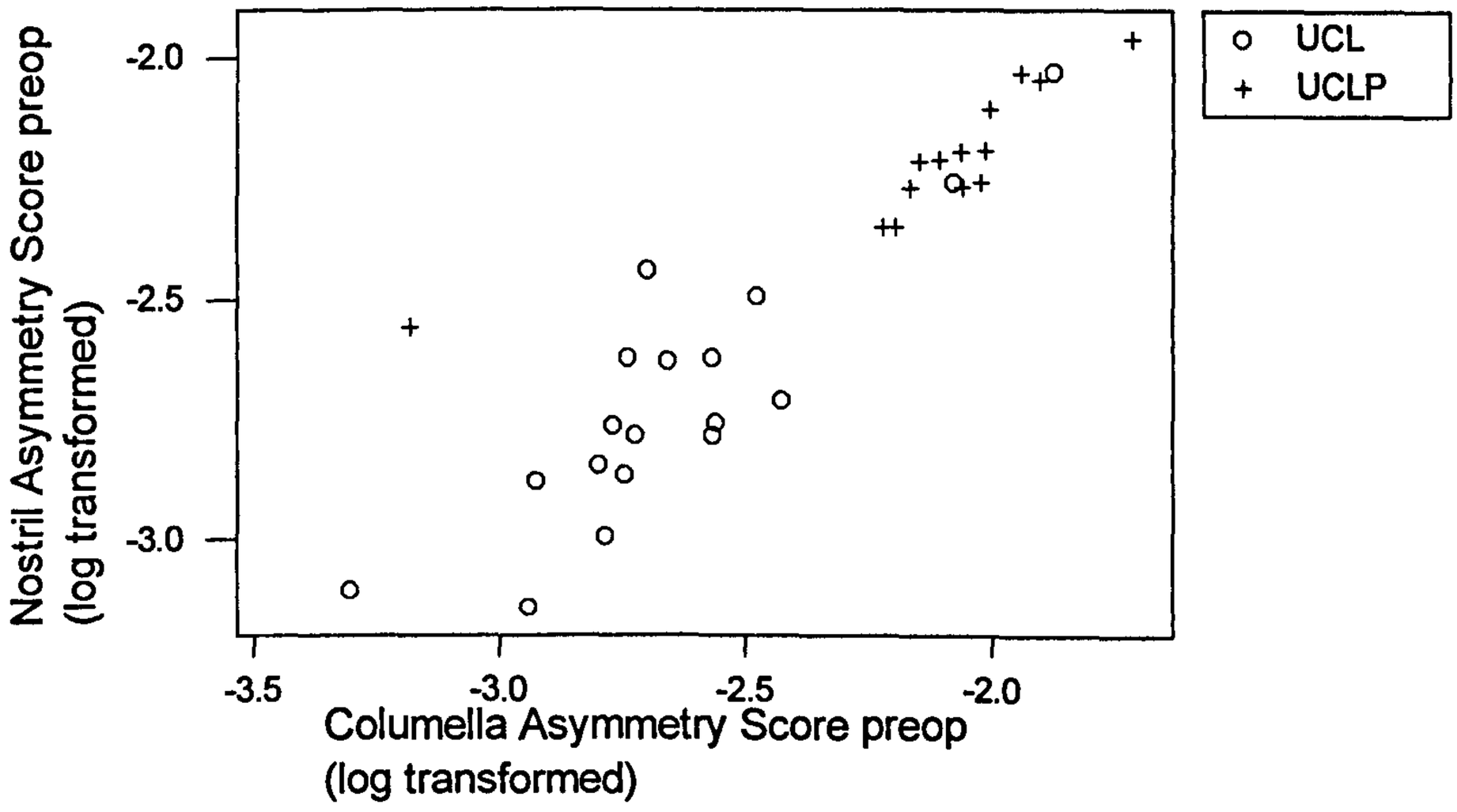


Figure 4.57 Correlation between columella asymmetry and nostril asymmetry, prior to surgery (preop)

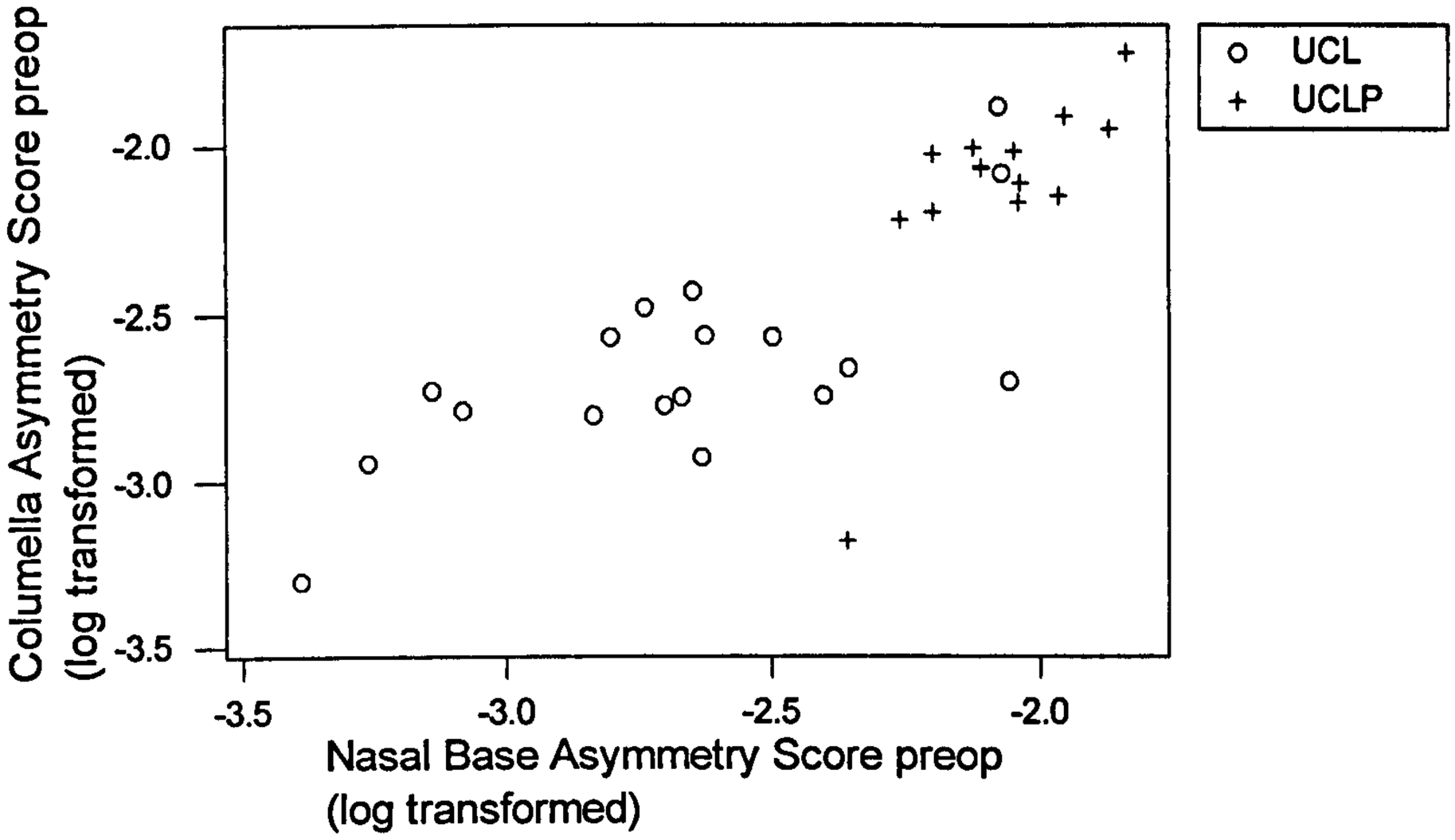


Figure 4.58 Correlation between nasal base asymmetry and columella asymmetry prior to surgery (preop)

4.9.2.6 Summary of Relationships between 3D Nasal Asymmetry Severity measures

Nasal base asymmetry was strongly associated with nostril asymmetry, nasal rim and columella asymmetry.

Nostril asymmetry was strongly associated with nasal base asymmetry, nasal rim and columella asymmetry.

Nasal base, nasal rim, and nostril asymmetry scores would be used as 3D indicators of cleft severity in the assessment of the correlation with outcome at age 2 years.

4.9.3 Correlation between measures of cleft extent (ratios) and 3D asymmetry scores, prior to lip/nose surgery

4.9.3.1 Nasal region

4.9.3.1.1 Relationship between size of cleft in the nostril floor and nasal base asymmetry, prior to primary surgery

A strong correlation was demonstrated between the extent of the cleft in the nostril floor and the degree of nasal base asymmetry (Fig 4.59). Pearson correlation coefficient = 0.7 (P-Value = 0.000). Just under half (49%) of the variability in nasal base asymmetry could be explained by its relationship with nostril floor ratio. As the size of the cleft in the nostril floor increased, so did nasal base asymmetry.

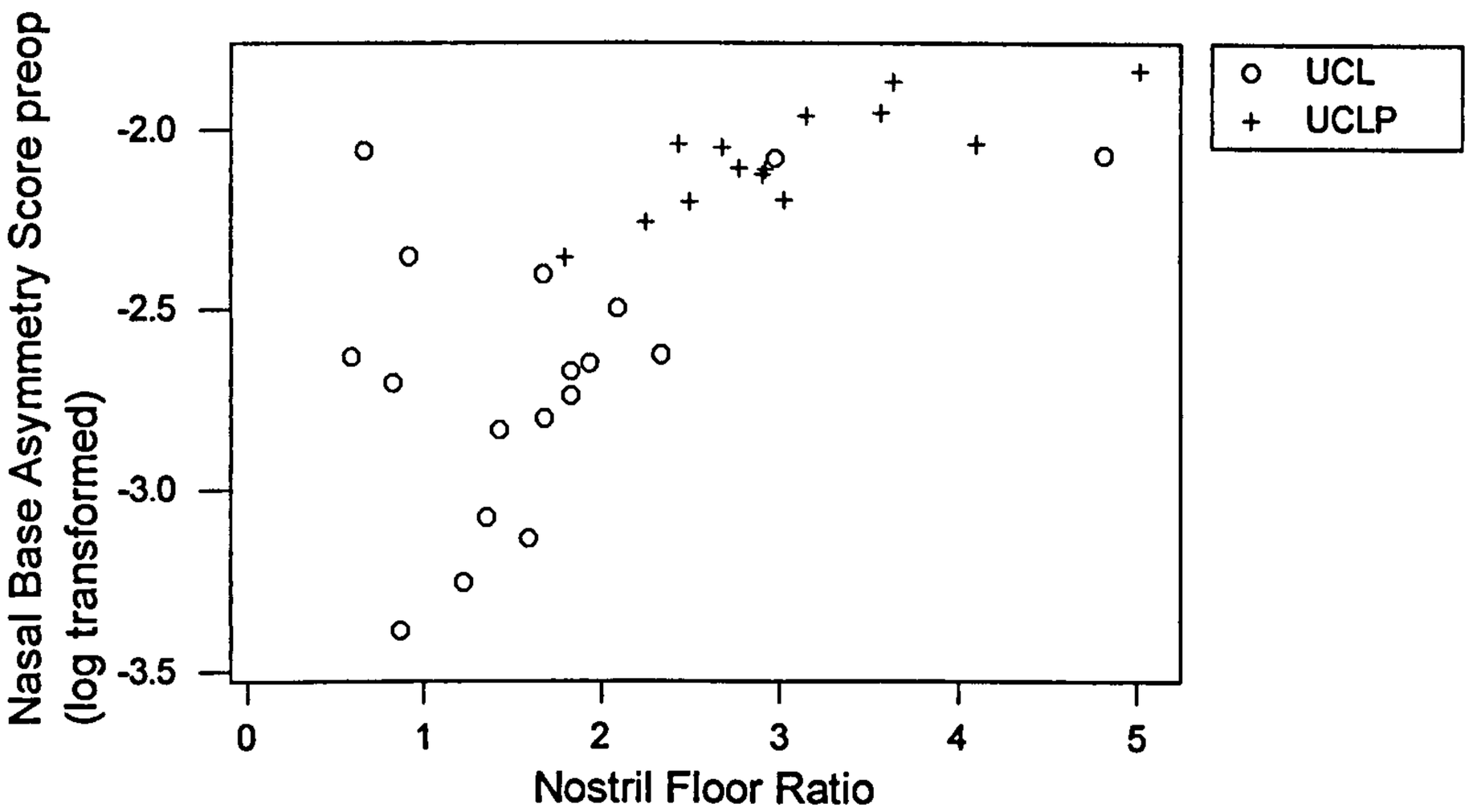


Figure 4.59 Strong correlation between nostril floor ratio and nasal base asymmetry, prior to surgery

4.9.3.1.2 Relationship between size of cleft in the nostril floor and nostril shape asymmetry, prior to primary surgery

A strong linear relationship was demonstrated between the size of the cleft in the nostril floor and nostril shape asymmetry (Fig 4.60, overleaf). Pearson correlation coefficient = 0.79 (P-Value = 0.000). 62.4% of the variability in nostril asymmetry was explained by its relationship with the size of the cleft in the nostril floor.

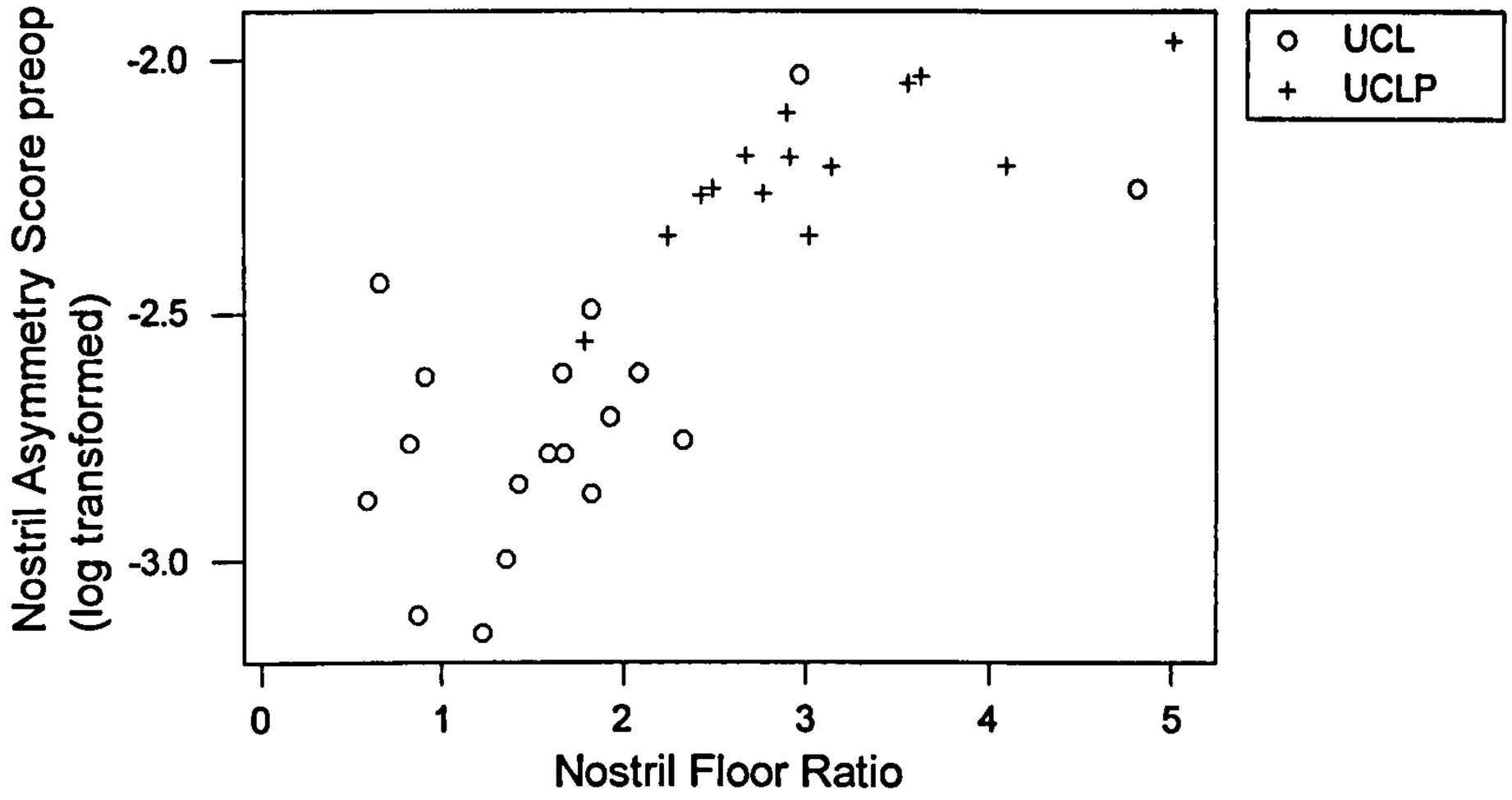


Figure 4.60 Strong correlation between nostril floor ratio and nostril asymmetry, prior to surgery

4.9.3.1.3 Relationship between size of cleft in the nostril floor on nasal rim asymmetry, prior to primary surgery

A weak correlation was demonstrated between the size of the cleft in the nostril floor and nasal rim asymmetry prior to surgery (Fig 4.61). Pearson correlation coefficient = 0.384 (P-Value = 0.03). Only 14.7% of the variability in nasal rim asymmetry could be explained by its relationship with the extent of the cleft in the nostril floor

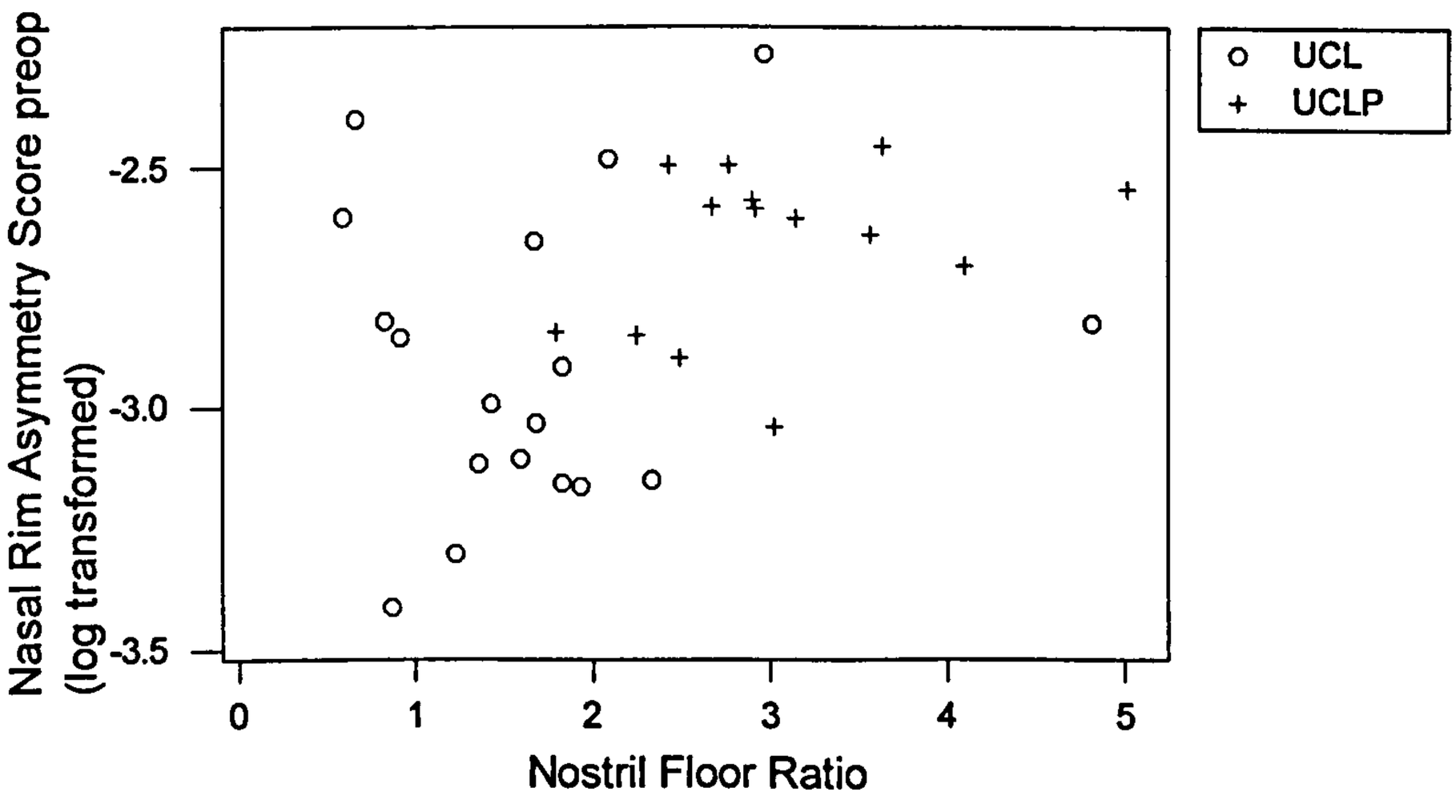


Figure 4.61 Correlation between nostril floor ratio and nasal rim asymmetry, prior to surger

4.9.3.2 Lip region

4.9.3.2.1 Relationship between philtrum height discrepancy and philtrum asymmetry prior to primary surgery.

There was no correlation between the philtrum height ratio and philtrum asymmetry pre-operatively (Fig 4.62). Pearson correlation coefficient = 0.325 (P-Value = 0.07).

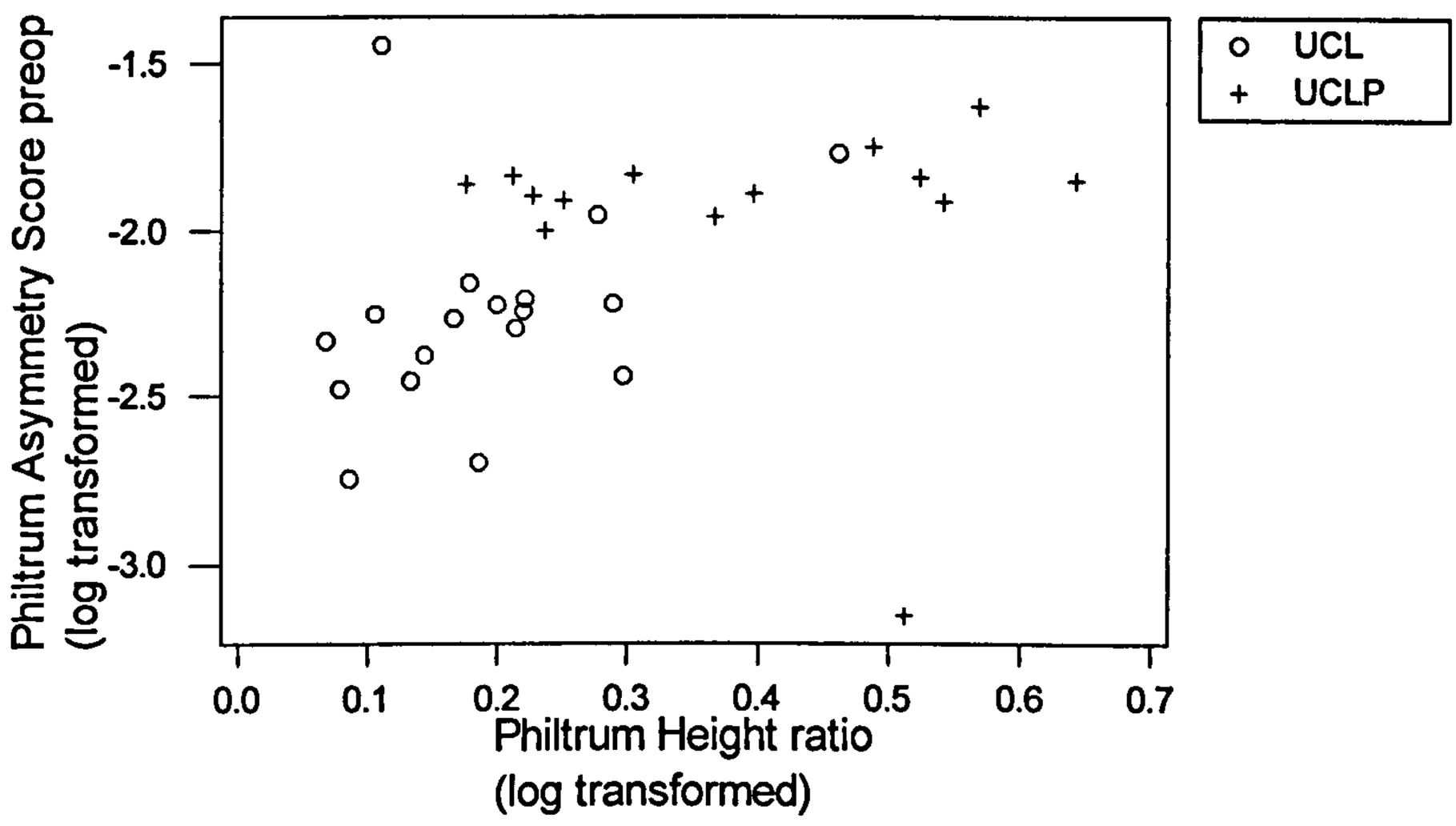


Figure 4.62 Correlation between philtrum height ratio and philtrum asymmetry, prior to surgery (preop)

4.9.3.2.2 Relationship between Cupid's Bow ratio and philtrum asymmetry prior to primary surgery.

There was a strong correlation between Cupid's Bow ratio and philtrum asymmetry, prior to surgery (Fig 4.63). Pearson correlation coefficient = 0.825 (P-Value = 0.000). Just over two thirds (68.1%) of the variability in philtrum asymmetry could be explained by its relationship with the size of the cleft in the lip before surgery.

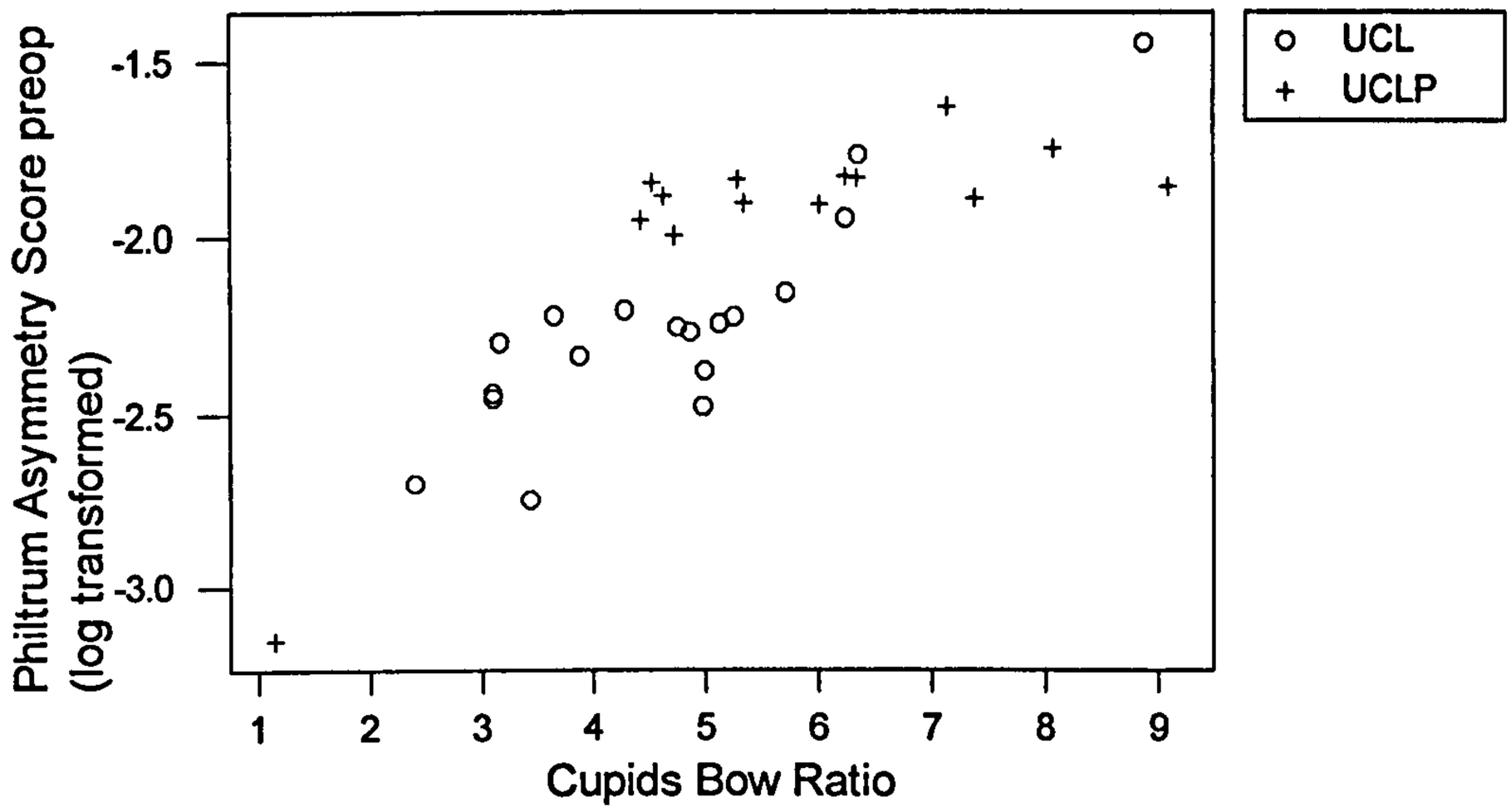


Figure 4.63 Correlation between Cupid's Bow ratio and philtrum asymmetry, prior to surgery (preop)

4.9.3.3 Summary of Correlation between measures of cleft extent (ratios) and 3D asymmetry scores

Nose
Nostril floor cleft extent was strongly associated with nasal base asymmetry and with nostril asymmetry, before surgery

Nostril floor cleft extent was weakly associated with nasal rim asymmetry, before surgery

Lip
Philtrum height discrepancy was not associated with philtrum asymmetry. Cupid's Bow ratio was strongly associated with philtrum asymmetry before surgery.

4.10 Relationship between initial cleft severity and shape outcome at age 2 years

In order to assess if there was association between initial cleft severity and residual deformity in the nose and lip, at age 2years, 19 cleft individuals (UCL=8; UCLP=11) for whom data were collected prior to primary lip/nose repair and at age 2 years, were examined. Pearson's correlation coefficients were calculated for the combined cleft sample in order to assess the strength and significance of any association between an individual's initial cleft severity and their soft tissue outcomes at age 2 years ($p>0.05$).

Table 4.60 shows the measures used to represent initial cleft severity in the nose and lip. Table 4.61 shows the measures used to represent residual shape deformity in the nose and lip.

Table 4.60 Initial Cleft Severity Measures

Severity Ratios	**Asymmetry Scores pre-op**
Cupid's Bow ratio	Nasal base asymmetry score
Philtrum height ratio	Nostril asymmetry score
	Nasal Rim asymmetry score
	Philtrum asymmetry score

Table 4.61 Measures of residual shape deformity at 2 years

Asymmetry Scores	**Procrustes 'distance from normal' (PDFN) Scores at age 2 years**
Nasal base asymmetry score	Nasal Complex shape
Nostril asymmetry score	Nostril shape
Nasal rim asymmetry score	Nasal rim shape
Philtrum asymmetry score	Philtrum shape
	Upper Lip shape

4.10.1 Nasal region

4.10.1.1 Relationship between severity of asymmetry prior to surgery and residual asymmetry at age 2 years

No correlation was demonstrated between the degree of asymmetry prior to surgery and residual asymmetry at age 2 years in either the nasal base, nasal rim or nostril. Figure 4.64 (overleaf) illustrates the absence of a linear relationship in the degree of nasal base asymmetry before surgical correction and at age 2 years.

4.10.1.2 Relationship between severity of asymmetry prior to surgery and residual shape deformity at age 2 years

No correlation was found between the degree of asymmetry prior to surgery in either the nasal base, nasal rim or nostril and residual shape deformity (PDFN score) in the nasal complex, nasal rim or nostril at age 2 years. Figure 4.65 (overleaf) illustrates the absence of a linear relationship in the nasal rim variables.

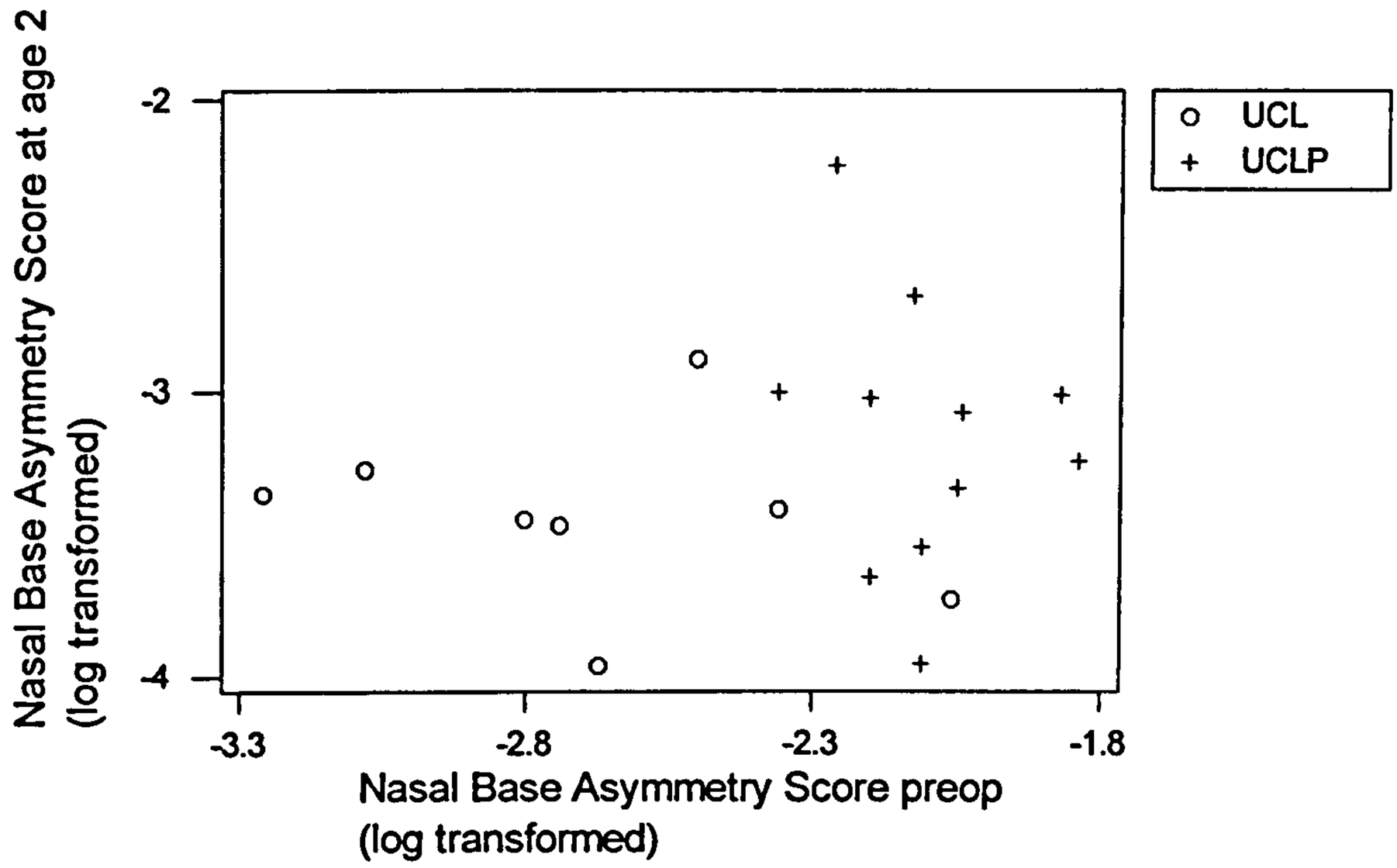


Figure 4.64 No correlation between nasal base asymmetry prior to surgery (preop) and nasal base asymmetry at age 2 years

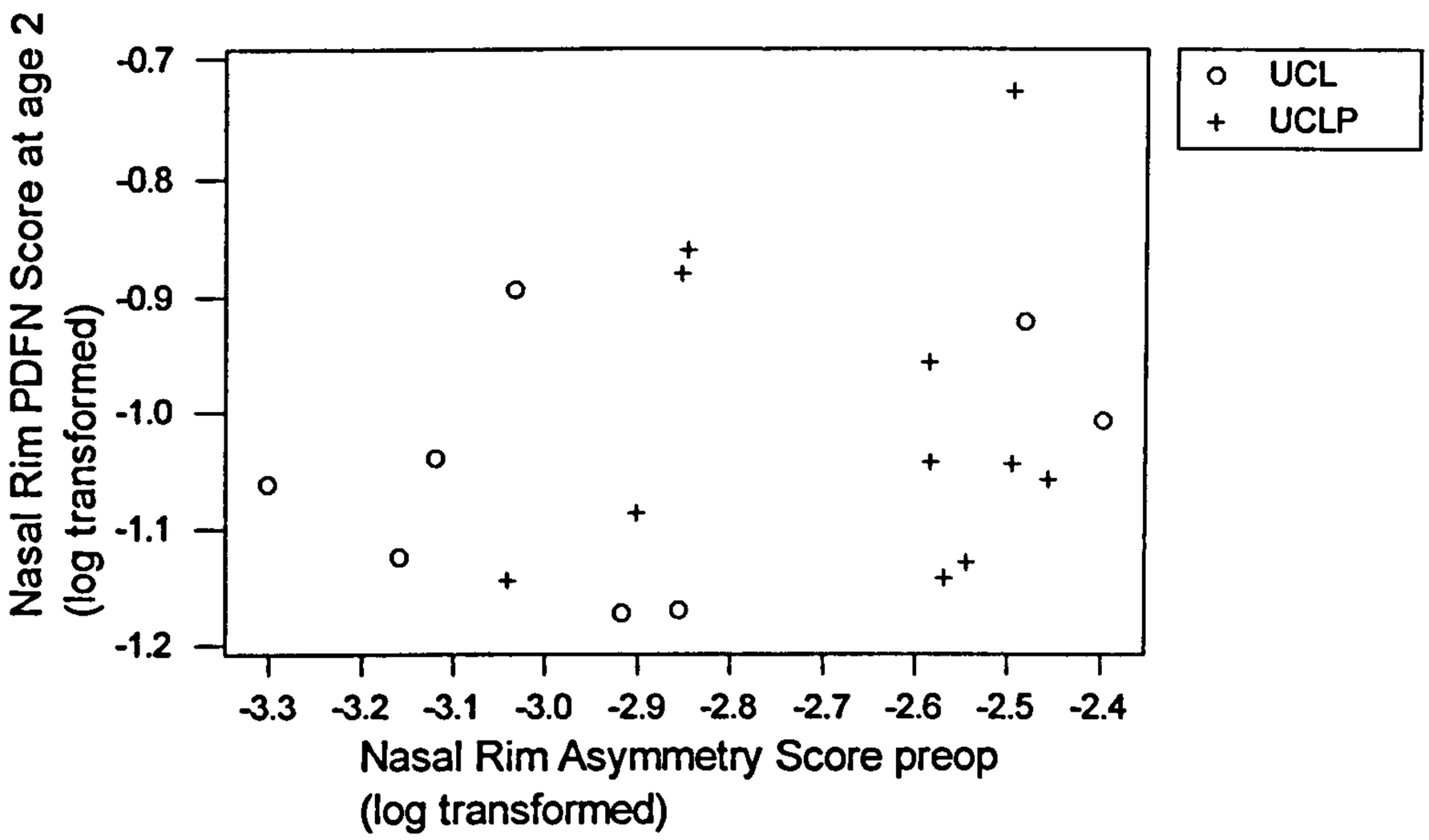


Figure 4.65 No correlation between nasal rim asymmetry prior to surgery (pre-op) and nasal rim Procrustes 'distance from normal' (PDFN) at age 2 years

4.10.2 Lip region

4.10.2.1 Relationship between severity of philtrum asymmetry prior to surgery and residual philtrum asymmetry at age 2 years

No correlation was demonstrated between philtrum asymmetry and residual philtrum asymmetry at 2 years (Fig 4.66 overleaf). Pearson correlation coefficient = 0.221 (P-Value = 0.364). The degree of severity of philtrum asymmetry prior to surgery was not significantly associated with residual philtrum asymmetry at 2 years.

4.10.2.2 Relationship between severity of philtrum height discrepancy prior to surgery and residual philtrum shape deformity at age 2 years

A moderate correlation was demonstrated between the ratio of philtrum height discrepancy prior to surgery and residual philtrum deformity (PDFN score) at 2 years of age (Fig 4.67 overleaf). Pearson correlation coefficient = 0.548 (P-Value = 0.015). Almost one third (30%) of the variability in residual deformity of philtrum shape could be explained by its relationship with philtrum height discrepancy pre-op.

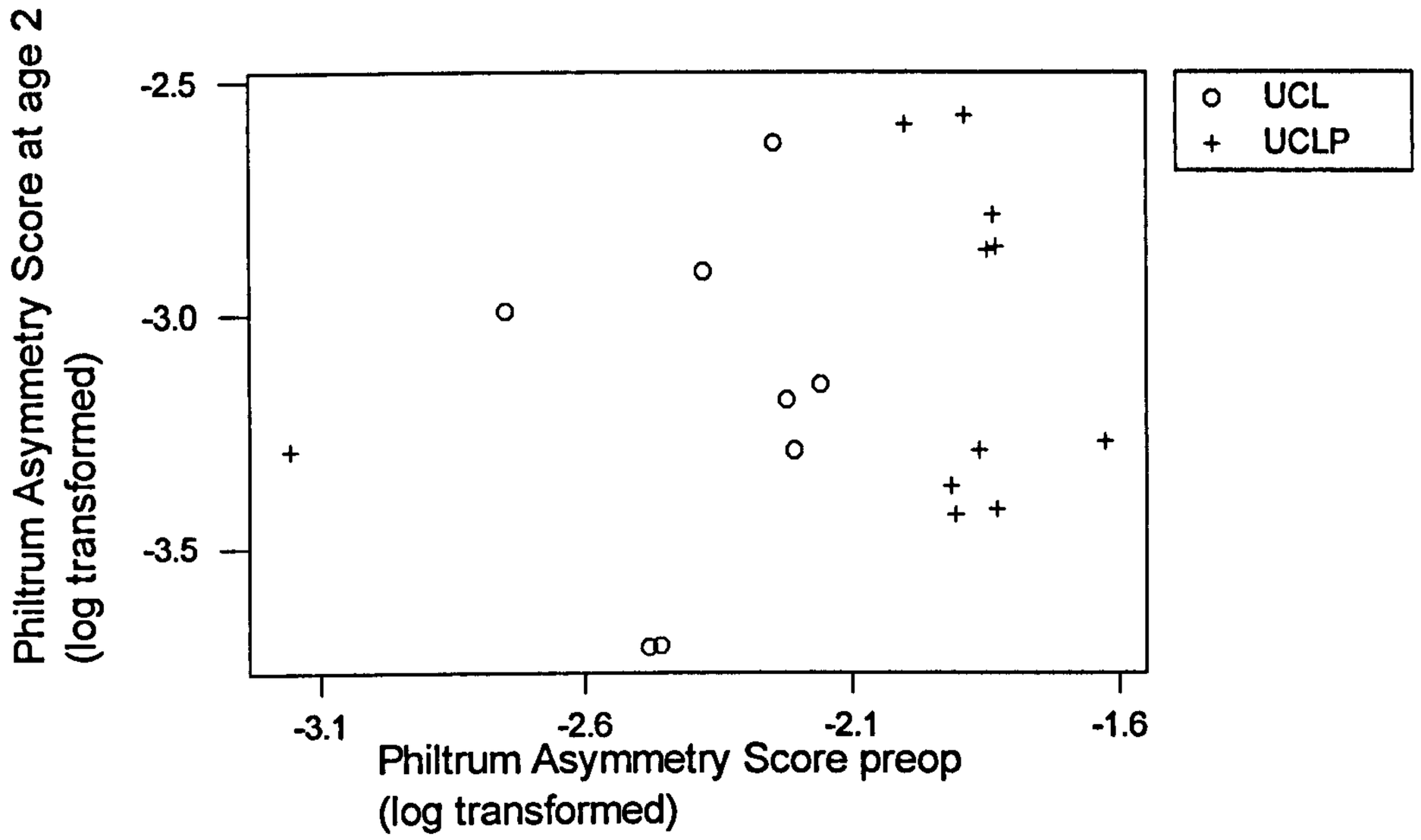


Figure 4.66 No correlation between philtrum asymmetry prior to surgery (pre-op) and at age 2 years

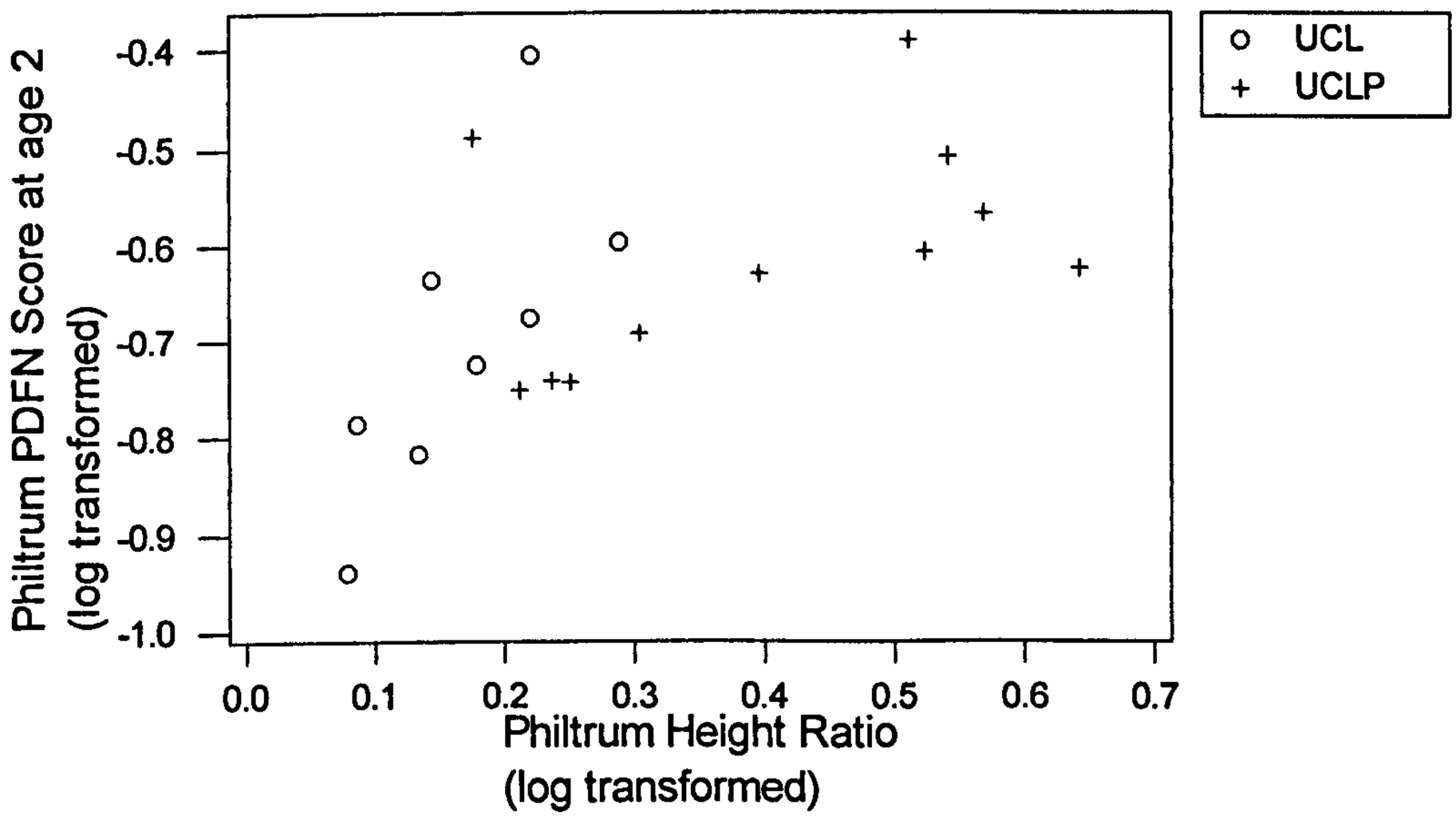


Figure 4.67 Correlation between Philtrum Height ratio prior to surgery (preop) and residual Philtrum deformity (PDFN Score) at age 2 years

4.10.2.3 Relationship between severity of philtrum height discrepancy pre-op and overall residual lip deformity at age 2 years

There was a strong correlation between philtrum ratio pre-operatively and overall lip deformity at 2 years, as determined by Procrustes 'distance from normal' (Fig 4.68). Pearson correlation coefficient = 0.654 (P-Value = 0.004). More than two fifths (42.7%) of the variability in overall lip deformity at 2 years could be explained by differences in pre-op philtrum height ratio.

4.10.2.4 Relationship between Cupid's Bow ratio prior to surgery and residual shape deformity at age 2 years

There were no correlations between Cupid's Bow ratio prior to surgery and philtrum or upper lip shape outcomes after surgery, represented by residual asymmetry at age 2 years, and the degree of residual shape abnormality represented by Procrustes 'distance from normal' scores (PDFN Score). Figure 4.69 (overleaf) illustrates the absence of a linear association between Cupid's Bow ratio prior to surgery and residual philtrum deformity at age 2 years.

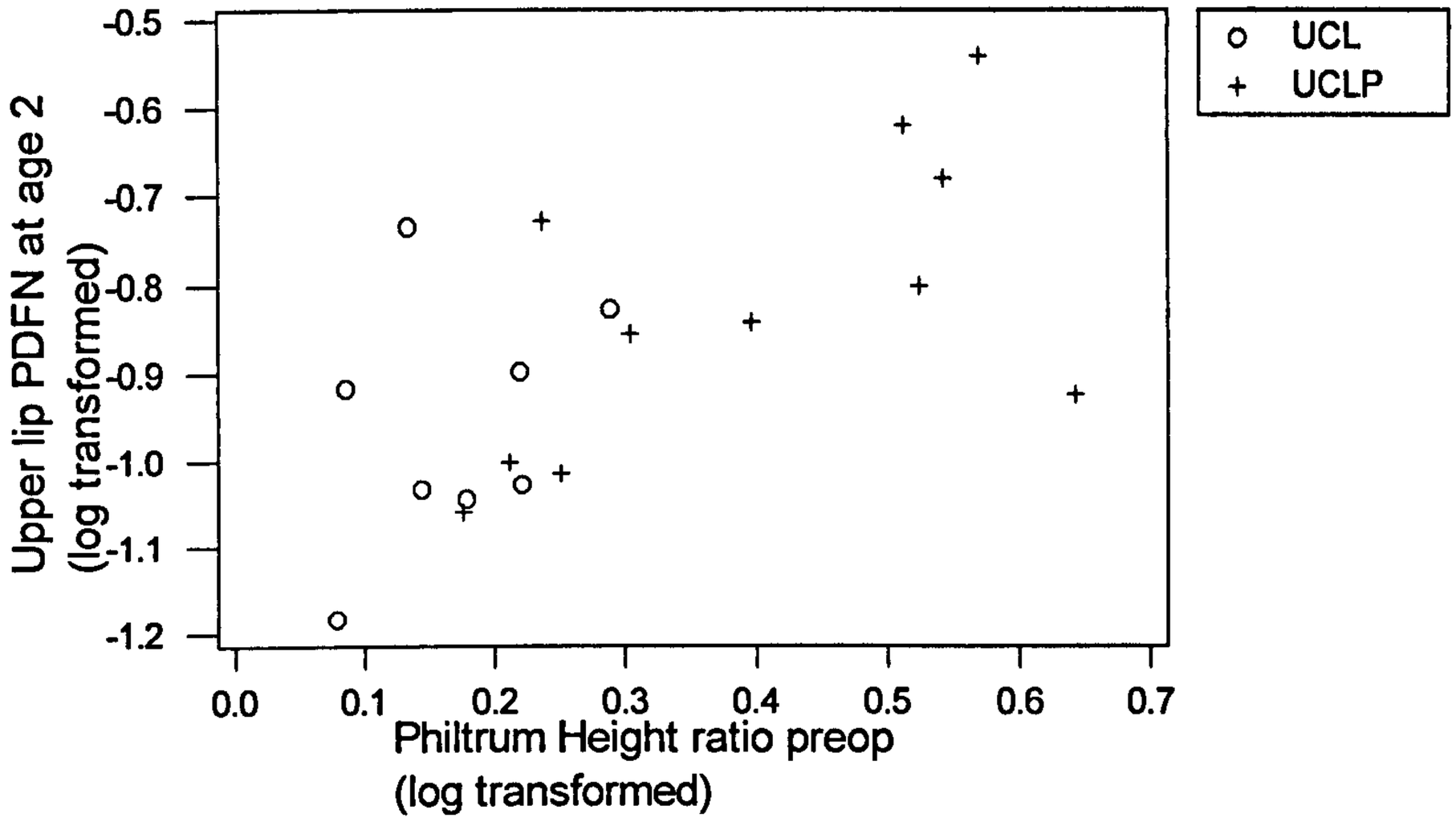


Figure 4.68 Strong correlation between philtrum height ratio prior to surgery (preop) and upper lip deformity (PDFN Score) at age 2 years

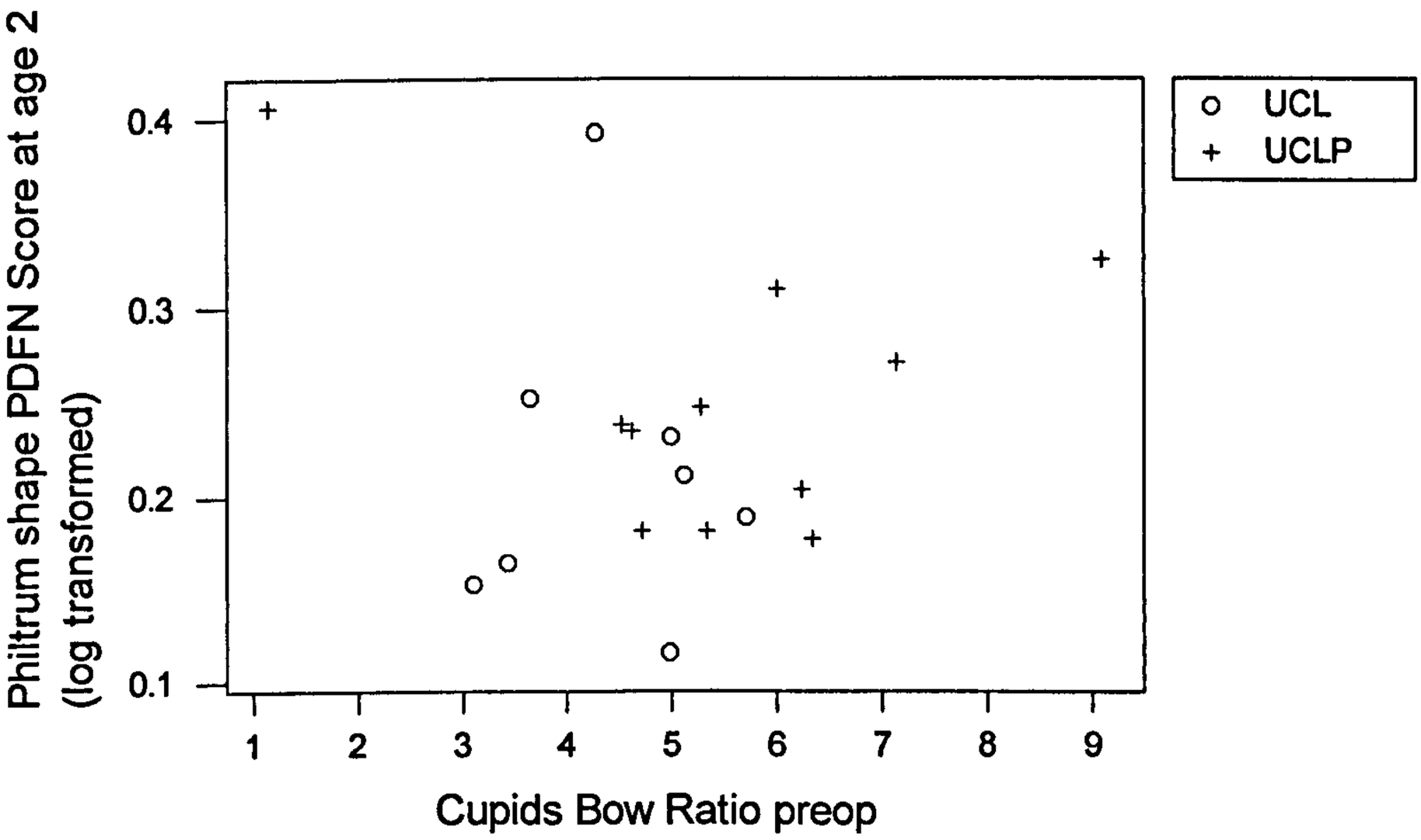


Figure 4.69 No correlation between Cupid's Bow width and residual philtrum deformity (PDFN Score) at age 2 years

4.10.3 Summary of relationship between initial cleft severity and outcome at age 2 years

Nasal region
There were no correlations between the degree of initial asymmetry and residual asymmetry at age 2 years in either the nasal base, nasal rim or nostrils.

Lip Region
No correlation was demonstrated between philtrum asymmetry prior to surgical correction and residual philtrum asymmetry at age 2 years.

There was a moderate to strong association between the degree of initial vertical discrepancy in the philtrum (philtrum height ratio) and residual philtrum and lip shape abnormality at 2 years of age.

No linear association was demonstrated between the initial size of the cleft in the lip (Cupid's Bow ratio) and residual deformity in philtrum or lip shape.

5 Discussion

5.1 Study Design

The data collected and analysis contained in this thesis formed part of a larger 3-dimensional investigation of facial morphology and growth in infants with UCL and UCLP and non-cleft infants, in the first 2 years of life. The study was designed as a prospective, longitudinal cohort study in which data collection for UCL and UCLP infants would be complete within 3 years. This evolved into a cross-sectional and mixed longitudinal design following a disappointing response to recruitment and a drop in the cleft birth rate during the period of the study.

A researcher collected data for non-cleft infants in a simultaneous PhD study (White, 2005). Some of this data was used to generate size-independent Asymmetry Score average 'norms' to facilitate comparison of cleft groups with a non-cleft baseline. In addition, data for 2-year-old non-cleft children facilitated investigation of cleft outcome by way of Procrustes 'distance from normal' scores.

5.2 Research Tool

5.2.1 C3D^{TM} Imaging system

The C3D^{TM} system has many advantages over other 3D data acquisition systems. High-resolution digital cameras and the speed with which images are obtained made it an obvious choice for application to the study of facial morphology in children.

5.2.1.1 Feasibility of Imaging small children with the C3D^{TM} System

The first aim of the study was to test the C3D^{TM} system and develop techniques for successful 3D-imaging of infants and toddlers. Whatever method is adopted, the capture of a facial image of a 3-month-old infant is a challenge. The age range of the infants in this study meant that they were capable of only limited co-operation for imaging procedures. Children were alert, unrestrained and did not require sedation. Nonetheless, this had obvious implications for standardisation of the capture procedure. The prototype C3D^{TM} system used in this investigation comprised of several components manufactured specifically for the project. This had advantages in that the system could be modified to meet the requirements for a pre-cooperative study population. The clinical development

studies demonstrated that the capture field area was relatively small and the addition of LED spot-lights to the camera pods was essential to aid optimal positioning of the infant for imaging.

Subject head movement and intrinsic facial movement were identified as potentially problematic early in the development studies. Despite advances, laser scanning systems and the liquid-crystal range finder systems are not capable of sub-second capture times or require more than one image recording from different angles (Yamada et al. 1998; Duffy et al. 2000; Kau et al. 2004). However, even in the short time interval between activation of the C3D ™ monochrome and colour cameras, intrinsic facial movement was detected. Minor muscular responses in the eyelid, lip and chin areas of laser-scanned subjects were noted by Kau et al. (2004) who tested a contemporary laser scanning system in 11 year old children (Minolta Vivid 900™ series). The authors concluded that a total scan time of 7.5 seconds and errors of 1.2mm in alignment of scans was clinically acceptable for the application in adults and children. Whilst this may be true in compliant older subjects, laser-scanning technology is not sufficiently robust to assess the intricate changes associated with cleft surgery in infants. It is also limited by a lack of ability to modify capture time to accommodate younger subjects. The potential for facial movement during image capture by the C3D™ system was minimised by reduction of the interval between monochrome and colour image capture from 200ms to 30ms, resulting in a total capture time of 50ms. To date, the C3D™ system out-performs all others in facilitating the most rapid acquisition of 3-Dimensional facial data.

C3D™ models form a permanent record of a child's facial morphology at a particular point in time and facial measurements and landmarks can be generated at any desired instance in the future. This has obvious advantages over conventional direct anthropometry in children, as subjects cannot be recalled months/years later to correct initial measurements, or perform new ones. In this respect, C3D™ affords the same benefits as computer-assisted analysis of static photographs favoured by others (Hurwitz et al. 1999; Russell et al. 2000; 2001), but the added advantage is that the models are a 3-Dimensional rather than a 2-Dimensional record and so depth perception is possible. Moreover, analysis methods have been developed to assess surface curvatures and whole-face surface topology and there is much scope for analysing the information contained in the 3D properties of the data further.

The disadvantages of using a prototype system included early hardware and software failures as the system evolved. Two data sets (one pre-op and one 2 year old) were un-usable because of early stability problems with camera shutters and focus. These models of were of insufficient quality for inclusion in the study. Hardware and software failure also influenced the timing of data collection, and forced re-scheduling of subjects. These problems were encountered early enough in the project that they were resolved. Three generations of C3D™ model software and seven of the Facial Analysis Tool™ evolved over the course of the study, but the final landmark data sets were extracted using the most up-to-date Facial Analysis Tool software.

5.2.1.2 Consistency of facial expression and lip pose

Throughout this study, maintaining the uniformity of facial expression was essential. The author noted that a resting expression with an open mouth was a remarkably consistent feature in the cleft group and multiple, similar open-mouth expressions were possible at each capture session. A plausible physiological explanation for the open mouth expression at rest is established oro-nasal breathing habits in cleft individuals. Reduced nasal airway patency and increased airways resistance usually results in obligatory oral breathing (Warren, Hairfield, Dalston et al. 1988). Open communication between nasal and oral cavities prevents the establishment of normal infant nasal breathing patterns and oro-nasal breathing has been shown to persist after cleft repair and into adulthood (Hairfield, Warren & Seaton 1988; Warren & Hairfield 1990). Surgical repair can further compromise nasal airways resistance in children (Hairfield, Warren & Seaton 1988). It could be argued that the presence of a cleft may reduce nasal airways resistance prior to repair and that a difference in mode of breathing may exist pre and post operatively. However, in the absence of evidence, the reasons why the open-mouth expression was prevalent in the cleft sample remains the subject of speculation.

In studies of facial morphology in children, the question of consistent facial expression is largely ignored. A study of laser-scanned cleft children aged 8-11 years did not attempt to standardise facial expression and mixed open mouth with closed mouth data (Duffy et al. 1999). In a study comparing Japanese cleft infant aged 3months to 4 years with controls, consistency of facial expression was not discussed and there were no illustrations to enlighten us (Yamada et al. 2002). Although there are no published reports of stability of resting expression in children, the C3D™ system was used to capture the faces of 3-year-old cleft and non-cleft children (Garrahy 2002). This study showed that intra-session, subjectively similar, resting facial expression was reproducible in young children. Most

recently a co-worker examined the stability of the lips together and lip-apart resting pose in infants aged 3 months to 2 years (White 2005). Although both resting facial expressions were found to be repeatable, results suggested that the lip-apart pose was more repeatable in 3 month olds. This confirmed the subjective impression of the author in this study, although reproducibility of the open-mouth resting expression in cleft infants was not tested. When measured with the lips apart and lips together, some facial dimensions were significantly different, most notably total face height (White 2004).

In respect to the question of how similar the lip pose of a child is likely to be over time, White (2005) showed that whilst the lip-apart resting pose was 'fairly repeatable' at 6 months, 1 year and at 2 years of age, it was not always consistent for each individual over time. A fundamental problem in comparing facial morphology over time is that as a child grows, so their ability to control their facial muscles develops. Moreover, inconsistencies in lip position at different capture times may affect the position of some facial landmarks, below the upper lip (Bock & Bowman 2005). This has implications for a small number of facial dimensions such as total face height. However the variation in lip pose over time was assumed to be a possible source of random error as it could have affected individuals in the study equally, at any capture time. In the shape studies, landmarks below the upper lip were omitted to minimise any potential effect of variation in lip pose. Caveats must be applied in every study of facial morphology of young children. Clinical judgement is required when comparing the facial soft tissues of growing children at different time points. In this study, all reasonable attempts were made to standardise data recording. Multiple captures were obtained for each infant at each session, and from these, C3D™ models were built and selected with similar lip-apart resting pose for all children, at all time points.

5.3 Validation studies

5.3.1 Accuracy

System error, operator error, and registration error of the study research tool were shown to be within acceptable limits for the study of facial morphology in infants and comparable with other 3D-imaging systems. Laser-scanning systems have been described with a system accuracy of 0.9mm and 0.5mm for individual points (Moss et al. 1989). Contemporary systems incorporating CCDs and laser technology such as the Minolta Vivid700™ have been shown to have an accuracy of 1.9mm± 0.8mm, when imaging a

facial cast (Kusnoto & evans 2002). A total system error of 0.5mm was reported for the liquid-crystal range finder (Yamada et al 1998). When imaging a planar surface, system accuracy of an early prototype C3D™ system was reported as 0.2mm. (Ayoub et al. 1998). This system differed from the current one in that it comprised only black and white cameras. The current C3D™ system error was 0.83mm, when C3D™ landmark co-ordinates of imaged facial casts were compared with actual landmark co-ordinates obtained via a co-ordinate measuring machine of high accuracy (CMM) (Ayoub et al. 2003). This highlights that stated system error values can be affected by choice of validation method.

Validation of new systems against a 'gold standard' of direct measurement of inanimate objects such as facial casts or precision models of known dimensions, or live subjects is common in the literature. However, the errors associated with obtaining 'gold standard' direct measurements must also be considered. The magnitude of the measurement and the ease of landmark identification can substantially affect the reliability of the measurements obtained (Ward & Jamieson, 1991). In validation studies of a laser scanning system, it was found that accuracy was better in capturing inanimate objects, rather than live subjects (Foong et al. 1999). Moreover, when compared to direct caliper measurements of the adult face, one study found that only a third of measurements from facial laser scans were within 1.5mm of caliper values (Aung et al. 1995). Shaner et al. (1998) compared calliper-derived facial measurements with those obtained from digitised landmarks on 3D photogrammetric models and found systematic differences in means and standard deviations. Stromland et al. (1998) found a systematic 3.2% (1mm) over-estimation in measurements obtained using a range scanner, compared with direct anthropometric measurements on adults. In the present study, the superior method of validation devised avoided these difficulties.

5.3.2 Landmark Identification

It has been shown that less than half of the common facial anthropometric direct measurements can be considered precise and reliable (Ward & Jamieson 1991). The highly accurate indirect anthropometry afforded by the C3D™ system made it particularly applicable in the study of young cleft children, where facial dimensions were small and measurement was not possible in the conscious subject. Moreover, manual identification of anatomic landmarks on the infant cleft C3D™ models was consistent across the whole face and compared favourably with systems that employ automatic landmark extraction means (Yamada et al. 1998). However, the ability to identify landmarks was occasionally limited by the optical quality of the 3D model and this affected a small number of landmarks

around the ears (Obs and Obi), and lower-most extent of the chin (gn). Where location of these landmarks was ambiguous, they were not marked on the models. The gnathion landmark could not be located with sufficient accuracy in the feasibility studies and was omitted from the main studies. Despite reasonable, reproducibility in the feasibility study, the ear landmarks were often indistinct due to poorer lighting of the periphery of the face or obscured by hair in the older children. Consequently, measurements involving the ear landmarks were omitted and therefore an analysis of face depth was not possible. Total face height was re-defined as the distance from nasion to pogonion (n-pg), instead of the anthropometric definition of nasion to gnathion (n-gn) (Farkas 1994; Duffy et al. 2000). This would have to be borne in mind when comparing face height measurements in this study with those of others. Interestingly, Yamada et al. (2002) did not include the gnathion landmark in their analysis of Japanese infants, possibly for similar reasons.

5.4 Analysis of facial size and shape

This study is the first to evaluate 3D facial morphology in cleft infants in terms of both size *and* shape. The goal of identifying how the facial dimensions were altered by primary lip/nose surgery and growth was achieved. In addition, the effect of these changes on the shape of the facial features was demonstrated. Nevertheless, measurement of over 40 facial dimensions and angles were necessary to characterise UCL and UCLP infant faces by indirect anthropometry. Knowledge of facial dimensions is clinically useful, but by definition, the 'shape' of a face cannot be derived from size-based measurements, since this takes no account of their relationships to each other. By adopting a geometric morphometric approach, (asymmetry score and Procrustes 'distance from normal') information about the change in shape of the facial features with surgery and growth was preserved and interpretation, as changes in the property of asymmetry, was simplified.

5.4.1 Statistical Assessment

The design of statistical approach measured changes within individuals as well as cleft group differences. This ensured that individual variability in initial condition or their response to surgery did not mask any small differences that existed between time points and between the two cleft groups. Significant findings in this study were interpreted in the descriptive sense, such that the broad pattern, over many variables gave a meaningful picture of where and how facial change occurred. Some of the variables were not necessarily independent and one might expect correlation between certain measurements in

the same facial region. This covariance might have implications for statistical analysis. In addition, future multivariate analysis would require exclusion of highly correlated variables to avoid unnecessary duplication. However, the study by White (2005) showed that correlation between facial dimensions in non-cleft children varied with age, and some dimensions were more independent than anticipated e.g. intercanthal width and palpebral fissure widths.

It has been suggested that where more than one statistical test is applied in a study, a correction for multiple-testing should be carried out (Bonferroni correction) (Bland & Altman 1995). Bonferroni corrections have been criticised as being inappropriate for clinical studies, as they pre-suppose one general null hypothesis e.g. 'there are no differences in the facial dimensions between UCL and UCLP'. If one difference were found, this would lead us to reject the null hypothesis. The problem lies in that whilst this approach protects against the chance of incorrectly producing a significant difference (Type I error), the chance of incorrectly accepting the null hypothesis when in fact the converse is true is inflated (Perneger 1998). An alternative approach was adopted in that each constituent study within the larger context of this thesis was considered on its own merits. In the studies of differences in somatic and facial dimensions between cleft groups and differences over time, a more rigorous statistical significance level of $p < 0.01$ was adopted to preserve statistical integrity, which was consistent with the approach adopted by Hermann et al. (1999b, 2000) in their cephalometric analysis of facial morphology in cleft infants aged 2-22months. Nevertheless the potential for inflated Type I error remains and is a limitation of the study. In the Asymmetry and Cleft Severity studies, a significance level of $p<0.05$ was adopted. The special feature of the asymmetry score is that it combines information across many different landmarks, thus reducing the 'multiple testing' problem by amalgamating the data before tests are applied. In effect, a facial feature is reduced to an independant variable, which quantifies asymmetry of its shape defined by multiple landmarks. This concept is analogous to the use of principal components analysis to define new independent measures of shape variation. Conclusions drawn about morphology or growth based on a set of such variables would not be expected to be influenced by inflated type I error (Hermann et al. 2001); however, the small sample size in the present study should be borne in mind.

5.4.2 Measurement of Asymmetry

The Asymmetry Score method developed for this study was independent of anatomically defined planes as it used the whole configuration to work out the best axis for reflection.

This overcame the main disadvantages of using symmetry planes based on bilateral landmarks for reflection, particularly when those baseline landmarks themselves may be asymmetric. Ras et al. (1995) showed clearly that evaluations of asymmetry based on such methods would be influenced by choice of reference landmarks and symmetry plane, as well as by data acquisition method. Unilateral cleft infants in this study were shown to have significant upper face asymmetry, and so the use of upper face landmarks to define a plane or axis for reflection for the assessment of asymmetry was inappropriate. This may also have implications for automatic landmark extraction methods favoured by Yamada et al. (2002a-c), which uses intercanthal landmarks (en) and pogonion (pg) landmark to define a reference plane and axes. This may result in a systematic error in landmark location in young cleft infants.

The application of Procrustes alignment techniques dealt with differences in subject size, by scaling configurations to a common 'unit' size (Bock & Bowman, 2005). This was a slight disadvantage in that the generated 'Asymmetry Score', was not expressed in a conventional metric value. However, this was out-weighed by the fact that statistical comparisons of shape changes over time were possible, which were independent of size changes with facial growth.

One of the most important aspects of this study was the ability to identify the source of asymmetry at feature level. Using the methods developed it was possible to quantify the contribution of each facial area to global facial asymmetry. This methodology could be applied to any combination of facial features, provided they can be defined without sharing landmarks. This was also a limitation, however as this method could not be used to explore the contribution of nostril shape asymmetry or philtrum asymmetry to global facial asymmetry, as both features had common landmarks with the nasal base complex (nasal base & columella) and the upper lip. Therefore, it was not possible to separate the effect of these features on each other. A separate analysis of the nasolabial area was undertaken. This was defined and decomposed into its component parts namely, nasal rim, nasal base and philtrum features. This has advantages over methods used to rate the appearance of the nasolabial area (Asher-McDade et al. 1992). The subjective assessment of nasal form (one of the component categories of the assessment) will be influenced not only by deviation of the nasal tip, but also by asymmetry of nasal rim shape, nostril shape and nasal base. These aspects may be weighted differently by each panel member. Furthermore, at least 3 examiners were required to produce a sufficiently reliable assessment. Asymmetry of the

nasolabial area is evident in 3-dimensions and it is quantifiable by the methods used in this study, and can be reliably evaluated by one independent observer.

To obtain the nostril Asymmetry Score, the left and right nostrils were defined by pairs of landmarks on the cleft and non-cleft sides as part of the same configuration. It was not possible to assess the asymmetry of each nostril independently. This may limit the Asymmetry Score's application in terms of identifying differences between cleft and non-cleft nostrils. However, it would be valuable in monitoring changes or improvement in nostril shape asymmetry over time and this is an area to be considered in future research.

The Procrustes matching process introduced another potential problem. Areas with high levels of asymmetry can influence the scores of other parts of the same configuration – the net result is artificially inflated scores. The upper face was an example of this. When pre-operative global face configurations were aligned using all of the landmarks, the upper face score was influenced by the high level of asymmetry of the lip landmarks. When Asymmetry Scores were recalculated with the lips omitted from the alignment (matching) process, a more realistic indication of the degree of asymmetry in this region was revealed. It is therefore important to ensure that highly asymmetric landmarks are not involved in the initial matching process, so that their influence on the rest of the global configuration is minimised (Bock & Bowman, 2005). Despite these methodological technicalities, the Asymmetry Score provides a clinically useful means of 3D shape assessment for cleft infants, and can be applied to any shape which can be defined by landmarks.

The Procrustes techniques rely on homology of landmarks within and between populations. Most confidence is placed in correspondence between Type I landmarks and least in Type III. The complexity of the soft tissues of the face necessitates analysis of landmark configurations which are a combination of landmark types. In this study, landmarks were predominantly Type I. Some Type III landmarks such as the tip of the nose, were redefined as Type II landmarks by standardising the selection method and orientation of the model. However, this is a potential limitation of Procrustes analysis techniques in terms of homology of certain landmarks before and after surgery. As it was not possible to tattoo the landmarks involved in the area of surgery, correspondence between landmarks before and after surgery was assumed. This may have influenced the measurement of asymmetry in this study, however, every study which uses a landmark-based analysis will suffer from this limitation. This is discussed further in relation to linear and angular measurements later.

5.4.3 Quantifying 'Distance from Normal'

The concept of 'Procrustes Distance' was used to quantify residual abnormality after cleft repair as the distance of each cleft case from the control mean shape at age 2 years. In common with the Asymmetry Score, this approach retained the geometry of the facial features, and made full use of the 3D nature of the data. The rationale behind this was that a facial feature may be symmetrical in shape, but that shape may not necessarily be normal. The control group consisted of approximately equal numbers of male and female infants, captured at the same time points and recruited from the West of Scotland. All control group children were born in Scotland to Scottish Caucasian parents, and were recruited prospectively, within the same period as this study. They formed a representative sample of the healthy Scottish infant population born during 2000-2001. The control group was large (more than 3 times the size of the combined cleft groups), and subject retention in the long-term was excellent. This adds to the validity of the control group in that it still represented the Scottish population at the end of the study. Loss of subjects from longitudinal studies can result in bias, and loss of validity of data is a potential problem in all lo

5.5 Sample

5.5.1 Recruitment & Loss to follow-up

The mean age at capture prior to primary lip/nose surgery, was 3.9 months (range 2.75 to 9 months) and the mean age at capture after lip/nose surgery (post-op) was 7.1 months (range 5.5 to 9.2 months). Both of these exceeded the original target capture times of 3 months and 6 months. There were several reasons for this. Failure to reply to letters and telephone-calls to schedule appointments complicated the longitudinal component of the study. Children were recruited from all over Scotland and although the majority had their primary surgery in Glasgow, others were treated in Edinburgh and Aberdeen. Childcare problems, illness and transport difficulties on the day of the capture, resulted in the parents having to re-schedule. Even when train tickets or parking vouchers and accommodation were pre-arranged and posted to the families, some had to cancel on the day due to unforeseen circumstances. Delays and cancellation of primary surgery and difficulties in families being able to travel specifically for 3D imaging appointments also had a significant impact on planned capture times. Children who were recruited prior to surgery, were aged almost 5 months on average at primary lip repair. This encroached in turn on the timing of the post-op capture, and some families were unable to make a return journey for

images in a short period, preferring to come again at the time of palate repair. The '6 month' capture thus became a 'post-lip / nose repair' capture and was the most difficult to co-ordinate. It was abandoned completely in 24.3% of the sample (9/37). Equipment failure and software crashes, necessitated re-appointment of several subjects and this further delayed the capture time.

Seventeen children failed to complete the study as far as the 2 year old capture point. Interestingly, as the study progressed, the proportions of cleft type within the groups changed from comprising fairly even numbers of UCL (17) and UCLP (15) infants at the beginning of the project, to being predominantly UCLP (21) children at 2 years (cf. 11 UCLP). The majority of children who failed to complete a 2-year capture were UCL cases. The drop- out rate for UCL children was more than twice that of the UCLP children (12 compared to 5). Garrahy (2002) also encountered this problem among 3-year-old cleft children. In her study, the UCL children proved hardest to recruit. Although recruitment of UCL children was not an issue in this study, retaining them was a major problem, with significant impact on final numbers and the study design. Why UCL children should prove less able to complete a study than those with UCLP remains a mystery. It may be that after lip / repair, families felt that as the surgery was over and their level of commitment to medical follow-up was reduced, and considered a return to Hospital purely for 3D-Imaging a low priority.

Incomplete data collection in longitudinal studies is a common theme in the cleft literature. In a large cephalometric study of craniofacial growth, only 93 of the 157 infants who had data collected at age 2 months, did so at 22 months. A randomised controlled trial evaluating the effects of intra-oral orthopaedics on maxillary arch dimensions reported loss of 9 subjects from an initial 48 by completion of the project at 78 weeks (Dutchcleft study) (Prahl et al. 2003). It is not surprising that families with young cleft children find it difficult to complete research projects such as this. They are coming to terms with having a child with a cleft and the inherent difficulties that may accompany. Moreover, during the first 2 years of their child's life, parents are most likely to change address due to family expansion. It is a testament to the dedication and support of the families who volunteer for such studies that research is concluded meaningfully at all.

5.5.2 Gender distribution

Unilateral clefts involving the lip and / or palate occur more commonly in males than females. The study sample reflected this in that 24 males and 13 females were recruited

prior to primary surgical repair. In the later stages of the study, a further 10 males and 3 females contributed data; this meant that the ratio of males to females was slightly increased. This compares well with the gender distribution in other studies of this age group (Hermann et al. 1999b, 2000).

5.5.3 Socio-economic status

The socio-economic status of cleft infants in this study was measured by Carstairs Score and deprivation categories (DEPCAT), which are the most commonly used measures of deprivation in relation to health and disease within Scotland. They measure the extent of material well-being or relative disadvantage experienced by populations in small geographic localities (postcode sectors) rather than individuals. In Scotland, lower socioeconomic status (i.e. high DEPCAT score) is associated with an increased prevalence of orofacial clefting and this effect is stronger for cleft lip and palate (Clarke et al. 2003). Almost a third of the cleft children in this study were categorised as DEPCAT 5 and 14% as DEPCAT 7; more than double the proportion of the Scottish population in both categories. This suggests that a greater proportion of cleft children in this study were living in more deprived areas, which tends to support Clarke et al. (2003). Sixty-eight percent of cleft children lived in areas designated as DEPCAT 3, 4 or 5, which was slightly more than the proportion of the Scottish population (62%) at the 1991 census (McLoone & Boddy 1994). This was surprising, as a much greater proportion of higher DEPCAT scores was anticipated in the cleft sample. There is a possibility of selection bias, since not every child born with a cleft in Scotland to participated in the study. Individuals of low socioeconomic status are commonly a difficult group to recruit for research projects and it is usually individuals who are of higher socioeconomic standing, who are more motivated to volunteer. This may have resulted in bias towards the more affluent DEPCAT areas.

Another possible explanation is that DEPCAT is a geographical area-based measure. Deprivation categories at the extremes of the scale (1, 2 or 6, 7) describe postcode sectors whose populations are homogenous i.e. either affluent or deprived. In the middle of the scale, (DEPCAT 3,4 or 5) areas are more mixed and reflect a combination of household types. It has been estimated that over half of the most deprived individuals may live outside the most deprived areas (McLaren & Bain, 1998), so it is possible that some of the families in this study fell into this group. DEPCAT is also a better indicator of deprivation in urban rather than rural areas as rural populations tend to be a mixture of more deprived and less deprived households, resulting in middle-ranking scores. The children in this study came from all over Scotland (rural and urban areas), and this may be reflected in their DEPCAT scores.

5.5.4 Body Measurements

Body measurements were examined in order to evaluate facial size in the context of overall body size. Cleft infants in this study were compared to the appropriate UK90 reference norms for boys and girls. Children were considered outside the normal range if they fell below the 0.4th centile. The 50th centile was taken as the 'average' norm. Numbers of subjects in the cleft type and gender sub-groups were small. Further sub-division of cleft type by gender would have rendered the study groups even smaller. For this reason, analysis was limited to differences between UCL and UCLP (combined males and females) and differences between males and females (combined cleft types).

A similar proportion of UCL and UCLP infants (82.4 % and 84.6% respectively) were of normal but low weight for age prior to primary lip/nose repair (under 50th centile). There was a tendency for UCLP infant weights to fall at the lower end of the scale. This trend was reported in a large retrospective study of South African cleft infants at the time of primary surgery (Lazarus et al. 1998). When compared to controls, infants with UCLP were significantly more underweight for age than infants with UCL. Felix-Schollart et al. (1992), on the other hand, detected no differences in weight between Dutch UCL or UCLP infants and controls. There were no gender differences in the proportion of low weight infants in the present study. This agrees in part with the findings of Jensen et al. (1988) in Danish 2 month old cleft infants. Male and female UCLP infants and UCL males were lighter than comparative average norms. These authors compared their data to that of a previous study of Danish infants and to North American anthropometric charts. However, their methodology did not detail how they defined the 'normal range'.

In respect to the parameter of head circumference, the majority of the sample had below average head circumference for age, and there were no differences in the relative proportions of males and females. This contrasts with Jensen et al. (1988) who reported that head circumference was similar to the control mean in UCL and UCLP infants, and in both genders.

Almost 60% of cleft subjects were of average height or taller and it was in this parameter that a striking difference between males and females was identified. A recent study of the facial and body characteristics of 3-month-old non-cleft Scottish infants found that boys were heavier, taller and had a greater head circumference than girls at 3 months (White et al. 2004). A similar finding was reported in a sample of 97 non-cleft Japanese infants at age 4 months (Yamada et al. 2002c). It has been demonstrated that cleft children do not

always fit this pattern. Felix-Schollart et al. (1992) reported that from birth to age 2.5 years, somatic growth in male and female UCLP infants was similar to controls, except in the parameter of height. In contrast with findings in non-cleft children, UCLP infant girls tended to be taller than UCLP boys. This was echoed in the present study in that 90% of females were on or above the 50th height centile for age. In contrast, approximately three fifths of males were of below average height, prior to cleft repair. This also agrees with Jensen et al. (1988) who reported that Danish cleft 2 month old cleft females were of normal height, when compared to controls, whilst males were shorter than the average norm.

An interesting finding is that the gender difference in height could not be explained by differences in the proportions of cleft type in the male and female groups. At birth, individuals with cleft lip and palate are generally smaller than unaffected individuals, whereas infants with cleft lip have been reported as having normal body dimensions (Becker et al. 1998). The majority of subjects in this study who were of below average height prior to lip / nose repair were male, and we might have expected that this could be explained by a predominance of 'shorter' UCLP subjects comprising this group. However, a similar proportion of UCL and UCLP subjects were found in the male group.

It is well documented, although widely debated, that cleft defects can lead to feeding difficulties resulting in compromised growth early in life. At birth, 25% of children with cleft lip and / or palate will have feeding difficulties (Jones 1998). Type of cleft is also related to severity of growth faltering. Children with clefts of the lip and primary palate appear to experience a negligible degree of compromised growth, whereas those with cleft palate are most severely affected. However, early growth faltering has been shown to be of a temporary nature, with children of all cleft types experiencing catch-up growth after cleft repair (Lee et al. 1997). Although information on feeding was not collected at the time of this study, it is a possible contributing factor in the variability in body measurements. Particularly in the parameter of weight, it is likely that some individuals may have been experiencing an early 'drop off', prior to surgical repair. This could be verified by obtaining Birth Registry data on birth weight and calculating the 'Thrive Index' for each child, such as in the study by Lee et al. (1997). The Thrive Index compares a child's attained weight Standard Deviation Score (SDS) to that predicted by their early weight measurements.

It is difficult to separate the effects of cleft type and severity from the underlying complexities of normal growth and genetic influences. Generally speaking, it has been recognised that children with palatal clefts do worse than those with isolated lip clefts in terms of somatic development (Lee et al. 1997). The results of the present study do not appear to support this and tentative conclusions may be drawn. When compared with norms for age and sex, children with UCL were just as likely to be of low weight, poor stature and to have below average head circumference as those with UCLP. This statement is made with caution however, as there was a great deal of variability among the sample groups in each body parameter and the number of study subjects was small. A further outcome of this analysis was that, regardless of cleft type, females were taller than their male counterparts, prior to primary surgery. Future study involving comparison of this cleft data with that from a non-cleft population would require cognisance of the fact that cleft infants were lighter and had smaller than average head circumference and they did not conform to the normal height pattern for gender.

Irrespective of cleft type or gender, or time point, there were no significant differences in weight, height or head circumference between the infants in the study sample. These findings agree with a similar study, which examined 3-year-old children with UCL and UCLP (Garrahy, 2002). As previously discussed, female cleft subjects in this study were of average or above average height pre-operatively, whilst their male counterparts were of below average stature for their age. This reversal of the normal pattern for height may explain why no differences were identified between the genders when cleft subjects were compared to each other.

The relationship between head size and body size in unilateral cleft children is unclear, as it appears to be related to weight, and not height in the early months of life, prior to lip/nose repair. Height, weight and head circumference correlated strongly after lip/nose surgery and at the age of 1 year. This finding was demonstrated in White's study of non-cleft infants at 3months and up to 2 years of age (White, 2005) In children with repaired unilateral clefts at age 2 years, however, head circumference did not correlate with either height or weight.

In all research, assumptions are made which affect how data is handled and subsequent interpretation of results. White et al. (2004) published facial dimension norms for 3-month-old non-cleft Scottish children. Gender differences were identified in some facial dimensions. However, almost all of these were explained by differences in body size and in particular, the fact that boys were heavier than girls. The only exceptions were in the nasal

base and selected nostril dimensions, where males had significantly larger dimensions than females. Few gender differences were found in facial dimensions in young Japanese non-cleft children, despite reported differences in body dimensions – boys were larger than girls (Yamada et al. 2002c). Moreover, the severity and heterogeneity of the cleft deformity may 'mask' sex differences pre-operatively, as reported in hard tissue studies (Krogman et al. 1982). In this study, no investigation of potential gender differences in facial dimensions was made and cleft groups were of mixed sex. As no size differences were detected between male and female cleft subject body dimensions at the beginning of the study, it was assumed that the study could proceed without the need to correct for general differences in body size between genders. Thus, differences in facial dimensions were assumed to be valid and not influenced by one group being larger or smaller than the other. Nevertheless, there were unequal ratios of males to females in each cleft group at various points throughout the study and a gender effect cannot be ruled out. This limitation is acknowledged and much larger sample sizes would be required to explore this further.

5.6 Facial soft tissue characteristics of UCL and UCLP, prior to primary surgery

This is the first study to characterize the facial soft tissues of Caucasian infants with cleft lip and cleft lip and palate in the Scottish population, prior to and following primary repair.

UCL and UCLP infants displayed a similar pattern of deformity in the soft tissues of the nose and lip prior to primary lip/nose repair, but differed in the extent to which this was expressed. Facial dimensions in the locale of the cleft tended to be larger in UCLP infants than in UCL infants. Discrepancies in individual cleft and non-cleft side dimensions in the nose and lip were accordingly larger in UCLP infants. UCL infants had significant nasal deformity associated with their lip deformity, but to a lesser extent than in UCLP. The UCLP infant face was characterised by greater deformity in the upper face, nose and philtrum. Key findings are discussed below.

5.6.1 Upper Face Deformity

In an early paper comparing pre-operative cleft subjects from this sample with age-matched controls, it was reported that an increased intercanthal width in UCLP infants was the result of a unilateral increase in the distance from soft tissue nasion to the innercanthus of the eye (en-n) on the cleft side (Hood et al. 2004, Appendix 10). A wide intercanthal distance was reported in 8 Japanese 3m UCLP infants compared with controls (Yamada et

al. 2002b), however the authors did not compare cleft and non-cleft sides and were unable therefore to comment on the exact location of the discrepancy. The results of the present study suggest subtle variation in the spatial relationship of the innercanthal points on the cleft and non-cleft sides. This is consistent with the findings of Zemann et al. (2002), who undertook 3D analysis of skull models of 21 3-month-old UCLP infants prior to surgery. Increased inter-orbital distance was attributed to asymmetry of the infraorbital rims, most often due to a caudal translocation on the cleft side (Zemann et al. 2002). Although skeletal morphology was not examined in the present study, results suggest that this is demonstrated in the soft tissues of the upper face in UCLP subjects as young as 3 months of age by comparing cleft and non-cleft side measurements. The same relationship was not detectable in UCL infants by this method. When Asymmetry Scores in the upper face were examined, a small but significant degree of asymmetry was present in UCL infants also, compared to control baseline. Thus, the 3D Asymmetry Score method was more sensitive as it considered asymmetry of the upper face in all three dimensions. In this respect, results demonstrate the potential limitation of defining asymmetry by comparing bilateral 2D measurements of a 3D structure, by virtue of the inability to relate measurements to each other.

Aberrations of the maxillary complex and overlying soft tissues are evident in clefting, but the calvaria, cranial base, orbital region and mandible also display abnormal morphology (Hermann et al. 1999b). It is generally accepted that combined cleft lip and secondary palate defects cause larger deviations from normal, than isolated clefts of the lip or primary palate (Dahl 1970; Molsted et al. 1995). Results of this study support the theory that clefting influences the underlying skeleton in the orbital region, and this manifests as significant three-dimensional asymmetry in the upper face in UCLP and to a much lesser extent in UCL infants, before cleft surgery. Although many have reported wider inter-orbital dimensions in unilateral cleft subjects (Ishiguro et al. 1976; Dahl et al. 1982; Yamada et al. 2002), this has not been previously definitively demonstrated as a true asymmetry in the shape of the upper face.

5.6.2 Nasal Base Deformity

The cleft deformity in the nasal base is characterised by increased anatomic nose width, an increased alar base width, and a splayed columella angle. All of these features were encapsulated as nasal base asymmetry. Anatomic nose width and alar base width were significantly wider in UCLP infants than in UCL infants prior to surgery. The degree of

anatomic nose width disruption is related to the position and contour of the alar crest, whereas alar base width is determined between subalare points. In UCLP infants, the alar base width was on average 7mm wider than in UCL infants. In UCL infants, the alar base width was also increased relative to controls but the anatomic nose width was shown to be within normal limits (Hood et al. 2004). This might be explained by a more postero-lateral and inferiorly positioned subalare point on the cleft side, and eversion of the alar base, as noted in Chinese UCLP children (Fisher et al. 1999). This alar flaring is thought to occur in response to the torque effect produced by contraction of facial muscles which have lost their medial insertion, whilst deeper soft tissue remains anchored to periosteum (Malek, 2001).

Nasal base asymmetry can be assessed by measuring the difference between nostril floor widths on the cleft and non-cleft sides of the face. This is useful, but for a truly size-independent, spatial evaluation of nasal base asymmetry, the asymmetry score method is more appropriate. The degree of nasal base asymmetry was strongly associated with the size of the difference in nostril floor widths. This finding is as expected, as the columella base and subalare (sbal) landmarks on cleft and non-cleft sides of the face are common to nasal base asymmetry score and nostril floor width ratios i.e they measure the same feature in 2D and in 3D. Similarly, nostril asymmetry scores strongly correlated with the size of the cleft in the nose.

5.6.3 Nasal Rim Deformity

The impact of the cleft on nasal rim shape varies. Fisher & Mann (1998) proposed that in cases of UCLP, the alar wing was deformed secondary to asymmetries in the relative positions of structures of the nasal base – the columella, alar base and lateral piriform margins. In this study, approximately two thirds of the variability in nasal rim asymmetry could be explained by its relationship with nasal base asymmetry. Columella asymmetry also explained just over half of the variability in nasal rim asymmetry, which tends to agree with Fisher & Mann (1998). Yet the remaining proportion of the variability in nasal rim asymmetry must also be related to the degree of deformation of the alar cartilage on the cleft side, aberrant position of the nasal tip and lack of support for the alar base. This suggests that correction of the nasal base alone will be insufficient to fully correct asymmetry, particularly of the nasal rim and nostrils. This has been noted in studies where primary nasal correction has not been performed (Brusse et al. 1999; Kim et al. 2004). This finding helps confirm the need for attention to nasal rim contour at the time of primary lip

repair, which has long been recognised as highly desirable (McComb 1985; Salyer et al. 2003).

The nasal rim Asymmetry Score method provides an overview of nasal rim shape as it describes the complex deformity and caudal rotation of the cleft side lower lateral (alar) cartilage, the depressed cleft side nasal dome, and eversion of the alar wing as previously described. This aspect of the cleft deformity should be evaluated in isolation from the influence of asymmetry of the nasal base. This has an important clinical application in the evaluation of pre-surgical and post-surgical therapies developed to mould the alar cartilage and improve nasal rim form (Bennun et al. 1999; Maull et al. 1999; Liou et al. 2003).

The nasal tip was displaced horizontally by approximately 7° more in UCLP than in UCL children, which might have been expected to be much larger, considering the degree of flattening of the alar wing in UCLP infants. In common with other studies (Yamada et al. 2002a; 2002b;2002c), the point chosen to represent the most prominent anterior point of the nose (prn) in this study did not necessarily coincide with the anatomical tip of the nose. Inherent difficulties in the identification and reproducibility of the anatomical tip necessitated the selection of a close surrogate. The clinical implication of this is that measurement of nasal tip displacement angle is likely to underestimate the degree of horizontal displacement of the nasal tip.

Nasal tip angle is a measure of prominence of the nasal tip. Flattening of the nasal tip is commonly described in UCLP infants of all nationalities prior to surgery, compared with UCL infants (Hermann et al. 1999b) or with controls (Yamada et al. 2002a; 2002b). In this study, the prominence of the nasal tip was similar in UCL and UCLP infants prior to surgery, in contrast to the findings of Hermann et al. (1999b). Methodological differences in study design may account for this, since soft tissue measurements were derived from lateral cephalometric radiographs, or it may reflect a worse degree of nasal deformity in the UCL subjects in this investigation.

5.6.4 Columella and Nostril Deformity

The more severe nasal deformity in the UCLP group in comparison to the UCL group, was not related to a deficiency of columella tissue, but to a more displaced columella position. The difference between columella heights on the cleft and non-cleft side was not significant in the UCLP group, but was significant in the UCL group. However, this amounted to 0.8mm and when considered with the system error, this is probably clinically negligible. Liou et al. (2003) reported a discrepancy in columella height in UCLP subjects and it was claimed that the cleft side was shorter than the non-cleft side by a mean of 4mm. They measured the difference in columella height on a basal view photograph with callipers. Therefore, it is doubtful whether accurate measurement would be possible as the severe malposition of the columella and outward rotation of the philtrum can obscure the cleft side dimension in this view. Columella assessment was not included in the computer-assisted NIH-Image-based anthropomentric analysis of Hurwitz et al. (1999), which also used basal view photographs. There is much interest in accurately documenting the pre-operative dimensions of the columella, particularly in relation to assessing the success of columella lengthening surgery (Cutting et al. 1998) and the effects of non-surgical therapies on columella symmetry (Grayson et al., 1999; Bennun et al., 1999). Many surgeons rely on direct anthropometric measurements at the time of surgery and thereafter, yet calliper derived measurements of the columella and philtrum are among the least reliable (Ward & Jamieson. 1991). Yamada et al. (2002a&b) did not specifically measure columella dimensions in their studies of UCLP infants and therefore the present study appears to be the only one that has accurately documented this important aspect of the cleft deformity. Furthermore, columella displacement is a significant morphological problem in both UCL and UCLP infants prior to surgery.

Although, linear dimensions cannot fully characterise the shape of the nostril, it was helpful to ascertain which dimensions varied most in the cleft infants in this study. There was no discrepancy in the cleft and non-cleft nostril long axis in UCL, whereas cleft side nostril floor and nostril width dimensions were larger than on the non-cleft side. In UCLP, all cleft side nostril dimensions were significantly larger than in UCL, reflecting the greater deformity in their nasal shape. Few researchers have managed to measure nostril shape and quantify the influence of different nasal parameters on nostril symmetry. Yamada's method for assessing nostril form in UCLP infants was limited to two points which were located on the upper and lower borders of each nostril. A pre-operative assessment was not possible with their system (Yamada et al. 2002a&b). Asymmetry of nostril shape was strongly

associated with the degree of asymmetry in the nasal base, nasal rim and the columella prior to surgery. To achieve symmetry of the nostrils therefore, correction of these three components of the nostril should be considered during surgical correction.

5.6.5 Nasolabial Deformity

Nasolabial dimensions were similar in UCL and UCLP infants before surgery except for the distance from the alar base to the lip commisure, on the cleft side. This dimension was shorter in the UCLP group (by approximately 2mm) than in the UCL group. The cleft side was also significantly shorter than the non-cleft side. This could suggest a degree of tissue hypoplasia in the upper lip. However, we believe that the lateral lip tissues are not deficient per se, but are distorted by the unopposed pull of abnormally inserted orbicularis oris and nasolabial muscles. This view is supported in other published data (Breitsprecher et al. 1999; 2002). This is compounded by bone separation of the cleft segments in UCLP infants. On the cleft side, heaping –up of muscle fibres which have not developed to their full extent, combined with a laterally and inferiorly displaced subalare point (Fisher et al. 1999) contribute to the 'shortening' of the distance from this point to the commisure.

No differences were found between cleft groups in upper lip prominence before surgical repair. These findings contrast with those of Hermann et al. (1999b) who reported that the upper lip was more prominent in 2 month old UCLP infants prior to surgery, compared to UCL infants. However, methodological differences in the way upper lip prominence was assessed may account for this, as Hermann's study was based on an evaluation of midline soft tissues from cephalogram radiographs and lip prominence was measured from the ls point to a defined facial plane.

5.6.6 Philtrum Deformity

The pattern of deformity in the philtrum was the same in UCL and UCLP infants but the magnitude was more severe in UCLP.

Cupid's bow width (width of the cleft in the lip) was significantly larger in UCLP infants (mean 20mm $\pm$ 4.1 compared to 14.8mm $\pm$ 3.6 in UCL). Many surgical descriptions refer to 'wide' clefts without qualification, and suggest 'wider' clefts may be more challenging to repair. Studies that include an evaluation of the horizontal extent of the cleft in the lip, measured across the cleft, are curiously absent from the literature. Therefore, it is difficult to say whether the infants in this sample had a range of clefts which were wider or

narrower than average. Yeow et al. (2002) reported the size of the cleft in the lip in UCLP infants, ascertained by direct anthropometry. Although it is not possible to compare results directly due to differences in landmarks chosen and measurement method (i.e. plastic ruler), subjects in their study showed more heterogeneity in the range of cleft widths than cleft infants in this study, but their sample size was much larger (125 infants).

There was significant discrepancy in the cleft and non-cleft side paramedial dimensions of the philtrum, in both cleft groups, and this was related to a shorter dimension bordering the cleft. Vander Woude & Mulliken (1997) demonstrated a similar finding in a study on the effects of lip adhesion on philtrum length. This involved measurements taken directly with callipers at the time of operation from 35 UCLP subjects. Although the origin of the paramedial measurements was different from that chosen in this study (sn point as opposed to sn0 point on each aspect of the columella), they reported the same shortening of the dimension bordering the cleft. However, they also reported a shortening of the philtral point to alar base dimension on the lateral lip element. This was not found in the present study in either the UCL or UCLP infants. Although Vander Woude & Mulliken (1997) did not state their methodology error, direct measurements were subject to error resulting from possible distortion of the skin surface with callipers and landmark placement error, since the philtral peak on the lateral lip element is an estimated point.

The size of the gap in the lip may be of clinical significance in terms of ease of surgical repair, but it does not appear to be of particular importance with respect to cleft severity. The previously mentioned study by Yeow et al. (2000), attempted to assess the relationship between the transverse and vertical aspects of cleft severity in the nose and lip using a plastic ruler to measure distances. The present study improved on the methodology of their study, which was open to question and prone to error. Results of the present study showed that as the extent of the cleft in the nose increased, so did the extent of the cleft in the lip, in the horizontal plane. However, a wide cleft in the lip was not necessarily accompanied by an asymmetric or deficient philtrum. Furthermore, the vertical deficiency in the philtrum was moderately associated with the magnitude of the discrepancy in nostril floor widths. This finding in UCL and UCLP children reflects the heterogeneity of the cleft deformity in *both* groups and may be different manifestations of the aberrant nasolabial muscle attachments. Failure of the cleft side of the philtrum to develop may be secondary to a lack of contribution from nasolabial muscles. These are abnormally attached to the piriform aperture and together with the pars marginalis fibres of the orbicularis oris

muscle, which run parallel to the cleft margin, contribute to the malposition of the cleft side alar base, thus widening the nostril floor.

In summary, soft tissue abnormalities are common to both UCL and UCLP cleft types and are related to muscular disruption primarily, except in the philtrum where a true hypoplasia may exist in both cleft types. The nasal defect that accompanies a cleft lip is significant for both cleft groups, though less severe in the UCL group. The presence of a worse underlying skeletal defect accentuates the nasal abnormalities in the UCLP group. It would appear from the results of this section that the presence of a secondary palatal cleft had a more obvious influence on nasal morphology than on lip morphology.

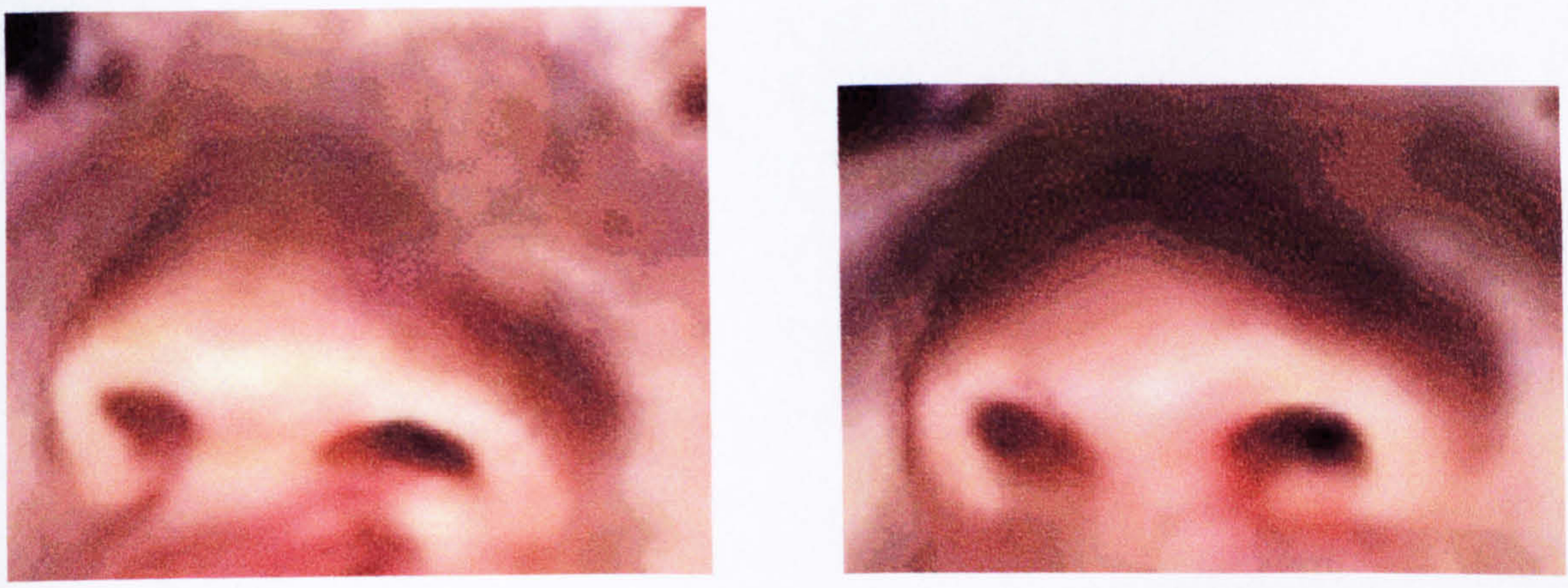
5.7 Changes in facial morphology with primary lip / nose surgery

Changes in facial dimension after lip/nose repair occurred as a direct result of the surgery and also secondary to facial growth. Surgery directly affected nose and upper lip dimensions and not surprisingly, there were some differences between UCL and UCLP groups in the magnitude of change achieved. This reflected the more extensive disruption of the soft tissues by the initial cleft deformity in UCLP infants. After this surgery, measurement of facial dimensions alone could not distinguish between cleft types.

Primary lip/nose surgery appeared to be most successful in improving lip and, more specifically, philtrum asymmetry. These were the dominant sources of facial and nasolabial asymmetry before surgical repair in both cleft groups. Surgery reduced the Cupid's bow width and increased the medial length of the philtrum. On the repaired side, the philtrum point to alar base dimension was significantly shorter than the non-cleft side in both UCL and UCLP, yet the paramedial philtrum dimensions were of equivalent lengths in both groups. The rotation advancement repair can result in a lip that is too short on the repaired side of the philtrum. This was noted immediately post-operatively by Lee et al. (1999). Yamada et al. (2002) also noted that the philtral point was higher in their rotation advancement cohort, compared to their triangular flap cohort, when measured 2 weeks after surgery. Millard maintains that the reason for this is insufficient rotation, however, rotation advancement surgery in the present sample was successful in producing philtral columns of comparable length, since philtral peak to columella distances were similar. This suggests that the shortened alar base to philtral point dimension on the

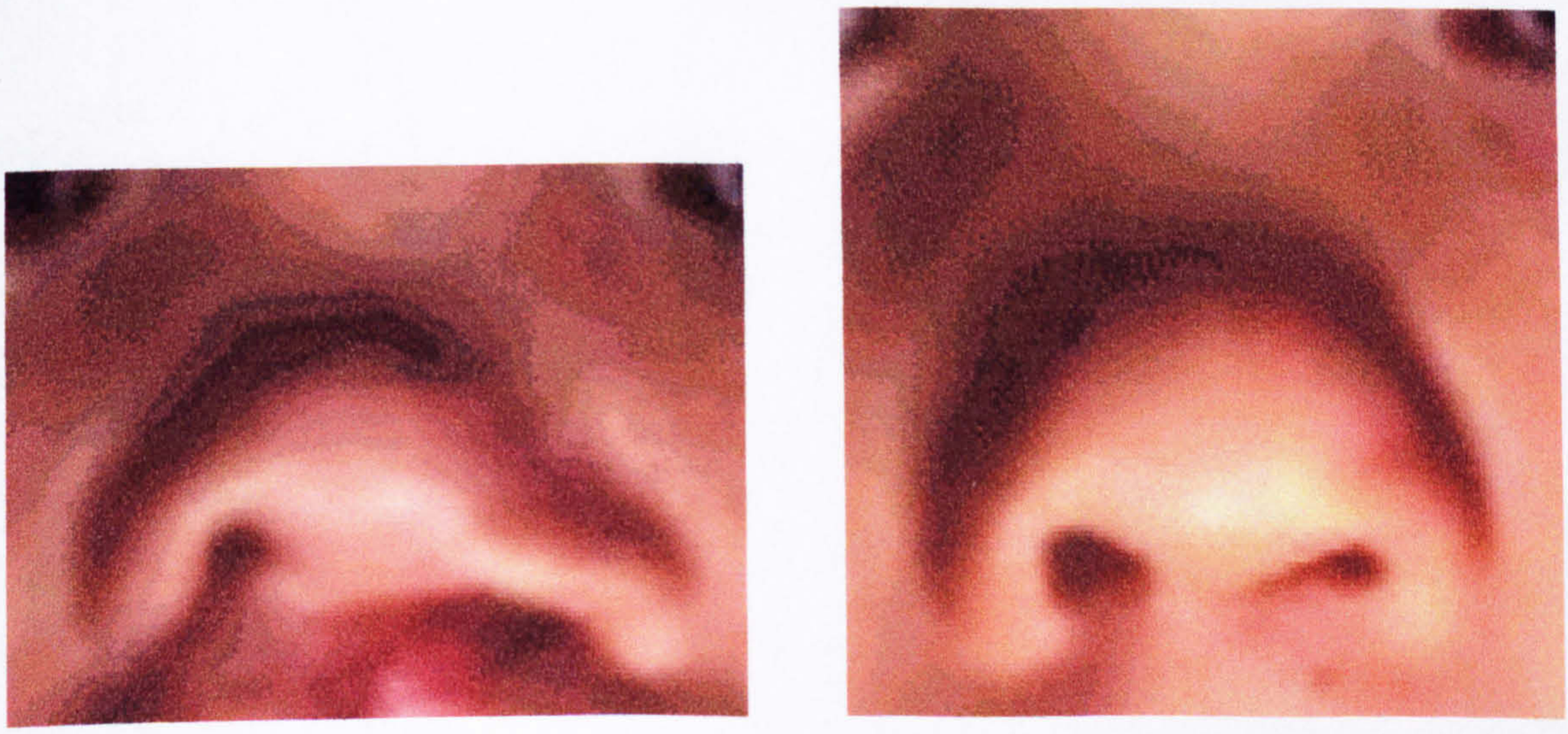
repaired side was due to asymmetric alteration of the alar base. It was closer to the philtral point on the repaired side. It is unclear whether the alar base was cinched in too much or whether it occupied a more inferior position than on the non-cleft side. Nevertheless, the median discrepancy between non-cleft and repaired sides only amounted to 1mm in UCL infants and 1.6mm in UCLP infants.

Primary surgery increased the length of the columella marginally (0.8mm) on the cleft side and the columella width was increased by 1mm. The Millard repair has been criticised for failing to correct a short columella, and so the technique has been modified by some to incorporate a columella lengthening procedure (Cutting et al. 2002). However, one could argue that this procedure is not necessary in UCLP cases since the columella is not in fact short, but just displaced (Broadbent & Woolf, 1984; Fisher & Mann, 1998). In the present study sample, the columella was not short in either cleft group, compared with controls, prior to surgery (Hood et al. 2004). Moreover, even though negligible length was attained with surgery, a columella lengthening procedure was probably unnecessary. Nonetheless, there was dramatic improvement in columella displacement. Surgery corrected the discrepancy between cleft and non-cleft side columella angle in UCL infants. A small residual deformity was still evident in UCLP infants (Figs 5.1 & 5.2 overleaf). This is probably due to the dislocation of the inferior edge of the nasal septal cartilage from the vomer groove and the deviation of its anterior edge towards the non-cleft side, together with bowing of the nasal septum into the cleft side nostril. These are more pronounced in UCLP children and difficult to fully correct.



(a) (b)

Figure 5.1 ***Nose of UCL child showing (a) columella displacement prior to repair (b) improved columella position after repair***



(a) (b)

Figure 5.2 ***Nose of UCLP child showing: (a) columella displacement prior to repair (b)residual columella displacement after surgical repair***

Surgery corrected the discrepancy between cleft and non-cleft side nostril dimensions in both cleft groups. This is important as the most frequent residual deformity of cleft repair is nostril floor width asymmetry (Farkas et al. 1993). Yamada et al. (2002a) were unable to quantify improvement in nostril symmetry with surgery in their rotation advancement cohort, and simply described the difference in the position of the upper limit of the nostril point as nostril asymmetry. Liou et al. (2004) reported improved nostril floor width dimensions after nasoalveolar molding and rotation advancement with no nasal dissection. No other nostril parameters were assessed. The nostril is a difficult area to document, as evidenced by the omission of a quantitative evaluation from almost every study of the nose and lip in young cleft children. Many describe surgical and non-surgical effect on nostril asymmetry, but do not quantify it (Bennun, et al. 1999; Yamada, et al 2002; Kim et al. 2004). The methods in this study present a fully comprehensive means of evaluating the nostril. Although nostril symmetry is one of the most desirable goals of cleft surgery, it is often the most inadequately assessed.

The degree of flattening of the nasal tip (nasal tip protrusion angle) was similar in both UCL and UCLP prior to surgery and was improved with surgery by a small but significant amount (2.7degrees), although this was probably clinically negligible. A flattened nasal tip is another of the common stigmata of cleft repair (Farkas et al. 1993), and the improvement with surgery demonstrated in the subjects in this study, is of comparable magnitude with that demonstrated by Yamada et al. (2002a). They reported an improvement in nasal tip angle to approximately that of controls with rotation advancement in 10 UCLP infants, but no such improvement was reported in the other group in their study treated by the triangular flap method.

The distance from the nasal tip to the nasal base was increased by surgery. As previously discussed, this is probably not attributable to a columella lengthening effect of the surgical procedure. The most likely explanation lies with the definition of the prn point, which was selected as the most prominent point on the curve of the nose in the region of the tip in 60 degree and profile views. It closely approximated, but may not always have coincided with the anatomical 'tip' of the nose. As the architecture of the nasal tip improved following primary surgery, this 'surrogate nasal tip' point becomes closer to the actual anatomical tip, in effect changing position. The degree of this change will depended on the initial degree of deformity of the nasal tip, which was more severe in children with UCLP. The amount of change demonstrated by the linear dimensions and angles relating to the nasal tip is likely to be an under-estimate of the improvement in nasal tip shape. This illustrates the

difficulty in interpreting linear measurements of 3D anatomical structures and it is more informative to assess the change in asymmetry of the nasal rim shape. McComb used the method developed by Coghlan et al. (1993) to demonstrate improved symmetry of isolated nasal features such as upper nasal perimeter from 2D photos, but was unable to comment on the relative contribution of these individual features to overall nasolabial asymmetry (McComb & Coghlan, 1996).

In the context of the whole face and nasolabial area, the present study showed that surgical repair was perhaps least successful in the correction of nasal rim asymmetry in UCLP children. Residual asymmetry remained higher in this group than in UCL infants, despite a similar initial level of asymmetry. This was also demonstrated in an increased cleft side alar wing length in UCLP children, which remained unchanged with surgery. However, the increased cleft-side alar wing angle was dramatically reduced and the discrepancy noted pre-operatively between cleft and non-cleft sides, in both cleft groups was fully corrected. This resulted from improved septal positioning and columella orientation, which could not be quantified with Coghlan's method (McComb & Coghlan, 1996).

5.8 Influence of Growth after primary surgery, on Facial Morphology.

No differences were detected in the pattern or amount of post-surgical facial growth in UCL and UCLP. Differential growth was demonstrated between facial features, and also within some facial features.

5.8.1 Growth in Upper face width, eyes and vertical face height

The amount of growth of the upper face (biocular) width and eyes in the first year was much larger than in the second year. This neural pattern of growth was normal, and reflects synchrony with an expanding cranial floor in response to brain growth. Intercanthal width increased more uniformly, but to a much lesser extent. This pattern is also normal (Ranly, 1980; White, 2005). Thus, the increase in upper face (biocular) width was mainly due to the increase in size of the eyes, which may mirror brain growth. Interestingly, there was no correlation between the amount of head growth and the increase in upper face (biocular) width in the first 2 years of life.

Head circumference was the only somatic measurement that correlated with upper face (biocular) width and vertical face height measurements prior to surgery. There was also a correlation between head circumference and upper face width at age 2 years. This is not unsurprising and would suggest that upper face size is maintained in proportion to head size, over time. This might have implications for assessing size differences between cleft and control groups when comparing differences in facial dimensions. It may be more appropriate to case-match on head circumference, rather than weight or height.

Total vertical face height increased to a greater extent in the first year, and by approximately half this initial amount in the second year, which was consistent with the pattern of growth in non-cleft children of similar age (White, 2005). Although this suggests a neural growth pattern, total vertical growth of the face correlated with neither head, nor body growth.

Vertical growth of the upper face in this study followed a normal growth pattern in both cleft groups (White, 2005). This strongly correlated with head circumference growth up to age 2 years. This would support the theory that growth of the maxilla is influenced by an advancing frontal bone, actively growing brain, the cartilaginous nasal capsule and nasal septum during this period. Furthermore a maxillary vertical 'push' is exerted by concurrent growth of the eyes (Markus et al. 1992a). The direction of upper face growth had a greater horizontal component than vertical component in the first 2 years of life, since upper face (biocular) width increased by a greater amount than upper face height.

The inability to demonstrate a correlation between growth in upper face width or total face height and head circumference growth, despite both these facial dimensions displaying a normal neural pattern of growth, is worthy of further discussion. This lack of association was also shown in non-cleft children by White (2005). Some believe that head circumference in children with unilateral clefts is more stable than weight or height, and less influenced by health or other somatic changes (Felix-Schollart et al. 1992). However, as the majority of cleft children in this study were of low weight and had smaller than average head circumference prior to surgery, it would appear that although general growth and development in these children was impaired, facial development proceeded in a normal manner. Results tend to support the theory that, in common with brain development, facial development is unlikely to be affected by fluctuations in general health and well-being.

UCLP children in this study had demonstrable unilateral telecanthus on the cleft side (increased en-n distance) before surgery, which contributed to upper face asymmetry. Furthermore, an apparent difference in the amount of longitudinal growth in en-n dimensions on the cleft and non-cleft sides did not reach statistical significance. However, upper face asymmetry was present in both cleft groups and improved dramatically around the time of lip / nose repair. Upper face asymmetry persisted only in the UCLP group, although this continued to improve with time. This might be explained in part by localised changes in the cleft side maxillary segment. Ishiguro et al. (1976) reported a tendency to hypertelorism in young UCLP infants which was not evident on PA cephalometric films by 3 years of age. Han et al. (1995) suggested that this might even persist up to age 8 years. Jain & Krogman (1983) who's study was similar to Ishiguro's also suggested that larger maxillary widths in UCLP might reflect segmental translocation. Zemann and others favour the theory of segmental translocation, rather than an alternative theory of maxillary hypoplasia (Zemann et al. 2002; Breitsprecher et al. 1999). Three-dimensional asymmetries of the infraorbital rim and nasal region were attributed to dislocation of the cleft side maxillary segment; a postero-lateral translocation being most common. In this study, results suggest that primary lip / nose repair improved muscular imbalance which resulted in a favourable growth direction and reduction in upper face asymmetry in all three dimensions. This may be a temporary early effect of surgery, which disappears as growth of the upper face normalises (Ishiguro et al. 1976, Han et al. 1995). The study comparing early craniofacial growth in UCLP and UCL infants of Hermann et al. (2000) was unable to demonstrate this, as they considered subjects at age 2 months and again at age 22months, therefore missing out the period in which the greatest change occurred (i.e. up to the age of 1 year).

5.8.2 Nose Growth

Growth of the nose did not differ in UCL or UCLP and was not dissimilar to the nasal growth pattern in non-cleft children (White 2005). Displacement of the nasal tip in cleft subjects continued to improve with growth. Nose dorsum length did not start to increase until the age of 1 year and this has also been shown to be normal (White 2005; Farkas et al. 1992). Therefore, primary surgery did not appear to have a detrimental affect on vertical or horizontal nose growth up to 2 years of age. Kim et al. (2004) similarly described no interference of nasal growth with primary nasal correction, in Asian subjects with cleft lip / nasal deformity compared to controls up to age 3 years. Primary nasal correction has been

demonstrated to exert no detrimental effect on nasal growth in the long term (McComb 1985; McComb & Coghlan 1996; Salyer et al. 2003). However it is also recommended by these authors that full assessment is delayed until after the adolescent growth spurt.

The amount of post-surgical growth in nose width and length was greater than the amount of growth in the protrusion of the nasal tip, which may explain persistance of a more flattened nasal tip in the cleft children in this study. In non-cleft children, it has been reported that growth in protrusion of the nasal tip is greater than growth in nose width, which results in forward and downward growth of the nasal tip (White 2005). The major part of nasal growth occurs between the ages of 7-12 years, and so nasal changes should be reassessed in the both cleft and non-cleft children at that time (Farkas et al. 1992).

5.8.3 Nasolabial Growth

It has been demonstrated that it is possible to detect differences in treatment outcome in relation to nasolabial development at age 5 years, using the soft tissue profile on cephalometric radiographs alone (MacKay et al. 1994). Although regarded as a valuable outcome measure (Molsted et al. 1992; Sadowsky et al. 1973; Smahel & Mullerova 1986), it is difficult to justify serial radiographs that have a poor diagnostic yield in young children, for this purpose. Furthermore, it has been shown that in cleft children, 'midline' landmarks are not coincident in the same plane (Garrahy 2003), and so evaluation in the sagittal plane may be subject to error. In the present study, the full 3D nature of the landmark's relationships to each other was utilised. Three angles were used to evaluate antero-posterior soft tissue development of the nasolabial area: nasal tip angle, nasolabial angle and protrusion of the upper lip, relative to the nasal base. Flattening of the nasal tip angle was apparent before surgery in UCL and UCLP infants (Hood et al. 2004) and the degree of flattening did not change with growth after surgery. This angle also did not change with growth in non-cleft children over the same 2 year period (White 2005). Nasolabial angle and the protrusion of the upper lip, relative to the nasal base did not change with growth in UCL or UCLP children, yet in non-cleft children, a slight decrease occurred over 2 years (White, 2005). It is likely, however that the magnitude of this difference is clinically negligible. It would appear that any potential detrimental effect of surgery on antero-posterior soft tissue nasolabial development was not evident by age 2 years. In this respect, there was no evidence of the lip 'tightness' as reported in 5 year olds (Zhu et al. 1994; Bardach et al. 1984) in this small sample of UCL and UCLP children at 2 years of age.

5.8.4 Alar Growth

Alar growth continued on the cleft and non-cleft sides of the nose, but there were no further improvements in alar wing angle. Symmetrical growth of the nasal rim was confirmed by examining changes in nasal rim asymmetry. In the non-cleft face, asymmetry tended to reduce with growth up to the age of 2 years except in the nasal rim (White 2005). Evidence suggests that improvements in nasal form obtained by primary nasal surgery persist into adulthood, but residual asymmetry is unlikely to improve with growth (McComb & Coghlan, 1996). This study confirms that after primary correction of the nasal rim, the degree of continued improvement that can be expected with growth up to age 2 years is negligible and this emphasises the importance of achieving symmetry by surgical or by non-surgical means. Pre-surgical nasoalveolar moulding (NAM) techniques have shown good results at age 4 years (Maull et al 1999) and age 6 years (Benunn et al. 1999). These may offer a solution for improving nasal rim symmetry further, although some advocate NAM more as an adjunct to primary surgery, rather than as a definitive treatment for nasal asymmetry (Liou et al. 2003).

5.8.5 Columella and Nostril Growth

Growth of the columella in the first 2 years of life was negligible in cleft children, and this was also true in non-cleft children (White 2005). As columella dimensions were shown to be normal prior to surgery (Hood et al. 2004) it would not be unreasonable to assume that these might also be close to normal at 2 years of age. Simple linear analysis does not give a clear understanding of how these dimensions relate to each other. This is highlighted by the fact that a degree of abnormality of shape was evident at age 2 years. This might be explained by residual malposition of the columella, as previously demonstrated (Figs 5.1 & 5.2). A septal deviation that is not fully corrected at the time of primary repair is unlikely to improve with time (McComb & Coghlan 1996). Any new therapy or surgical modification designed to improve columella dimensions may be assessed in the first 2 years of life, without the clouding effects of growth. However, full evaluation should be delayed until nasal growth is complete.

A small amount of growth of the nostrils occurred in the first 2 years of life in UCL and UCLP children and can be considered normal for this age group (White 2005). Interpretation of changes in the nostrils using linear measurements is difficult, as it is hard to visualise the relationship between them. There were differences in the amount of growth

in certain nostril dimensions on the cleft and non-cleft sides, pointing to a potential for subtle change in nostril shape and symmetry, if this were to continue over time.

5.8.6 Philtrum Growth

After surgery, philtrum length appeared to normalise on the cleft side. It has been suggested that the repaired cleft lip retains the configuration and length determined at the time of repair (Saunders et al. 1986). This study indicates that growth in length occurred, albeit for a short period after lip repair, but philtrum width did not grow. Changes in philtrum dimension did not affect residual philtrum asymmetry. According to Farkas, the cutaneous lip is 75% of the adult size by the age 3 months and 83% by the age of 2 years, i.e. lip growth is very slow in early childhood (Farkas, 1992). It is not surprising therefore that the lip form 'determined by primary surgery' did not alter much with growth in the first 2 years of life. Therefore, the changes in the philtrum length may have simply resulted from restoration of normal muscle balance after lip repair, rather than a growth effect, although this cannot be entirely ruled out.

5.9 Distribution of Facial Asymmetry in UCL and UCLP

Early pilot work from this study (Hood et al. 2003) showed that the degree of asymmetry varied according to facial feature and it was possible to localise these asymmetries, and quantify the effects of surgery and growth of the face (Appendix 10). The present study developed this further and is the first to describe how asymmetry is distributed in the cleft face and to quantify the relative contribution of feature asymmetry to residual facial and nasolabial asymmetry. Differences were identified in the pattern of distribution of asymmetry across facial regions and nasolabial features, between UCL and UCLP infants. In general, UCLP infants displayed more asymmetry than UCL infants and age-matched non-cleft controls, prior to primary surgery to repair the cleft.

UCL facial morphology was characterised by dominant residual lip region asymmetry immediately after surgery and at age 1 year, but at age 2 years, no distinction could be made between residual asymmetry in lip or nasal features. In the UCLP group, despite more elevated lip and philtrum asymmetry prior to surgery, residual asymmetry remained higher than in the UCL group and was distributed more uniformly across facial regions and nasolabial features.

Upper face asymmetry in the UCL group was similar to controls after primary repair, but persisted in the UCLP group up to 2 years of age. This distinct difference between cleft groups at 2 years, was only detected by comparing asymmetry scores, and this reiterates the greater sensitivity and more appropriate application of 3D methods to the study of asymmetry.

Surgical correction of nasal base asymmetry was successful and dramatic improvement was demonstrated in both cleft groups, which had a similar degree of post-operative asymmetry. However, residual asymmetry was significantly greater in the UCLP group at age 2 years than in the UCL group which appeared to be associated with a slight deterioration in initial improvement gained in UCLP combined with continued improvement in UCL nasal base asymmetry with growth, however the changes over time in individual cleft groups were not significant. This is unlikely to be a result of asymmetry in the amount of growth as there was no evidence of statistically significant differences between the cleft and non-cleft nasolabial dimensions. However, asymmetry in the direction of growth of the nasal cavity, as others have demonstrated in UCLP infants by cephalometry, could not be ruled out (Ishiguro et al 1976). Residual asymmetry of the alar base is a relatively common problem. Mulliken & Martinez-Perez (1999) reported that a third of their series of 105 patients with unilateral cleft lip nasal deformity who were treated with the rotation advancement technique needed alar base revisions, and so the reason for the significant difference in nasal base asymmetry between cleft groups may be entirely related to the surgery. The Millard rotation advancement may not fully correct nasal base asymmetry for a number of reasons such as lack of bone foundation or failure to free the alar base sufficiently. Alar base lateral creep has also been recognised (Millard 1976) and nasal septum shift due to unbalanced muscle forces. Methods that pay particular attention to the functional repair of the nasolabial muscles, such as the Delaire reconstruction are claimed to produce better nasal symmetry than the Millard repair at age 4-5 years (Horswell & Pospisil, 1995). McComb demonstrated that poor placement of the alar base at the time of primary repair did not correct itself until after alveolar bone-grafting (McComb, 1985). Further study of this sample is required to ascertain whether the nasal base symmetry further deteriorates beyond the age of 2 years.

5.10 Facial Feature Residual Shape Deformity at 2 years

There is much interest in quantifying the shape of facial features to determine how well the goals of surgical correction or non-surgical interventions have been achieved (Maull et al. 1999; Yamada et al. 2002a; 2002b). Studies of soft tissue morphology outcomes in children with UCL as a distinct group are largely absent from the literature, as much research is primarily concerned with UCLP subjects. This may also be partly because of an assumption that a cleft of the lip and secondary palate is a more 'severe' defect, and thus poorer outcomes are more likely than in UCL infants (Markus, 1992). For facial soft tissue morphology, however, this has not been proven.

New outcome measures were developed, which preserved the 3D properties of the facial feature in question, and has not been previously reported. Residual shape deformity or 'distance from normal', was measured as the Procrustes distance to a control mean shape at 2 years of age, for each individual cleft child. Results revealed that only nostril shape was more abnormal in UCLP children than in UCL children. Unfortunately, the PDFN score technique considers both nostrils together and so it is not possible to comment on the exact nature of the abnormality. UCL and UCLP children had a similar degree of residual deformity in the nasal rim shape and in the shape of the philtrum at 2 years of age. When considered with the previous finding of no difference in nasal rim asymmetry between cleft types at 2 years, this might suggest that the same amount of abnormality remained in the nasal rim, regardless of whether a nasal surgical procedure was performed or not. Whilst philtrum symmetry was improved with corrective surgery, particularly in the UCLP group, it did not necessarily achieve a 'normal' shape in either UCL or UCLP children.

5.11 Relationship of Initial Cleft severity and Outcome

In terms of soft tissue morphology, this study confirms that significant facial deformity exists in UCL as well as in UCLP children, prior to surgical correction. When judging the early success of a particular surgical or non-surgical intervention on soft tissue morphology, there is an argument for pooling UCL and UCLP data and stratifying by clinical 'severity' of disruption of the facial features. The subjects in this study were categorised according to an embryological classification, in other words, according to whether they had a cleft of the secondary palate. This appears to have little relevance to the

configuration of the soft tissues. The majority of the UCL group had an incomplete cleft lip with varying degrees of nasal deformity, whilst the UCLP group were predominantly complete clefts of the lip and nose. In terms of soft tissue disruption, the UCL children represented a 'milder' group and the UCLP children a more 'severe' group.

Until now, little was known about the potential influence of the initial severity of a cleft on the morphological development of soft tissues of the face. Mortier et al. (1997) reported a moderate correlation between pre-operative severity ratings of soft tissue deformity and post-operative outcome, however, the interval between pre and post-op ratings varied and the method was subjective. Hurwitz et al. (1999) demonstrated a weak correlation between initial severity and outcome at 5 years of age. However their limited assessment used a composite score of different abnormalities in both lip and nasal features, derived from 2 photographic views. In the present study, nasal and lip features were assessed separately. Surprisingly, no correlation could be demonstrated between any of the measures of severity of nasal deformity devised (ratios and Asymmetry Scores) and shape outcome in any aspect of the nose at age 2 years. Moreover, none of the asymmetry scores prior to surgery, correlated with asymmetry outcome at 2 years. The reasons for the failure to demonstrate a relationship are unclear. It may be due to the relatively small number of subjects examined, however the study group was the same size as that in Hurwitz et al. (1999). Although the cleft infants received the same lip repair, not everyone had a McComb primary nasal repair. This may have had an effect, in that the subjects receiving the primary nasal repair were assumed to have had a worse nasal defect (determined by the surgeon). Equally, the subjects who did not have a primary nasal repair were assumed to have had less severe nasal defects. Given that there was no correlation in any aspect of nasal form, this may suggest that some of the 'less' severe cases had in fact a more severe underlying defect which influenced their outcome. It may also mean that surgical correction produced an acceptable nasal shape, irrespective of the initial degree of severity. This warrants further investigation in a larger study sample. Moreover, the factors influencing the surgeon's decision to operate on the nose or not should be taken into consideration.

The only measure of initial cleft severity that demonstrated a correlation with outcome at 2 years was philtrum height discrepancy. There was a moderate correlation with residual philtrum shape deformity and a strong correlation with lip shape deformity at age 2 years. Surprisingly, there was no corresponding correlation between philtrum asymmetry pre-operatively and at age 2 years. This may be explained by inadequacy of sample size, or the

fact that it is possible to have a symmetric, but still abnormally shaped philtrum i.e. too long, too short or malpositioned. Results favour the latter, but warrant further investigation.

The common landmarks in philtrum shape and lip shape define the shape of the Cupid's bow. A greater discrepancy in the vertical height on either side of the philtrum means that it is more difficult to achieve symmetry of the philtral peaks by the classic Millard repair. This has been recognised by Millard himself and he and several others have introduced modifications to overcome this problem (Millard 1968, 1976; Mohler 1987; Cutting 2003). It follows that initial deficiency in available tissue should have some impact on outcome if it means that surgery is more challenging. Another possibility is that greater scar contraction may occur because of the need for more complex surgical manipulation. Regardless of the true nature of the association, it is important to recognise that this has implications for UCL as well as UCLP cases. Results of this investigation suggest that the Millard repair was least successful in achieving a 'normal' 3-D Cupid's bow shape in cases where a large vertical discrepancy existed in the philtrum. The advantages of modifications to surgical technique proposed by others could be tested objectively using the C3D^{TM} system. Stratification of cases by philtrum severity and comparison with this study sample may yield the most informative results.

5.12 Recommendations and Future Research

Advances in imaging technology have now superseded the prototype system used in this investigation. It is currently possible to build high quality 3D models using only digital colour cameras. Stereo-matching can be preformed on high-resolution colour images, simplifying the equipment requirements by removing the need for additional flashes and texture pattern projection. This will reduce even further the time taken to acquire images and will be a major advantage in the imaging of young subjects. The disadvantage is that there is a greater demand on computational power and 3D model building is still limited by PC processor speed. However, as information technology continues to progress, so will the area of 3D imaging.

At present, the number of steps from acquisition of images to useful data output and the considerable burden on operator time are the greatest hurdle to the translation of this technology to the clinical setting. Automatic landmark extraction has been recommended and is in general use in a number of systems (Yamada et al. 1998, 1999; Naftel &

Trenouth, 2004) and this would significantly enhance the C3D™ system. In addition to the obvious benefits such as reduction of operator time, it would also reduce the errors of the method. With these enhancements, 3D-imaging could become an integral part of routine assessment and monitoring of facial development for all cleft cases throughout Scotland and the UK.

This thesis was concerned with a landmark-based analysis of linear distances and shape asymmetry in the face. It is now possible to generate surface curves between landmarks to map surface contours between anatomical points, and to generate facial surface meshes. These can be used to measure shape change over the entire facial surface, particularly in areas where few natural landmarks exist. These techniques can be used to measure contour changes and volume changes and have many applications in the study of facial phenotype in syndromes, in cosmetic surgery and in maxillo-facial surgery.

The characterisation of facial development and somatic variability in UCL and UCLP is a starting point for deciding what type of variability may be important. The cleft subjects in this study could be further compared with a shape 'norm' of matched non-cleft children in order to explore the variability in the outcome for facial morphology at 2 years of age. Principal component analysis, a geometric morphometric technique that explores variation in shapes, could be applied to determine exactly how each cleft individual deviates from the normal population. Visual representations of facial contours can be generated to display individual cleft cases against a norm. In this way, abnormalities may be readily appreciated and quantified and this would be of great benefit to cleft surgeons to facilitate audit of surgical results and future research.

In addition to quantifying the degree of asymmetry, the asymmetry score can be decomposed into the three properties of asymmetry, namely orientation, positional and intrinsic asymmetry (Bock & Bowman, 2005). This may be useful in determining the exact nature of the asymmetry in a face.

An area for further study might involve a more detailed examination of the landmarks themselves and comparison to a control norm. At the landmark level, the asymmetry score method can also explain the contribution that certain anatomical points make to the overall asymmetry of the region of interest. However where bilateral landmarks are concerned, it is difficult to discriminate between sides. Nevertheless, this could be easily overcome by comparison with the same configuration in non-cleft individuals.

An interesting area for future research is the relationship between subjective assessment of asymmetry / attractiveness / deformity and objective measurements. Shape, asymmetry and relative spatial position cannot be specifically measured by rating-panel assessment methods and there is a lack of correlation between methods that measure specific facial features and ratings of appearance (Russell et al. 2001). The data from the subjects in this study could be compared to data from a panel assessment of subject appearance, which would allow exploration of the relationship between objective measurement and subjective perceptions of deformity.

A database of facial soft tissue measurement in infants with unilateral clefts is now established which could be utilised as a benchmark for cleft management in Scotland. This should also be expanded to include bilateral cleft types and isolated cleft palate cases. The cohort in this study should be followed up to see how trends in facial growth and asymmetry continue through childhood and adolescence, in accordance with the recommendations of CSAG and ethos of the Eurocleft projects.

6 Conclusions

The C3D™ system is particularly apt for objective early assessment of facial soft tissue morphology in young children. It provides a possible solution to the problem of standardization of methods of interpretation of findings before surgery and during follow-up. The non-invasive, computer-assisted, indirect anthropometry technique used in this thesis overcame many of the limitations of direct measurement of infant faces, and had the added benefit of a 3D co-ordinate based analysis.

Accurate, repeatable soft tissue measurements were used to quantify facial shape and size characteristics in cleft infants and distinguish between UCL and UCLP infants.

Differential growth was demonstrated between facial features and within some facial features. In particular, the columella, nostrils and philtrum did not grow significantly after surgery, although this was would be considered normal in the age group studied.

Facial growth in children with UCL and UCLP was independent of the head and body growth.

The presence of a cleft of the secondary palate accentuated the amount of soft tissue disruption by the cleft in the lip and nose, but did not alter the pattern of disruption.

Primary lip / nose repair had no detrimental effect on early growth and development of the facial features. Palatal surgery had no discernable effect on facial soft tissue growth at age 2 years.

Primary lip / nose repair had a beneficial effect on facial morphology in terms of reducing asymmetry and was most successful in the improving philtrum and nasal base symmetry, less successful in improving the nasal rim asymmetry. A possible early beneficial effect of cleft repair remote from the surgery site was noted in the reduction of Upper face asymmetry in the first year of life.

After lip/ nose repair, residual asymmetry in the facial features is unlikely to change by age 2 years, despite increases in size with growth. There is a need to continue to follow this cohort to see how their soft tissues change in future with differential growth.

Facial morphology outcomes for UCL and UCLP children in this study were generally similar at 2 years of age, despite initial differences in facial form. However nasal base asymmetry, upper face asymmetry and residual nostril shape deformity were significantly greater in UCLP children at 2 years of age, than in UCL children. These shape differences were not detectable by measurement of facial dimensions alone.

Nasal shape outcome reflects the success achieved by surgical design and skill and does not appear to be associated with initial deformity in the nose. Philtrum deformity and lip deformity at age 2 years may be related to initial deformity in terms of philtrum height discrepancy.

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Appendices

Appendix 1 Parent Information and Consent Form & Follow up letters

Dept Child Dental Care
378 Sauchiehall St
Glasgow
G2 3JZ

How Does Your Child's face Grow?

November 27, 2005

Dear Parent

My name is Kay Hood and I am writing to you with permission from your Hospital Doctor, Mr Ray / Mr Amad, to ask if you would be kind enough to take part in a study to look at how the face of a child develops.

Children with clefts of the lip and / or palate usually have surgery within their first year of life. There is very little information available to parents and the specialists involved in providing care for children with clefts, about how a baby's face grows after surgery.

We have a new way of recording the shape of the face in **3D** using digital cameras, linked to a computer. With your help, we will be able to build computer programmes to measure and predict the appearance of the face after different types of surgery. We need to photograph as many young cleft children in Scotland as possible, therefore we would be grateful if you would consent for your child to have pictures taken **4** times over the **next 2 years**, at age:

- **3 months**
- **6months**
- **1 year**
- **2years**
-

The study will benefit all children with clefts and is supported by **CLAPA**, and funded by the **Scottish Office.**

The cameras are in **Glasgow Dental Hospital** and the **Royal Hospital for Sick Children, Yorkhill, Glasgow.** Children will also be weighed and measured at each visit and none of the procedures involve any discomfort for you or your child. All information recorded is strictly confidential and will be used for research purposes only. Travel expenses are available and we will take up no more than an hour of your time.

Your child's medical care will not be affected if you decide not to participate in the study.

If you would like further information please contact Kay Hood (Specialist Paediatric Dentist) at Glasgow Dental Hospital & School: **0141 211 9699 (3D answering machine);** c.hood@dental.gla.ac.uk**, mobile: 079XX XXX XXX**

Please complete the consent form and return it in the envelope provided. Your time is very much appreciated.

Sincerely

Kay Hood
Lecturer / Specialist in Paediatric Dentistry

West of Scotland Cleft Research Team

CONSENT TO PARTICIPATE
Please return in envelope provided

I.....

of.....

.....

Telephone contact number.....

give permission for my child.....

to be enrolled in the 3D imaging project.

I understand that pictures of my child will be taken 4 times over the next 2 years. In addition, their weight, height and head circumference will be recorded each time.
I understand that participation in the study is entirely voluntary and I may withdraw at any time.
I understand that the images collected may be used in presentations of this work and publications.

Signed.....Date.....
Mother/father/ legal guardian (delete as appropriate)

Department of Child Dental Health
University of Glasgow Dental School
378 Sauchiehall Street
Glasgow G2 3JZ

How Does your Child's Face Grow?

Dear Parent

Just a note to remind you that it's time for ..... to have 3D images taken. An appointment has been arranged for

Date.....

Time.....

in the Royal Hospital For Sick Children, Yorkhill, Glasgow

Please come to the Main Entrance and take the lift to **level 1**. Follow the signs to **Medical Illustration**. Continue on past and the **3D Imaging** room is the last door on the **Right** at the end of the corridor. The visit should take no longer than 45 minutes and we'll weigh and measure ..... too. Please bring your red Child Health Book with you, if you have one.

If you are unable to attend or have any questions please contact me as soon as possible on: **0141 211 9699 (answering machine - please state "Message for Kay Hood"). If you have trouble finding us on the day, my Mobile number is 079XX XXX XXX.**

Many Thanks and I look forward to seeing you soon.

Kindest Regards

Kay Hood
Lecturer / Specialist in Paediatric Dentistry

West of Scotland Cleft Research Team

Department of Child Dental Health
University of Glasgow Dental Schoo
378 Sauchiehall Street
Glasgow G2 3JZ

How Does your Child's Face Grow?

Dear Parent

I need to organise a date for .....to come to **Glasgow Dental Hospital** or **RHSC Yorkhill** to have 3D images taken in the next few weeks.

Your support for my project so far has been invaluable. Please help me to complete my study by arranging an appointment as soon as possible. I will organise train tickets / parking vouchers, as required.

Please leave a current contact telephone number on the answering machine and I'll call you back:

0141 XXX XXXX (answering machine for Kay Hood)
Mobile: 079XX XXX XXX.
email: c.hood@dental.gla.ac.uk

Many Thanks and I look forward to seeing you again soon.

Kindest Regards

Kay Hood
Lecturer / Specialist in Paediatric Dentistry

Appendix 2 Ethical Approval

Yorkhill Research Ethics Committee
Room 1 Harley Street
Yorkhill NHS Trust
Glasgow
G3 8SJ

Tel number 0141 201 0728
Fax number 0141 201 6976

BH/EM

10 March 2000

Ms Catherine Anne Hood
Glasgow Dental Hospital
Sauchiehall Street
GLASGOW

Dear Miss Hood

P7/2000 Three Dimensional Analysis of Orofacial Malformations in Infants.

Thank you for forwarding your proposal to the Yorkhill Research Ethics Committee.

Your study was approved subject to clarification and amendments.

It is unclear how and by whom parents will be approached to take part in the study. If parents are going to be approached in the Yorkhill hospitals then a Yorkhill consultant supervisor is necessary. The committee would wish assurance that the surgeons who treat the patients agree to this study.

The patient information sheet should be on Yorkhill headed paper the information and consent sheet should be separate. The names of the researchers should be on the patient information sheet which should start with an invitation to take part in the study ie the 6th paragraph in the current patient information sheet should be the first.

The information sheet should outline what will happen to the pictures, whether they will be kept or destroyed after the study. (the committee would wish to know how the researchers propose to ensure that they act in accordance with the Data Protection Act.)

Parents should be assured that they do not have to take part in the study and that declining to do so will not affect their child's care. If it is proposed that the pictures will be shown to anyone outside the clinical team and in particular at public meetings then specific consent for this should be sought from the parents It should be made clear to parents that their child may be recognisable.

One copy of your amendments forwarded to me will be sufficient.

With kind regards

Yours sincerely

Dr B Holland
Secretary Yorkhill Research Ethics Committee

Appendix 3 Socio-economic Status of Scottish population at 1991 census

Socio-economic Status of Scottish population at 1991 census (Source: McLoone 1994).
Distribution of the Scottish population by Deprivation Category (DEPCAT) 1991

DEPCAT SCORE	Scottish Population	%	Postcode Sectors	%
1	305,725	6.1	94	9.4
2	688,018	13.8	171	17.1
3	1,090,483	21.8	226	22.6
4	1,270,597	25.4	231	23.1
5	741,664	14.8	125	12.5
6	567,492	11.4	97	9.7
7	334,285	6.7	57	5.7
Total	**4,998,264**	**100**	**1001**	**100**

Appendix 4 Table of Surgical procedures

Surgical procedures performed in study sample of UCL and UCLP children [continued overleaf]

ID	Cleft type	Lip	Nose	Nasal Floor	Primary Hard palate	2ndry Hard palate	Soft palate
3 month cohort							
1	UCLP	Millard	McComb	Single layer closure	*	Veau Wardill	Intravelar veloplasty
2	UCL	Millard	McComb	*	*	*	*
3	UCL	Millard	Other	*	*	*	*
4	UCL	Millard	*	*	*	*	*
5	UCLP	Straight line Manchester	McComb	Single layer closure	*	Von Langenbeck	Furlow
6	UCL	Millard	*	*	*	*	*
7	UCLP	Millard	McComb	2 layer closure	Alveolus Perioplasty	No releasing incisions	Furlow
8	UCLP	Millard	*	*	*	*	Radical muscle dissection
9	UCL	Millard	*	*	*	*	*
10	UCLP	Adhesion	McComb	*	*	Veau Wardill*	Intravelar veloplasty
11	UCLP	Millard	*	*	*	*	Radical muscle dissection
12	UCL	Millard	McComb	Single layer closure	*	*	*
13	UCLP	Millard	McComb	*	Vomer flap	Veau Wardill	Intravelar veloplasty
14	UCLP	Millard	McComb	*	*	*	Radical muscle dissection
15	UCL	Millard	Other	2 layer closure	*	*	*
16	UCL	Millard	*	*	*	*	*
17	UCL	Millard	McComb	*	*	*	*
18	UCL	Millard	McComb	*	*	*	*
19	UCLP	Millard	McComb	Single layer closure	2 layer closure	Veau Wardill	Intravelar veloplasty
20*	UCLP	Millard	McComb	Single layer closure	N/A	N/A	N/A
21	UCLP	Millard	1y rhinoplasty	*	*	Von Langenbeck	Furlow
22	UCL	Millard	McComb	2 layer closure	*	*	*
23	UCL	Millard	McComb	*	*	*	*
24	UCL	Millard	McComb	*	*	*	*
25	UCLP	Millard	*	Single layer closure	Vomer flap	*	Furlow
26	UCL	Millard	*	*		*	*
27	UCL	Millard	*	*	*	*	*
28	UCL	Millard	McComb	*	*	*	*
29	UCLP	Millard	McComb	*	Vomer flap	*Von Langenbeck	Intravelar veloplasty

Surgical procedures performed in study sample of UCL and UCLP children [continued]

	Cleft type	Lip	Nose	Nasal Floor	Primary Hard palate	2ndry Hard palate	Soft palate
3 month cohort (continued...)							
30	UCL	Millard	*	*	*	*	*
31	UCL	Millard	McComb	*			
32	UCL	Millard	*	*	*	*	*
34	UCLP	Millard	McComb	Single layer closure	*	Veau Wardill	Intravelar veloplasty
35	UCLP	Millard	McComb	*	*	Veau Wardill	Intravelar veloplasty
36	UCLP	Millard	McComb	*	2 layer closure	Von Langenbeck& unilateral releasing incision	Intravelar veloplasty
37	UCLP	Millard	*	*	*	Von Langenbeck	Furlow
38	UCL	Millard	*	*	*	*	*
1 year old augmentation cohort							
101	UCL	Millard	1y rhinoplasty	*	*	*	*
102	UCLP	Millard	McComb	2 layer closure			Furlow
103	UCLP	Millard	McComb	Single layer closure	*	Veau Wardill	Intravelar veloplasty
104	UCLP	Millard	McComb	2 layer closure	2 layer closure	Von Langenbeck	Furlow
2 year old augmentation cohort							
201	UCLP	Millard	*	*	*	Hard palate closure no details	Soft palate closure no details*
202	UCLP	Millard	McComb	Vomer flap	*	Von Langenbeck unilateral release	Radical muscle dissection*
203	UCLP	Millard	*	*	*	no releasing incisions	Radical muscle dissection
204	UCLP	Millard	*	*	*	Von Langenbeck	Furlow
205	UCLP	Millard	McComb	*	Vomer flap	no releasing incisions	Radical muscle dissection *
206	UCL	Millard	*	*	*	*	*
207	UCLP	Millard	McComb	Single layer closure	*	Veau Wardill	Intravelar veloplasty
208	UCL	Millard	McComb	*	*	*	*
209	UCLP	Millard	*	*	*	Von Langenbeck	*