The Factors Which Affect Mid-Facial Growth in Unilateral and Bilateral Cleft Lip and Palate Patients

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Abstract

Aims

The aim of this study was to ascertain which factors influence mid-facial growth, when evaluated with the 5-year index.

Method

This was a retrospective cohort longitudinal study. One hundred and eighty-seven unilateral and bilateral cleft lip and palate patients that had undergone cleft lip and palate surgery, from 2000 to 2009, at [redacted] were included. There were two different but consistent techniques being used for the last 13 years. Factors investigated were surgical technique, severity of the cleft, anomalies of deciduous lateral incisors, and presence of bone in the cleft. Clinical notes, the cleft database, radiographs and dental study models were used. Comparisons were made using chi-squared tests at $p<0.05$.

Results

Technique B had significantly worse mid-facial growth for unilateral and bilateral cleft lip and palate patients ($p<0.001$; $p=0.045$) and a significantly higher number of cases with bone forming in the cleft ($p=0.014$; $p=0.005$). The severity of the cleft had a significant effect on the mid-facial growth ($p=0.018$; $p=0.031$). Anomalies of

deciduous lateral incisors did not have a significant affect. A trend was present between the presence of bone and worse mid-facial growth.

Conclusions

Surgical technique, the severity of the cleft and the presence of bone have a significant effect on mid-facial growth.

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Contents

Chapter 1

Literature review

1.1 Incidence of cleft lip and palate

Cleft lip and palate is the most common craniofacial abnormality. It is reported by Coupland and Coupland, (1988) and Gorlin et al, (1971) that non-syndromic cleft lip and palate occurs in approximately every 1 in 700 live births in the United Kingdom. Of these, 40% are classified as unilateral cleft lip and palate and 10% as bilateral cleft lip and palate. Gorlin et al, (1971) also recorded clefts as being more common in Indian and Oriental ethnicities, at an incidence of 2.3 per 1,000 live births. The lowest incidence was found in Afro-Caribbean ethnicities at 0.6 per 1,000 live births. Coupland and Coupland, (1988) had assessed children that were born with cleft lip with or without palate and isolated cleft palate from 1973 to 1982 in the Trent region of the United Kingdom. Of the 930 children born during this period, 39% had isolated cleft palates and 61% had cleft lip with or without cleft palate. There were more females than males in the isolated cleft palate group, with 55% being female and 45% being male. The opposite was true when assessing the cleft lip with or without palate group. A majority of this group, at 62%, was male whereas females formed 38% of this group. Between the period 1973 to 1982, the overall incidence of cleft lip with or without palate was recorded as 1.12 per 1,000 live births and the incidence of cleft palate only was recorded as 0.70 per 1,000 live births. The seasonal variation of cleft births was also examined. It was observed that a higher number of children with cleft palate only were born in the three month periods from July to September and August to October. There were a reduced number of births in the three month periods from February to April, March to May and April to June. In the cleft lip with or without palate group, there were a reduced number of births in the three month periods from April to June and May to July, whereas in the winter months from

November to January and December to February, there was an increased number of births.

Bister et al, (2010) conducted a study to examine the incidence of facial clefting in the Cambridge area of the United Kingdom, from 1993 to 1997. During this period, there were 22,765 live births of which 21 had facial clefts. The incidence of facial clefts in live births was 1 in 1084. In total there were 23,577 live births, still births and terminations, of which 30 had facial clefting. 10% of these had an isolated cleft lip and 3% had an isolated cleft lip with other abnormalities. 30% had an isolated cleft lip and palate and 23% had an isolated cleft lip and palate with other abnormalities. 17% had an isolated cleft palate and 17% had an isolated cleft palate with other abnormalities.

Owens et al, (1985) examined data of patients with facial clefts between 1960 and 1982, which covered the areas of Liverpool, Bootle, Sefton North, Sefton South, St Helens, Knowsley and Wirral. During this period, there were 544 children with facial clefts of the 325,727 births. Of these 544 children, 88 were excluded from the study as they had a syndrome and multiple congenital anomalies. After this exclusion, the incidence of facial clefts was 1.4 every 1000 births. 30% of the children had a cleft lip only, 36% had a cleft lip and palate and 34% had a cleft palate. There were more males in the cleft lip group with a ratio of 1.52:1 and the cleft lip and palate group with a ratio of 1.98:1. In the cleft palate only group there was a 1:1 ratio for males and females.

1.2 Formation of the palate

The maxilla, mandible and the dentition is derived from the first pharyngeal arch. At four weeks in utero the frontonasal process, the paired maxillary processes and the paired mandibular processes are present. The frontonasal process subsequently enlarges and forms median and lateral nasal processes. The primary nasal septum and the primary palate are derived from this frontonasal process. The primary nasal septum separates the nasal cavities by the sixth week in utero (Moxham, 2003). The oral cavity is divided into a small oral cavity, inferiorly to the primary palate, and a larger oronasal cavity, posteriorly to the primary palate. Between the sixth and eighth week in utero, the secondary palate forms through the movement of the palatal shelves. The two lateral palatal shelves develop posterior to the primary palate. The oronasal cavity is divided by a secondary nasal septum. By the seventh week in utero, the tongue fills the oral section of the oronasal cavity. During the eighth week in utero, the vertical palatal shelves lift to lie horizontally following the tongue moving to lie inferiorly into the stomodeum. The fusion of the lateral palatal shelves occur after the palatal shelves contact and the medial edge epithelia fuse to form a midline epithelial seam. This seam later degenerates to allow mesenchymal continuity across the palate. The fusion of the lateral processes takes approximately two weeks and is completed by the tenth week in utero.

Failure of the lateral processes to rotate horizontally from the vertical position, where they are placed on either side of the tongue, can cause a cleft of the palate. A cleft in the palate can also occur despite successful movement of the lateral processes from

a vertical to a horizontal position. The cause for this is usually insufficient contact in the midline between the two lateral processes when they are in a horizontal position.

1.3 Aetiology of cleft lip and palate

The aetiology of cleft lip and palate is unknown and described widely as being multifactorial.

1.3.1 Aetiology – Genetics

There are various reasons present for believing that genetics are involved in the aetiology of cleft lip and palate. This includes the difference in the incidence of cleft lip and palate between ethnicities (Gorlin et al, 1971). The incidence of cleft lip and palate observed in Indian and Oriental ethnicities was 2.3 per 1,000 live births compared to 0.6 per 1,000 live births, in the Afro-Caribbean population. Wong and Hägg, (2004) noted that there were more than 200 syndromes which would include a cleft lip as a feature and approximately 400 syndromes that had cleft palate as a feature. The authors described certain genes thought to cause orofacial cleft syndromes. Mutations of the T-box transcription factor-22 gene (TBX22) is thought to cause X-linked cleft palate, which would involve an isolated cleft palate and a tongue-tie. In some males, sometimes only a high-arched palate, bifid uvula or a tongue tie may be the only features present. The presentation of X-linked cleft palate in females, can vary from an asymptomatic carrier to expressing all the features of the syndrome. The expression of TBX22 was described as being restricted to the

lateral processes when they are in a vertical position and are due to rotate and elevate to a horizontal position. Mutations of TBX22 was observed by Braybrook et al, (2001) in a large Icelandic family with X-linked cleft palate and in various other families from different countries.

Mutations in the Poliovirus receptor like-1 (PVRL1) gene, has been reported by Wong and Hägg, (2004) as causing cleft lip/palate ectodermal dysplasia syndrome (CLPED). A cleft lip, with or without palate, hidrotic ectodermal dysplasia, syndactyly and learning difficulties are features found in CLPED. The protein product of PVRLI was renamed as nectin-1 from its original name as poliovirus receptor-related protein. PVRL1 was expressed at the medial edge epithelium of the palatal shelves and the skin surface epithelium in animal studies. Mutations in the PVRL1 gene was also found as a cause in non-syndromic cleft lip and palate. The involvement of the interferon regulatory factor-6 in Van der Woude's syndrome and popliteal pterygium syndrome has also been described by the authors.

Wong and Hägg, (2004) also reported on genes that can cause non-syndromic cleft lip and palate. These include transforming growth factor-alpha which could be susceptible to various types of mutations and has been recognised as an aetiological factor in cleft lip and palate. The authors reported the risk of cleft palate increasing by six to eight times. The risk of cleft lip, with or without the palate, doubles when a variant of the transforming growth factor-alpha gene, the TaqI C2 allele, is combined with maternal smoking. The risk of cleft lip, with or without the palate, increased by three to eight times in circumstances where the transforming growth factor-alpha TaqI C2 allele is present and the mother has not used multivitamins in the first

trimester of pregnancy. Jezewski et al, (2003) detected mutations of the drosophila msh homeo box homolog-1 (MSX1) gene in 16 subjects with cleft lip, with or without cleft palate, from a total of 917 cleft lip/palate subjects. It was reported that 2% of non-syndromic cleft lip and palate cases were due to mutations of the MSX1 gene. Jugessur et al, (2003) reported that the risk of non-syndromic cleft palate could increase by 9.7 times with an interaction of mutated transforming growth factor-alpha genes with mutated MSX1 genes.

The effect of 5,10-methylenetetrahydrofolate reductase (MTHFR) on the risk of non-syndromic cleft lip and palate has been discussed by Prescott et al, (2002). MTHFR is an enzyme which is involved in the metabolism of folic acid. After heating the MTHFR C677T variant, it's enzyme activity reduces. Prescott et al, (2002) reported that the risk of having a cleft lip and palate child increased by 4.6 times in mothers which had the MTHFR C677T genotype. Van Rooij et al, (2003) carried out a case control study which involved investigating the interaction between folate and the MTHFR C677T genotype. Their results demonstrated an increased risk of giving birth to a cleft lip/palate infant by almost six times, if the mother did not use folic acid during the period, from before conception to early pregnancy, and carried the MTHFR C677T genotype.

Jugessur et al, (2003) carried out a population based study of cleft lip with or without palate and cleft palate only cases in Norway. Two hundred and sixty-two case-parent triads were analysed, where a 1.7 times increase in the risk of cleft lip and/or palate was found in the presence of two of the copies of the transforming growth factor beta-3 CA (TGFB3-CA) variant. Vieira et al, (2003) studied subjects from South

America and reported a variant for TGFB3 showing significant transmission distortion for cleft palate patients. This study suggested an interaction between TGFB3 and MSX1 in the development of cleft lip with or without palate and cleft palate only cases, in the South American population. Kim et al, (2003) studied the association of the single nucleotide polymorphism (SfaN1) in TGFB3 and the risk of non-syndromic cleft lip with or without palate in a Korean population. Twenty-eight non-syndromic cleft lip with or without palate subjects were compared to 41 healthy control subjects. The risk of cleft lip with or without palate increased as the G allele number increased. Comparing the non-syndromic cleft lip with or without palate group to the healthy control group, the frequency of the G allele was significantly increased in the non-syndromic cleft lip with or without palate group. There was a strong association between the male non-syndromic cleft lip with or without palate subjects with the G allele type in comparison to the females, where the association was weaker.

1.3.2 Aetiology – Environmental factors

Folic acid and multivitamins

The interaction between maternal folic acid use and other maternal exposures such as maternal fever, cigarette smoking or alcohol use was investigated by Shaw et al, (2002). Subjects were identified from 1987 to 1989 in California, of these 265 were orofacial cleft cases. The authors had excluded orofacial cleft cases with at least one accompanying major anomaly or that had single gene disorders such as trisomies. A four month periconceptional period was defined for each female, from one month before to three months after conception. Females were interviewed on their use of vitamins containing folic acid, whether they had a fever, number of cigarettes

smoked and alcohol consumption during this period. Using females who reported vitamin use and no periconceptional fever as a reference, the risk of an infant developing an isolated cleft lip/palate was increased with an odds ratio of 1.5 (95% confidence interval [CI] = 0.9-2.6) among mothers who used vitamins and had a fever during the periconceptional period. This risk was also increased for females who did not use vitamins and did not have a fever during this period with an odds ratio of 1.9 (CI = 1.4-2.7). Infants of females who did not use vitamins and had a fever during this four month periconceptional period, had an increased risk of cleft lip/palate with an odds ratio of 2.9 (CI = 1.4-5.7). The odds ratio of an infant with an isolated cleft palate was 1.3 (CI = 0.6-2.8) for females who used vitamins and had a fever during the periconceptional period. The odds ratio was also 1.3 (CI = 0.4-3.9) for females who had a fever but did not use vitamins. Females who neither used vitamins or had a fever during this four month periconceptional period, had an increased risk of a child with an isolated cleft palate with an odds ratio of 1.5 (CI = 1.0-2.4). When considering the interaction between maternal vitamin and cigarette use, the risk of isolated cleft lip/palate was the lowest for mothers who used vitamins but did not smoke cigarettes during the periconceptional period. The highest risk of isolated cleft lip/palate were for females who did not use vitamins but had smoked cigarettes, at an odds ratio of 2.8 (CI = 1.8-4.3). The risk of isolated cleft palate was the most increased for mothers who did not use vitamins and smoked cigarettes at an odds ratio of 2.0 (CI = 1.0-3.9).

Hall and Solehdin, (1998) described the reduced risk associated with periconceptional maternal folic acid and orofacial clefts. Folic acid is involved in the synthesis of DNA and RNA which leads to the important role it plays in growth. Kelly

et al, (2012) reported the results of data collected from over 11, 000 infants at 9 months of age in Ireland. The association of folic acid and cleft lip and palate was investigated. It was reported that pregnant women who consumed folic acid in the first three months of their pregnancy, had a likelihood of giving birth to a cleft lip and palate baby of 1.5 per 1,000. However, women who did not consume folic acid during the first three months of their pregnancy, had an increased risk of delivering a baby with cleft lip and palate at 6.8 per 1,000. Women who had not used folic acid within the first three months of their pregnancy were 4.36 times more likely to have a child with cleft lip, compared to women who had been consuming folic acid during this period. The authors advised the use of a daily 0.4mg dose of folic acid a month before conception to the first three months of pregnancy to reduce the risk of cleft lip with or without palate.

Smoking

Little et al, (2004) conducted a case control study which involved 190 cleft subjects who had been born between September 1st 1997 to January 31st 2000 in Scotland, Manchester and Merseyside. The control group consisted of 248 subjects. It was reported that expectant mothers who had smoked during the first trimester of their pregnancy, were 1.9 times more likely to give birth to a baby with cleft lip with or without palate and 2.3 times more likely to give birth to an infant with a cleft palate. It was suggested for cleft lip with or without palate and cleft palate only, there is a dose dependant association. Van Rooij et al, (2003) reported a combined effect of maternal smoking and the glutathione s-transferase 0-1 genotype which leads to a 4.9 times more risk of giving birth to a cleft lip and palate baby. Beaty et al, (2002) used 269 case-parent trios for a non-syndromic cleft lip, cleft palate or cleft lip and

palate. They were recruited through treatment centres located in Maryland, USA. The authors reported an interaction between MSX1 and maternal smoking which increased the risk of cleft lip with or without palate or cleft palate by 7.16 times.

Alcohol

Munger et al, (1996) conducted a study in Iowa of children born between 1987 to 1991. There were 118 isolated cleft lip and palate subjects, 56 isolated cleft palate subjects, 51 cleft lip and palate subjects with other birth defects present and 62 cleft palate subjects also with other defects present. This was compared to a control group consisting of 302 subjects. The amount of alcohol consumed by the subjects' mothers was self-reported. There was a positive correlation present with the amount of alcohol consumed and the risk of isolated cleft lip and palate. Mothers who consume 1-3 drinks per month are 1.5 times more likely to have a cleft lip and palate child. The odds ratio increases to 3.1 times more likely as the consumption of alcohol also increased to 4-10 drinks per month. This risk continues to increase to 4.7 times more likely to have a child with cleft lip and palate, when the amount of alcoholic drinks being consumed increases to over 10 per month. The authors found no significant association between maternal use of alcohol and cleft palate only or clefts associated with other birth defects.

Shaw and Lammer, (1999) investigated the association between periconceptional alcohol consumption and orofacial clefts. The subjects were from California, who had been born between January 1987 and December 1989. There were 731 cleft infants and 734 control subjects. Low level alcohol, consuming less than 1 alcoholic drink a week to 1 every day, was found to not have a significant effect on the likelihood of

giving birth to a child with an orofacial cleft. The authors investigated whether periconceptional “binge” drinking increased the risk of giving birth to an infant with an orofacial cleft. In this study, binge drinking was described as expectant mothers who had been consuming more than 5 alcoholic drinks in a sitting. Females who had been binge drinking weekly or more regularly than that, had an increased risk of giving birth to a child with an isolated cleft lip with or without palate at an odds ratio of 3.4 (95% confidence interval [CI] = 1.1-9.7). This increased to an odds ratio of 4.6 (CI = 1.2-18.8) of delivering a baby with cleft lip with or without palate and other congenital anomalies. The risk of a child with a syndromic orofacial cleft was comparatively high at 6.9 (CI = 1.9-28.6). Hoyt et al, (2016), assessed the effect of maternal exposure to second hand smoke and major birth defects. It was reported that the odds ratio of a child with cleft lip without palate was 1.41 (95% confidence interval [CI] = 1.10-1.81) if there had been periconceptional exposure to second hand smoke. The odds ratio of giving birth to an infant with cleft lip with or without palate was 1.24 (CI = 1.05-1.46) and cleft palate only was 1.31 (CI = 1.06-1.63) .

1.4 Classification of cleft

1.4.1 Veau Classification

Victor Veau’s classification of cleft, 1931, are divided into the four following groups:

1. Clefts of the soft palate
2. Clefts of the soft and hard palate up to the incisive foramen
3. Clefts of the soft and hard palate extending unilaterally through alveolus

4. Clefts of the soft and hard palate extending bilaterally through the alveolus

1.4.2 Kernahan and Stark

In 1958, Desmond Kernahan and Richard Stark had developed their classification system. They described the incisive foramen as an embryologically sound dividing line, hence their classification is based around this idea. The classification involves the following three groups:

1. Clefts of structures anterior to the incisive foramen – clefts of the primary palate
2. Clefts of structures posterior to the incisive foramen – clefts of the secondary palate
3. Clefts affecting structures anterior and posterior to the incisive foramen – clefts of the primary and secondary palates

Additional descriptions added to the classification include the side of the cleft for example unilateral, bilateral or median and the severity which is classified as a complete or incomplete cleft.

1.4.3 LAHSHAL code

Kriens in 1989, developed the LAHSHAL classification which is able to describe the cleft in detail as it can differentiate between a soft or hard palate cleft, complete or incomplete and unilateral or bilateral. The letters of LAHSHAL represent the lip, the alveolus, the hard palate and the soft palate. This allows the side of the cleft to be

recorded. Lower case letters are used to record an incomplete cleft and upper case letters are used to record a complete cleft.

1.5 Features

1.5.1 Feeding

Feeding is one of the difficulties that a cleft lip and palate patient may encounter. The severity of the feeding problem will depend on the type and severity of the cleft (Miller, 2011). In the presence of a severe palatal cleft the difficulty in feeding would be increased. A cleft nurse specialist would carry out an initial assessment and manage the symptoms through feeding interventions. Feeding difficulties in non-syndromic cleft patients are usually due to structural causes which are restricted to the oral cavity. Swallowing is generally not an issue as the pharyngeal phase of swallowing is undisturbed, which may not be the case if the patient had other medical problems present as well as the cleft. The feeding problems described by Miller, (2011) are restricted to the oral phase and include poor oral suction, longer feeding times, nasal regurgitation, excessive intake of air and reduced oral intake.

Children who have a cleft present with a craniofacial malformation, can suffer from increased difficulty in feeding and swallowing compared to clefts without the presence of additional craniofacial abnormalities. Miller, (2011) describes the risk of airway obstruction that may be present due to maxillary or mandibular hypoplasia, with or without hypoplasia of the midface. The airway may become compromised if

the patient has existing multiple cranial nerve palsies present, which would in turn affect the oral-motor and sensory nerve functions and lead to airway compromise during feeding. Chronic aspiration is a possible consequence which can lead to recurrent respiratory problems, pneumonia and lung damage.

1.5.2 Hearing

Difficulty in hearing is one of the complications that exist with cleft patients. Conductive hearing loss from otitis media with effusion, is common in patients with cleft lip and palate and cleft palate only. Skuladottir et al, (2015) carried out a study to investigate the hearing outcomes in cleft lip and palate patients. The subjects recruited were born in Norway between 1985 to 1994. One hundred and fifty-nine of the subjects had non-syndromic cleft lip and palate and 158 had non-syndromic cleft palate only. The authors reported a significant improvement in hearing as the patient grows from a child to an adolescent, for both the non-syndromic groups of cleft lip and palate and cleft palate only. At the age of 15 years, patients who had undergone palate closure at 18 months had a significantly better pure tone average compared to patients who had undergone palate closure at 12 months. The authors reported no significant difference in the hearing levels between the cleft lip and palate group and the cleft palate only group.

1.5.3 Speech

Speech impairment is often observed in cleft patients with varying levels of severity. Rohrich et al, (2000) reports that if the palate is repaired later than 2 years, speech

may not improve significantly. The child learns to speak from a very early age and the mechanism for speech would have already been developed before reaching the age of 2. To restore the normal velopharyngeal mechanism, speech therapists recommend early surgical closure of the palate.

1.5.4 Disruption of facial growth

Growth is commonly restricted in cleft palate patients. Midfacial hypoplasia is often observed. Rohrich et al, (2000) reported the restriction in maxillary growth after repair does not differ significantly than in patients with unrepaired clefts. Restriction in maxillary growth usually leads to a class III malocclusion and skeletal base, which may require orthognathic surgery in the future to correct it.

1.5.5 Disruption of dental development

Ranta et al, (1983) describes the dental anomalies that are found in cleft patients. The authors report the lateral incisor in the cleft region, as being the tooth that is most likely to suffer from hypodontia or be present as a supernumerary. Supernumeraries of the lateral incisor are more likely to be present in patients who have a cleft lip only. As the severity and extent of the cleft increases, the incidence of a lateral supernumerary also decreases. The side of the cleft and the sex of the patient did not have an effect on the presence or absence of a lateral incisor. Hypodontia is more common in cleft patients compared to non-cleft patients. The second maxillary premolars, the second mandibular premolars and the upper lateral incisors are the most likely to suffer from hypodontia outside the cleft area, otherwise

it would be the lateral incisor in the cleft area which would be the most likely to be missing. Hypodontia has been observed more frequently in the maxilla in cleft patients compared to the mandible. No significant differences have been observed between hypodontia occurring on the left or the right side, outside the cleft area. Hypodontia is more common in patients with more severe clefts. The authors reported on the prevalence of hypodontia of the permanent dentition outside the cleft region, excluding the third permanent molars, in different populations. In patients that had a cleft lip with or without palate, hypodontia was more prevalent in German patients at 21.4% followed by Finnish at 10.1%. Danish patients were the least likely to exhibit hypodontia in this group at 4.5%. In patients with unilateral cleft lip and palate, hypodontia was more likely in patients of Finnish origin at 48.8% followed by German and Danish Norwegian at 42.4% and 42.3% respectively. American German patients had the lowest incidence at 28%. In patients with bilateral cleft lip and palate, the highest incidence of hypodontia was reported in Finnish patients at 68.4%, followed again by German and Danish Norwegian patients at 44% and 43.4% respectively. American German patients who had a bilateral cleft lip and palate had the lowest incidence at 17.9%. German patients with cleft palate had the highest incidence of hypodontia at 36.8%, followed closely by Finnish patients at 32.7% and Danish Norwegian patients at 32.3%. American German patients from Iowa had the lowest incidence in this group at 22.7%. This data clearly demonstrates how the incidence of hypodontia in cleft patients can vary depending on the ethnicity and origin of the patient.

Ranta et al, (1983) reports hypodontia as being more common in females compared to males, however this difference is not statistically significant. The maxillary second

premolars are the most common teeth to be missing outside the cleft area at 7.5% to 32.3%. The mandibular second premolars are the second most common teeth to be missing outside the cleft area at 0.4% to 10.8%. This is followed by the upper lateral incisors outside the cleft area at 3.1% to 10.4%. The incidence of hypodontia in patients that do not have a cleft are lower than this. The incidence of hypodontia can increase dramatically in some syndromic cleft groups, such as in Pierre Robin syndrome, where it has been reported that 50% of 56 Finnish children demonstrated hypodontia (Ranta, 1986). A difference observed in the Pierre Robin group is that hypodontia is more common in the mandible rather than the maxilla outside the cleft area. This is un-expected because in cleft patients the hypodontia is usually more prevalent in the maxilla.

Delayed tooth formation could be observed in cleft patients in the permanent dentition, which has been reported by Ranta et al, (1983) as approximately being delayed by six months. The maxillary lateral incisor on the side of the cleft is commonly microdont. Hellquist et al, (1979) reported that a minority of the 172 subjects that they had analysed, had a dentition of average size and shape. Only 6.2% of this group did not have microdont teeth. Less than half of this group had an upper central incisor of a normal shape on the side of the cleft, with an incidence of 44%.

1.5.6 Caries

Bokhout et al, (1997) investigated the incidence of dental caries in primary teeth in Dutch cleft lip and palate patients. Eighty-one cleft lip and palate subjects were

compared to 77 subjects who did not suffer from a cleft. The incidence of dental caries was reported as being significantly increased in the cleft lip and palate group compared to the control group. The mandibular molars and teeth located beside the cleft, were reported as being the most susceptible to dental caries. The cleft lip and palate group had subjects who had significantly poorer oral hygiene when compared to the control group. The cleft lip and palate subjects also had more gingival inflammation present at an odds ratio of 1.95.

1.5.7 Psychological

Patients who have cleft lip and palate can be susceptible to psychological problems such as lowered self-esteem, self-confidence and depression. Turner et al, (1998) discusses the psychological aspects of cleft lip and palate. This includes cleft lip and palate patients noticing social rejection from outsiders. Sixty-nine percent of males had exhibited psychological problems compared to 42% of females, which included behavioural, cognitive, emotional and family problems. It has also been reported that the suicide rate of cleft lip and palate adults is double of an adult without cleft lip and palate.

1.6 Management

1.6.1 Cleft team

The cleft team includes the following:

- Plastic surgeon
- Oral maxillofacial surgeon
- ENT surgeon
- Orthodontist
- Speech therapist
- Psychologist
- Specialist nurse
- Audiologist
- Paediatrician
- Geneticist
- Audiologist
- Restorative dentist
- Paediatric dentist

1.6.2 Treatment

The management of cleft patients is discussed by Colbert et al, (2015). The authors outline the current treatment protocol used by cleft units in the UK. Each regional cleft centre would treat a minimum of 80 – 100 cleft babies a year. A multi-disciplinary approach is used to manage these patients from birth until they are at

least 20 years. Before birth, cleft can be diagnosed with ultrasound imaging. The local obstetric unit would contact the cleft team, with a referral, within 24 hours of this diagnosis. Contact would be made by a clinical nurse specialist from a main cleft centre, within 24 hours of the referral. Printed information would be provided to the parents as well as offering contact with the cleft lip and palate association. A face-to-face meeting would also be arranged at this stage.

At birth, the cleft team would be contacted within 24 hours. The clinical nurse specialist would visit the parents and the baby, within 24 hours of this referral. Counselling would be provided to the parents of the cleft baby. During the first 8-week period following birth, the parents would meet the cleft team. A lip repair may be carried out at this stage. Routine hearing and ENT assessments would be commenced within the first few days of birth, which would continue until adulthood. The infant would be assessed by the cleft orthodontist who would take neonatal records including dental study models. Dental health education would be provided to the parents. Advice on feeding is given, which includes types of feeding bottles to use and possibly the use of a feeding plate. A speech therapist would provide counselling. The babies would be under surveillance for coexisting conditions and syndromes. Genetic counselling would be provided to the parents if required.

At three months of age a lip repair would be carried out which could be a straight line repair for example the Veau technique, a rotation – advancement technique (Millard) or a Z-plasty technique (Tennison, Fischer). The anterior hard palate could also be closed with a vomer flap. A review visit with the orthodontist would be carried out to reinforce oral health advice and deliver any further advice which may be required.

At 6 months a palate repair would be carried out which could be undertaken using the Von Lagenbeck technique from 6 to 18 months of age. This technique is reported to result in reduced scarring. Another technique which could be used is the Veau technique which helps to lengthen the palate, however there is increased scarring associated with this. The Delaire technique could be used which involves a lip and soft palate repair at approximately six months.

At 10 months, a hearing test is carried out if treatment for the cleft palate is necessary. If the infant has a cleft palate, they will receive an annual hearing assessment up to 3 years of age. Within 9 weeks and 2 years of birth, a speech and language assessment is carried out.

During the ages of 3 to 5 years, if velopharyngeal competence is needed there are various options to correct this including a pharyngoplasty. A lip revision is also performed if necessary. Regular orthodontic reviews are continued to reinforce oral hygiene advice. A set of impressions would be taken when the child is 5 years old to construct study models. These study models can later be used as part of the 5-year index. At the main cleft centres, speech and language assessment and management is provided. If required, there would be an ENT assessment and audiology management. Prior to the child attending school, psychological support would be offered.

From the age of 7 years to 10 years, an alveolar bone graft is carried out. This would later help with the eruption of the canine in the cleft region. The orthodontist is further

involved to expand the upper dental arch, to prepare the cleft site for an alveolar bone graft. At this stage, the orthodontist could also start to align the anterior teeth. The expanded upper arch would have to be stabilised to avoid relapse of the space created for the bone graft. Oral hygiene advice is further reinforced. Upper and lower alginate impressions and a wax bite is taken at 10 years, which would form part of the Goslon scoring process. The speech therapist would assess the child and provide treatment if it is needed. Approximately 50% of cleft patients require speech therapy.

During the ages of 11 to 20, multidisciplinary orthodontic, paediatric and restorative dental care would take place. Once the cleft lip and palate patient is 18 years old and above they can undergo orthognathic surgery, if it is required, to correct their skeletal anterior-posterior relationship or the patient's malocclusion. A rhinoplasty can be performed from this age, if the patient requires it. If the patient is considering orthognathic surgery, the orthodontist would carry out orthodontic treatment to facilitate the surgery. Restorative work could be provided at this stage if needed. The cleft centre would take a complete set of records at 15 and 20 years.

1.7 Cleft surgery

It is thought that better speech can be obtained if the palate is repaired earlier. This is because the patient will start to develop their speech and talking habits from a very young age, however it is also generally accepted that if the cleft palate is repaired

too early, this will have an adverse effect on maxillary growth by causing growth retardation.

Noverraz et al, (1993) analysed 88 patients who were born between 1970 and 1984 with a complete unilateral cleft lip, alveolus and palate. The authors wanted to investigate if there was an association in the type of malocclusion, Class I, II or III, with the timing of the surgical closure of the hard palate. It would have been thought that the timing of the surgery could result in deficient maxillary growth and lead to a class III malocclusion. The subjects in this study, had received lip repair surgery. The soft palate was repaired using a modified von Lagenbeck palatoplasty which was carried out at a mean age of 1.1 years. A modified von Lagenbeck procedure was used for repair of the hard palate. The subjects were divided into four groups based on the timing of the hard palate closure. Group A had subjects who had received hard palate repair at a mean age of 1.5 years. Group B had subjects who had received hard palate repair at a mean age of 4.6 years. Group C had a mean age of 9.4 years for repair of the hard palate and group D had subjects where the hard palate was still open. The subjects in group D were not over 10 years of age. There were no differences observed between the four different groups when the malocclusion, in terms of Class I, II or III, was assessed using the Goslon yardstick.

Friede et al, (1987) assessed and compared maxillary growth in unilateral and bilateral cleft lip and palate subjects. These subjects had their hard palate repaired either at infancy or still had an unrepaired palate at 7 years. The authors reported significantly better midfacial growth and occlusion, in unilateral cleft lip and palate

subjects, that had a hard palate repair after the age of 7 years. A difference between the maxillary growth of the bilateral cleft lip and palate subjects was not observed.

Friede and Enemark, (2001) carried out a study to assess the effect of delayed hard palate closure on maxillary growth in unilateral cleft lip and palate patients. Thirty consecutive patients were used from each of the two Scandinavian centres. One of the Scandinavian centres, in Sweden, would carry out an early velum repair at 8 months followed by closure of the hard palate at a mean age of 8.5 years. A bone graft would also be performed at the same time. The other centre in Denmark would carry out primary closure of the palate in two stages. The lip and hard palate repair would be carried out at the same time at approximately 3 months. The posterior palate repair would be carried out at approximately 22 months with a push-back technique. Lateral cephalograms were used to assess mid-facial growth. The authors reported significantly better mid-facial growth in the subject group who had delayed hard palate closure. Friede, (2007) analysed published papers on the effect of two-stage palatal repair with delayed hard palate closure, in unilateral cleft lip and palate patients. It was reported that most papers described either an excellent or very good maxillary growth outcome.

Stein et al, (2006) carried out a study comparing the cephalometric and occlusal outcomes in unilateral cleft lip and palate patients, who had either undergone a one stage palate closure or a two stage palate closure. Twenty-two of the subjects had undergone a one stage closure of the hard and soft palate, at a mean age of 23 months. Twenty-one of the subjects underwent hard palate repair at 86 months. There were no significant differences in the cephalometric measurements between

the two groups. Upper anterior arch constriction was recorded in the subjects who had received one-stage palate repair between the ages of 6 and 10 years. By the time the patients reached between 15 and 18 years, the difference in the anterior width of the maxillary arches could no longer be detected.

Lilja et al, (2006) investigated the dental arch relationships in unilateral cleft lip and palate Swedish subjects, who had delayed hard palate closure, in a retrospective study. One hundred and four subjects were included. These patients underwent delayed hard palate closure at 8 years. The authors reported the Goslon yardstick outcomes as 85% in groups 1 and 2 which are predicted as requiring little or no orthodontic treatment. Twelve percent of the subjects had a Goslon score of 3, who are predicted as requiring orthodontic treatment. Three percent of the subjects had a Goslon score of 4, who are predicted as requiring orthognathic surgery in the future and no subjects were given a score of 5.

1.8.1 The Goslon yardstick

The Goslon (Great Ormond Street, London and Oslo) Yardstick is used at 10 years of age, for unilateral cleft lip and palate patients. This was described by Mars et al, (1987). The authors developed the Goslon Yardstick as a way to compare the long-term results of different approaches to the early treatment these patients received, by categorizing the malocclusions in order of its severity and the difficulty of correcting it. Dental study casts are used with the Goslon yardstick to rank the malocclusion present into the following five groups:

- Group 1 = excellent outcome. Patients have occlusions that require either straight forward orthodontic treatment or no treatment at all.
- Group 2 = good outcome. This is similar to group 1, where patients have occlusions that require either straight forward orthodontic treatment or no treatment at all.
- Group 3 = fair outcome. Patients require complex orthodontic treatment to correct the Class III malocclusion and other features of this malocclusion but a good result is anticipated.
- Group 4 = poor outcome. The malocclusion is at the limit of orthodontic treatment without orthognathic surgery to correct the skeletal relationship. If facial growth is unfavourable, orthognathic surgery will be required.
- Group 5 = very poor outcome. These patients require orthognathic surgery to correct the skeletal relationship to achieve a satisfactory occlusion.

However, it must be borne into mind that this is a normative index but the overall decision for treatment requirements also depends on a number of other factors including patient's expressed and desired need, medical history, suitability for general anaesthetic and social circumstances.

1.8.2 The 5-year index

The 5-year index was presented by Atack et al, (1997b). This index is used to assess the outcome in terms of mid-facial growth in patients with unilateral cleft lip and palate at 5 years. The authors had used the same format of the original Goslon

Yardstick by Mars et al, (1987) which consisted of ranking study models from 1 to 5, with 1 being an excellent outcome and 5 as a very poor outcome.

1.9 CSAG

Due to the outcome of two studies in the 1980s, it became apparent that the delivery of cleft treatment had to be changed in the UK. The GOSLON Yardstick was used to compare cleft centres in the UK and Norway. The outcomes of the UK centre were considered to be poor (Mars et al, 1987). The other study which was carried out was a European multi-centre audit of treatment outcome for complete unilateral cleft lip and palate patients. It was reported that two of the UK centres had fallen short on many aspects of patient care (Shaw et al, 1992). Due to this information the Clinical Standards Advisory Group (CSAG) carried out a national investigation into the cleft care that was being provided to patients in the UK. Recommendations were made to improve the delivery of cleft care in the UK and improve the standards of patient care. It was decided to centralise cleft care into 8 to 15 national centres. Initially there were 57 centres present. Centralisation would ensure cleft surgeons would treat large quantities of patients, which would improve their skills and build on their experience. In 1998, only 7 surgeons in the UK repaired 5 or more unilateral cleft lip and palates in a year (Colbert et al, 2015). Centralisation would prevent this from happening. One of the recommendations made included a nationwide database, to store data of all the cleft patients. This would help in data collection for audits and further improvements in cleft care. Training for cleft surgeons was recommended to

be restricted to cleft centres where there were a high-volume of patients and a high quality of clinical experience readily available.

Chapter 2

Participants and Methods

2.1 Research problem

An audit of treatment outcome was carried out nationally utilizing the 5-year Index (Atack et al, 1997a; Atack et al, 1997b) on patients born with a complete unilateral cleft lip and palate. There is a perceived difference in the 5-year index outcomes between the two techniques being used at a single cleft unit. This project is carried out to ascertain which factors influence midfacial growth when evaluated with the 5-year index. The two techniques used are different but follow stable protocols for 13 years each and we have consecutive analysable data for the last nine years.

2.2 Aims

To explore the possible causes for the difference in the proportion of “excellent/good” and “poor/very poor” surgical outcomes, when using the 5-year Index between two different surgical techniques at this unit. The factors to be considered are:

- surgical technique
- the severity of the case
- agenesis and dental anomalies of the maxillary primary and permanent lateral incisors and other teeth
- presence of bone in the cleft prior to alveolar bone grafting

2.3 Hypothesis

1. The surgical technique is a determinant of mid-facial growth of unilateral and bilateral cleft lip and palate patients.
2. The severity of the cleft is a determinant of mid-facial growth of unilateral cleft lip and palate patients.
3. Dental anomalies and agenesis of the dentition are determinants of mid-facial growth of unilateral and bilateral cleft lip and palate patients.
4. Presence of bone in the cleft is a determinant of mid-facial growth of unilateral and bilateral cleft lip and palate patients.

2.4 Method of investigation

Ethical approval was sought for research at [redacted]. The population consisted of all the unilateral and bilateral complete cleft lip and palate patients, that have undergone cleft lip and palate surgery from 2000 to 2009, at [redacted]. This is a retrospective cohort longitudinal study using clinical records such as dental study casts, radiographs, the cleft database and clinical notes. Eligible subjects were recruited using the cleft database. Subjects would be eligible for inclusion in the study if they satisfy the following inclusion criteria:

- Subject has a complete bilateral or unilateral cleft lip and palate - the Simonart's band should be non-bony and less than 5mm
- Surgical technique used is clearly recorded in the clinical notes

- 5 year index is present
- Consecutive patients who received initial cleft lip and palate surgery from 2000 to 2009

The following exclusion criteria was applied:

- Incomplete unilateral cleft of the lip and palate - thickness of the Simonart's band is greater than 5mm
- Unable to ascertain key data from the clinical records such as the surgical technique used
- No 5 year index was recorded
- If there are no radiographs present that can be used to assess the presence or absence of bone in the cleft prior to alveolar bone graft surgery, then these subjects will be excluded from the subgroup that will be assessed for the presence of bone in the cleft.

2.5 Outcome

The 5-year index was used to measure the outcome in terms of mid-facial growth in patients with unilateral cleft lip and palate at 5 years of age. If study models were not available, clinical photographs of the patient would be used to assess the outcome. This is because photographs have been shown to be a reliable alternative (McAuliffe et al, 2011). No formal index has been established for measuring the treatment outcome, in terms of dental arch relationship for bilateral cleft lip and palate patients. A separate yardstick would be used to measure the outcome in bilateral cleft lip and

palate patients, described by Ozawa et al, (2011). This is an extension of the 5-year index and has been recorded as having inter-rater weighted kappa scores between 0.74 and 0.92, which is in the ‘‘good’’ to ‘‘very good’’ categories. The ranking system for both unilateral and bilateral cleft lip and palate patients consists of scoring study models from 1 to 5 as follows:

- Group 1 = excellent outcome. Patients have occlusions that require either straight forward orthodontic treatment or no treatment at all.
- Group 2 = good outcome. This is similar to group 1, where patients have occlusions that require either straight forward orthodontic treatment or no treatment at all.
- Group 3 = fair outcome. Patients require complex orthodontic treatment to correct the Class III malocclusion and other features of this malocclusion but a good result is anticipated.
- Group 4 = poor outcome. The malocclusion is at the limit of orthodontic treatment without orthognathic surgery to correct the skeletal relationship. If facial growth is unfavourable, orthognathic surgery will be required.
- Group 5 = very poor outcome. These patients require orthognathic surgery to correct the skeletal relationship to achieve a satisfactory occlusion.

However, it must be borne into mind that this is a normative index but the overall decision for treatment requirements also depends on a number of other factors including patient’s expressed and desired need, medical history, suitability for general anaesthetic and social circumstances.

2.6 Exposures

2.6.1 Sex, Race/Ethnicity

- Caucasian
- Pakistani
- Indian
- Bangladeshi
- Afro-Caribbean
- Chinese
- Mixed
- Other

2.6.2 Surgical technique

The clinical notes recording the operation would be used to distinguish which surgical technique was used. Unilateral and bilateral techniques were different.

1. Unilateral cleft lip and palate patients - the surgical technique fell into one of the two following categories:
   - Technique A: the lip has been repaired first at approximately 3 months and the hard and soft palate have been repaired together at approximately 6-8 months, using a vomer flap at this point.
   - Technique B: the lip and the hard palate have been repaired simultaneously using a vomer flap at 3 months, including a bi-lobed flap from the pro-labium in the lip repair, and an anteriorly based inferior turbinate flap laterally. This

facilitates complete closure of the alveolar flap with soft tissue at the time of the lip repair. Repair of the soft palate is carried out at 6 months.

2. Bilateral cleft lip and palate patients - each of the subjects fell into one of the three following categories:
    - Technique A: A lip adhesion at 3 months, followed by a definitive lip repair when the patient is slightly older (18-36 months). Cleft palate repair at 6-9 months.
    - Technique B: The lip and one vomerine anterior repair is carried out at 3-4 months. At the second operation the other vomerine flap is performed in continuity with the soft palate repair. It is often not possible to completely close the alveolus anteriorly in this second operation.
    - Technique C: The lip repair is carried out at 3-4 months. The cleft palate is closed at 6-9 months.

2.6.3 Severity of the case

The severity of the case was determined by using the method described by Peltomaki et al, (2001) on neonatal study models, using digital calipers on recognized landmarks. The ratio of cleft width to arch circumference and the ratio of arch width to arch length was calculated. The measurements were repeated one month apart.

2.6.4 Presence of dental anomalies

The presence of dental anomalies of the upper lateral incisors was recorded by a combination of assessing the subject's occlusal radiograph, OPG and the 5 year dental study cast. The primary dentition was assessed using the 5 year dental study casts and any clinical illustrations that were present. The cleft lip and palate patients have a routine radiograph taken prior to their bone graft surgery which usually occurs at approximately 7-9 years. The mixed dentition would only be assessed for these patients that have had a radiograph taken.

The lateral incisors were recorded as falling in one of the following groups:

1. Hypodontia
2. Supernumerary
3. No dental anomaly present

The 5-year study models and available clinical illustrations and radiographs were used to explore dental anomalies and agenesis of other teeth.

2.6.5 Presence of bone in the cleft

An occlusal radiograph was used to assess the presence or absence of bone in the cleft, prior to alveolar bone graft surgery. This was a subgroup of the study where patients have had radiographs taken prior to an alveolar bone graft, at approximately 7-9 years old.

2.7 Data management

Anonymised data was collected and entered directly into a research database. Decision on inclusion/exclusion was made and all exposure variables were collected first. Outcome data was collected subsequently in blinded fashion, i.e., the investigator determining treatment outcomes was not aware of the exposures.

2.8 Statistical analysis

This is an exploratory study and no formal sample size calculation is presented. Based on the results of the previously conducted audit, we expected to include approximately 80 patients.

Summary statistics were calculated as appropriate for all collected variables, stratified by surgical technique and treatment outcomes. To explore the association between exposure variables and treatment outcomes, treatment outcome was dichotomized (excellent/good/fair vs. poor/very poor). Comparisons between outcome groups were made using chi-squared or Fisher's exact tests, as appropriate. Furthermore, multivariable logistic regression analysis was carried out to evaluate the effect of surgical technique on treatment outcome, adjusting for other exposure variables. Odds-ratios and 95% confidence intervals were estimated, and all statistical test would be 2-sided at alpha=0.05.

Chapter 3

Results

3.1 Characteristics of the sample

One hundred and eighty-seven subjects were included in this study, after meeting the inclusion criteria. One hundred and thirty-eight of these subjects had a unilateral cleft lip and palate and 49 had a bilateral cleft lip and palate. In the unilateral cleft lip and palate group, 85 were male and 53 were female. In the bilateral cleft lip and palate group, 39 subjects were male and 10 were female. There were 44 neonatal study models present from the unilateral cleft lip and palate group, that were used to measure the severity of the initial cleft.

The results are presented in the following tables.

Table 3.1.1: Unilateral cleft lip and palate – Gender

Gender	Frequency	%
Male	85	61.59
Female	53	38.41

A higher proportion of the unilateral cleft lip and palate subjects were male at approximately 62%, compared to females at approximately 38%.

Table 3.1.2: Unilateral cleft lip and palate – Ethnicity

Ethnicity	Frequency	%
Caucasian	112	81.16
Pakistani	11	7.97
Indian	5	3.62
Bangladeshi	2	1.45
Afro-Caribbean	4	2.90
Chinese	2	1.45
Mixed	1	0.72
Other	1	0.72

A majority of the patients were Caucasian.

Table 3.1.3: Unilateral cleft lip and palate – Surgical technique

Technique	Frequency	%
A	75	54.35
B	63	45.65

Table 3.1.4: Unilateral cleft lip and palate – 5-year index

Index	Frequency	%
1	22	15.94
2	44	31.88
3	37	26.81
4	26	18.84
5	9	6.52

Table 3.1.5: Unilateral cleft lip and palate – Presence of bone in the cleft

Bone	Frequency	%
Yes	**36**	**37.11**
No	**61**	**62.89**

Table 3.1.6: Unilateral cleft lip and palate – Anomalies of the deciduous lateral incisor

Lateral Incisor	Freq.	%
No anomaly	77	56.20
Hypodontia	41	29.93
Supernumerary	19	13.87

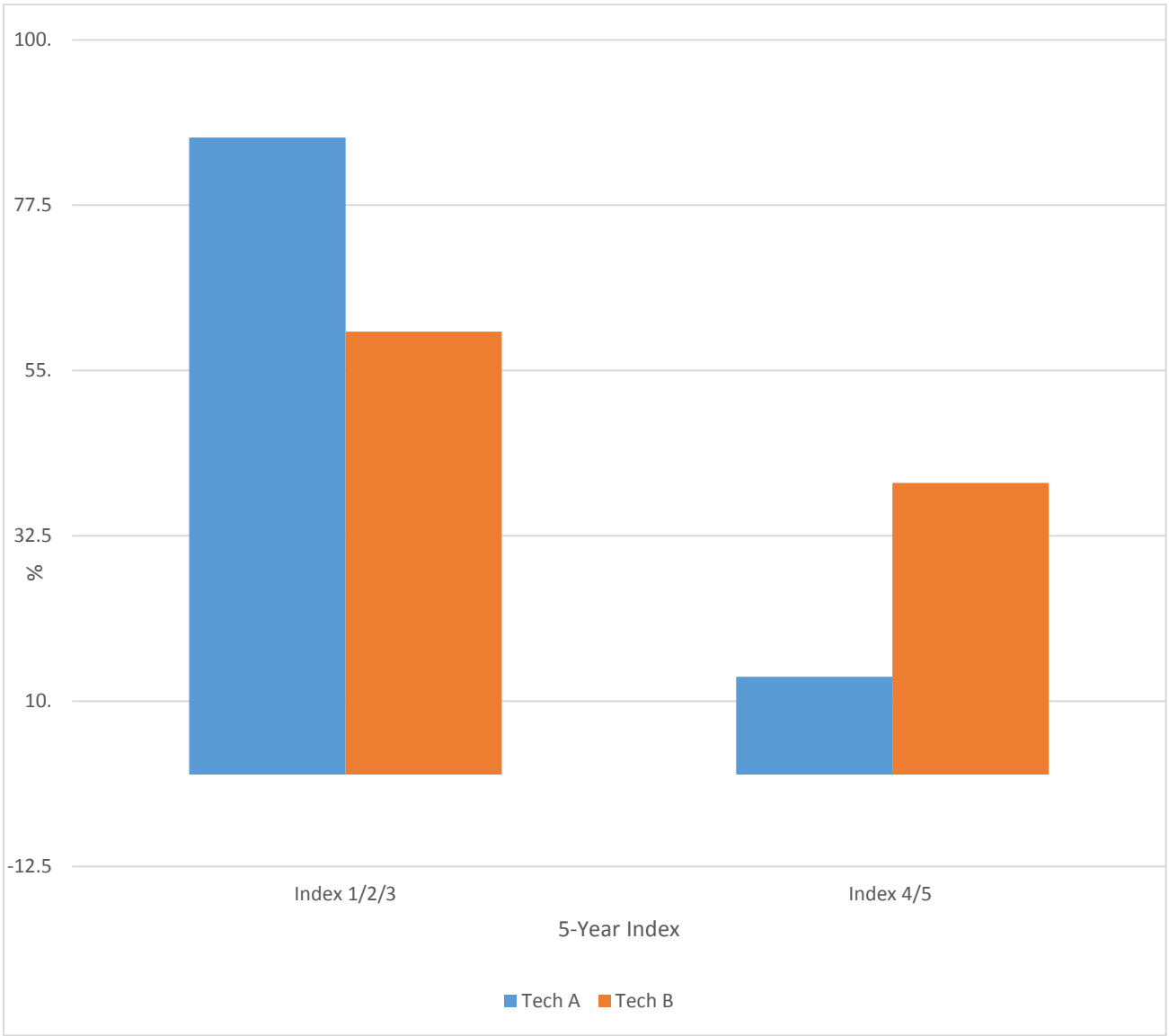
Table 3.1.7: Unilateral cleft lip and palate – Age of patient (days) at time of palate closure

Technique	Frequency	Mean (Days)	Min (Days)	Max (Days)
A	75	231.6	184	365
B	63	103.8	81	200

Table 3.1.8: Unilateral cleft lip and palate – Effect of technique on facial growth

Outcome	Tech A	Tech B
Index 1/2/3 (Freq.)	65	38
Index 1/2/3 (%)	**86.7**	**60.3**
Index 4/5 (Freq.)	10	25
Index 4/5 (%)	**13.3**	**39.7**

Figure 3.1.8: Unilateral cleft lip and palate – Effect of technique on facial growth



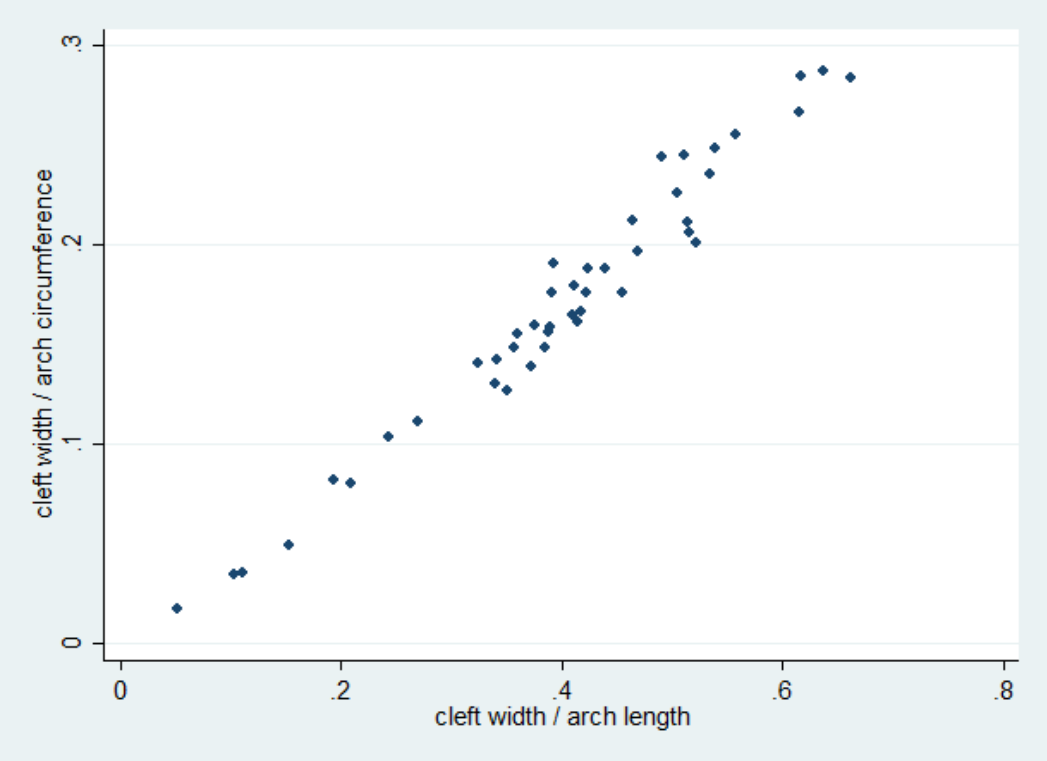
A Pearson chi-squared test was carried out which had a p value < 0.001. The Fisher's exact test resulted in a p value of 0.001. Statistical analysis showed technique B has worse 5-year index scores and this is statistically significant.

Table 3.1.9: Unilateral cleft lip and palate – Effect of gender on facial growth

Outcome	Male	Female
Index 1/2/3 (Freq.)	64	39
Index 1/2/3 (%)	**75.29**	**73.58**
Index 4/5 (Freq.)	21	14
Index 4/5 (%)	**24.71**	**26.42**

A Pearson chi-squared test gave a result of a p value of 0.82 and a Fisher's exact test resulted in a p value of 0.843. The effect of gender on the 5-year index was not statistically significant.

Figure 3.1.10: Unilateral cleft lip and palate – A scatter diagram showing the cleft width to arch circumference ratio plotted against the cleft width to arch length ratio.



This scatter diagram shows the cleft width: arch circumference ratio compared to the cleft width: arch length. These ratios are used to measure the severity of the initial cleft prior to cleft lip and palate surgery. There was a Pearson correlation coefficient of 0.98 with a p value of less than 0.0001. These two ratios are highly correlated, with the cleft width to arch circumference ratio increasing as the cleft width to arch length ratio increases and vice versa.

Table 3.1.11: Unilateral cleft lip and palate – Effect of the cleft width to arch circumference ratio on facial growth

Outcome	Frequency	Mean
Index 1/2/3	29	0.15
Index 4/5	15	0.20

Table 3.1.11 demonstrates the effect of the cleft width to arch circumference ratio on the 5-year index, for unilateral cleft lip and palate patients. The mean cleft width to arch circumference ratio was 0.15 for subjects which had a 5-year index score of 1 (excellent), 2 (good) and 3 (fair). These subjects may require either no treatment in the future to correct their malocclusion or only orthodontic treatment which may be simple or complex. The mean cleft width to arch circumference ratio is increased at 0.20 for subjects with a 5-year index score of 4 (poor) or 5 (very poor). Subjects which have scored a 4 are at the limits of orthodontic treatment and may need surgery to correct the skeletal relationship, if the patient would like this to be corrected. If subjects which have scored a 4, have unfavourable facial growth, then they would be likely to need orthognathic surgery. Orthognathic surgery would be elective treatment and therefore would be carried out if the subject would like the skeletal relationship to be corrected, rather than a normative need based solely on a 5-year index score of 4. Subjects receiving a 5-year index score of 5, may need orthognathic surgery to correct the skeletal relationship to achieve a satisfactory occlusion, if they had a desire and want to do so. A two-sample t test with equal variances was carried out which showed a p value of 0.018. This is statistically

significant. The severity of the initial cleft does have an effect on the 5-year index. The larger the cleft width to arch circumference ratio, hence the more severe the initial cleft is, the more likely the subject would have a poorer 5-year index result and may require orthognathic surgery in the future, if the subject wished to correct their skeletal relationship.

Table 3.1.12: Unilateral cleft lip and palate – Effect of the cleft width to arch length ratio on facial growth

Outcome	Frequency	Mean
Index 1/2/3	29	0.37
Index 4/5	15	0.46

Table 3.1.12 demonstrates the effect of the cleft width to arch length ratio on the 5-year index for unilateral cleft lip and palate patients. The mean cleft width to arch length ratio was 0.37 for subjects which had a 5-year index score of 1 (excellent), 2 (good) and 3 (fair). These subjects may need either no treatment or only simple or complex orthodontics to correct their malocclusion, if they desired. The mean cleft width to arch length ratio is increased to 0.46 for subjects with a 5-year index score of 4 (poor) or 5 (very poor). Subjects which have scored a 5-year index of 4, are more likely to be at the limits of orthodontic treatment without orthognathic surgery, if the subject wanted to correct their malocclusion. The need for orthognathic surgery would be more likely if the subject was to have unfavourable growth and the subject wanted the skeletal relationship to be corrected. Subjects scoring a 5-year index of

5, may need orthognathic surgery to correct the skeletal relationship if they were unhappy with it and wanted to have this corrected. The overall decision for treatment requirements also depends on a number of other factors including the patient's expressed and desired need, medical history, suitability for general anaesthetic and social circumstances, rather than being purely based on a normative need using the 5-year index score. A two-sample t test with equal variances was carried out which demonstrated a p value of 0.031 which is statistically significant. The severity of the initial cleft does have an effect on the 5-year index. The larger the cleft width to arch length ratio, hence the more severe the initial cleft is, the more likely the subject would have a poorer 5-year index result and require orthognathic surgery in the future, to correct their class III malocclusion and class III skeletal base.

Table 3.1.13: Unilateral cleft lip and palate – Effect of anomalies of the deciduous lateral incisors on facial growth

Outcome	No Anomaly	Hypodontia	Supernumerary
Index 1/2/3 (Freq.)	59	27	16
Index 1/2/3 (%)	**76.6**	**65.9**	**84.2**
Index 4/5 (Freq.)	18	14	3
Index 4/5 (%)	**23.38**	**34.15**	**15.79**

A Pearson chi-squared test gave a result of a p value of 0.255. A Fisher's exact test gave the p value of 0.295. This was not statistically significant. Anomalies of the deciduous lateral incisors do not have a significant effect on the 5- year index of a subject.

A logistic regression was carried out on the 138 unilateral cleft lip and palate observations. This showed technique B is 4.3 times more likely to have a mid-facial growth than technique A. Once the confounding factors, gender & anomalies of the

lateral incisor had been accounted for, technique B is 4 times more likely to have a worse outcome than technique A.

A logistic regression was carried out on the neonatal model subgroup, which consisted of 44 neonatal models. This showed technique B is 2.4 times more likely to have a worse outcome. Once the confounding factors of gender, anomalies of the deciduous lateral incisor & severity of the initial cleft have been accounted for, technique B is 3 times more likely to have a worse outcome in terms of the 5-year index compared to technique A.

Table 3.1.14: Unilateral cleft lip and palate – Effect of technique on the presence of bone in the cleft

Bone	**Tech A**	**Tech B**
Yes (Freq.)	17	19
Yes (%)	**27.87**	**52.78**
No (Freq.)	44	17
No (%)	**72.13**	**47.22**

A Pearson chi-squared test was carried out which showed a p value of 0.014. A Fisher's exact test showed a p value of 0.018. This demonstrated technique B as being more likely to result with the presence of bone in the cleft prior to alveolar bone grafting and this was statistically significant.

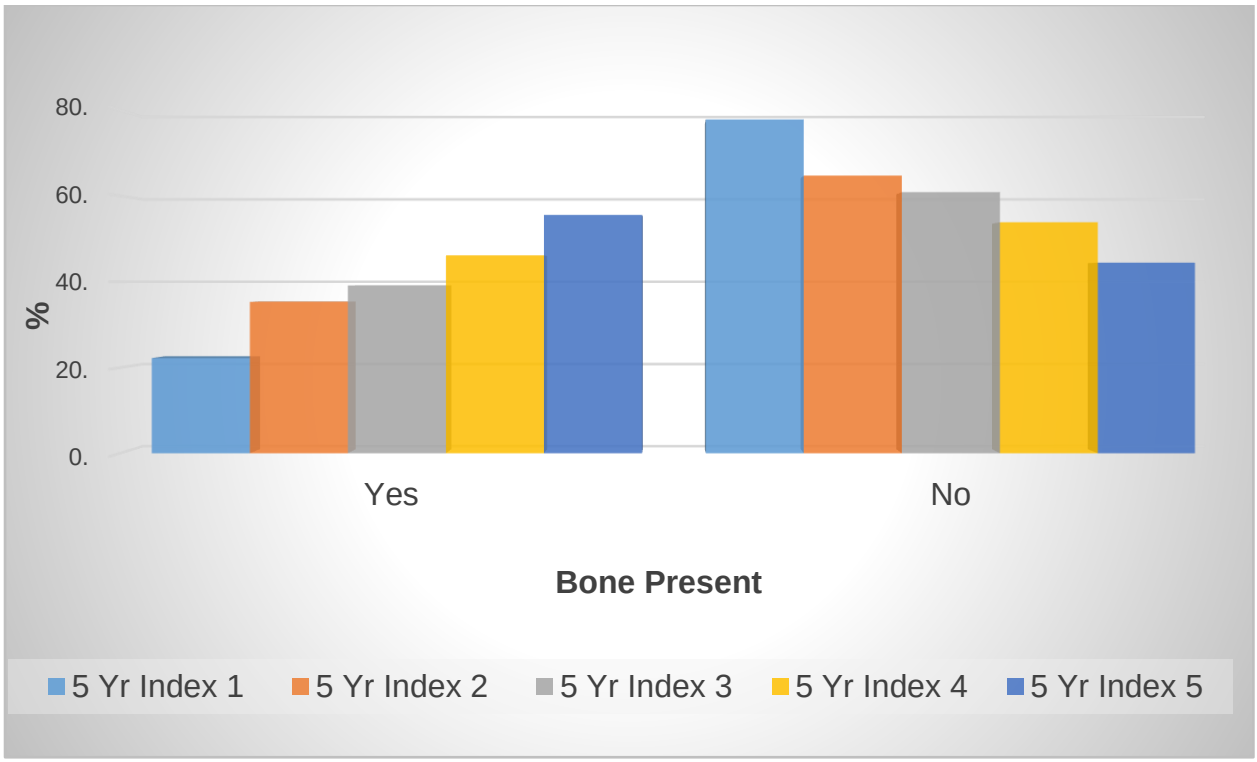
A logistic regression on 97 observations showed technique B as being 2.9 x more likely to have bone in the cleft prior to alveolar bone grafting. Once the confounding factors of gender and anomalies of the deciduous lateral incisor have been accounted for, technique B is 3.3 times more likely to have bone in cleft prior to alveolar bone grafting, compared to technique A.

A logistic regression was carried on the neonatal model subgroup, which consisted of 42 neonatal models, which also had radiographs to assess the presence and absence of bone in the cleft prior to alveolar bone grating. Technique B was shown to be 4.3 times more likely to have bone in the cleft prior to alveolar bone grafting, compared to technique A. Once confounding factors of gender, anomalies of the deciduous lateral incisor & severity of the cleft had been accounted for, this increased the odds ratio of technique B being 6.6 times more likely to have bone in the cleft, prior to alveolar bone grafting, compared to technique A.

Table 3.1.15: Unilateral cleft lip and palate – Effect of the presence of bone on facial growth

Bone	5 Yr Index 1	5 Yr Index 2	5 Yr Index 3	5 Yr Index 4	5 Yr Index 5
Yes (Freq.)	4	12	9	6	5
Yes (%)	**22.22**	**35.29**	**39.13**	**46.15**	**55.56**
No (Freq.)	14	22	14	7	4
No (%)	**77.78**	**64.71**	**60.87**	**53.85**	**44.44**

Figure 3.1.15: Unilateral cleft lip and palate – Effect of the presence of bone on facial growth



A Pearson chi-squared test showed a p value of 0.468 and a Fisher's exact test showed a p value of 0.470. This was not statistically significant however a trend is visible. A logistic regression showed a p value of 0.07 for trend. Therefore, the presence of bone in the cleft prior to alveolar bone grafting is more likely to result in a worse 5-year index score. However, this is not statistically significant although a trend has been observed.

Table 3.2.1: Bilateral cleft lip and palate – Gender

Gender	**Frequency**	**%**
Male	39	79.59
Female	10	20.41

A higher proportion of the bilateral cleft lip and palate subjects were male at approximately 80%, compared to females at approximately 20%.

Table 3.2.2: Bilateral cleft lip and palate – Ethnicity

Ethnicity	Frequency	%
Caucasian	40	81.63
Pakistani	6	12.24
Afro-Caribbean	1	2.04
Mixed	1	2.04
Other	1	2.04

Table 3.2.3: Bilateral cleft lip and palate – Surgical technique

Technique	Frequency	%
A	24	48.98
B	17	34.69
C	8	16.33

Table 3.2.4: Bilateral cleft lip and palate - 5-year Index

Index	Frequency	%
1	21	42.86
2	12	24.49
3	5	10.20
4	5	10.20
5	6	12.24

Table 3.2.5: Bilateral cleft lip and palate – Presence of bone in the cleft

Bone	Frequency	%
Yes	11	28.95
No	27	71.05

Table 3.2.6: Bilateral cleft lip and palate – Anomalies of the deciduous lateral incisor

Lateral Incisor	Frequency	%
No anomaly	25	51.02
Hypodontia Right & Left	10	20.41
Hypodontia Right	4	8.16
Supernumerary Right & Left	3	6.12
Supernumerary Right	5	10.20
Supernumerary Left	2	4.08

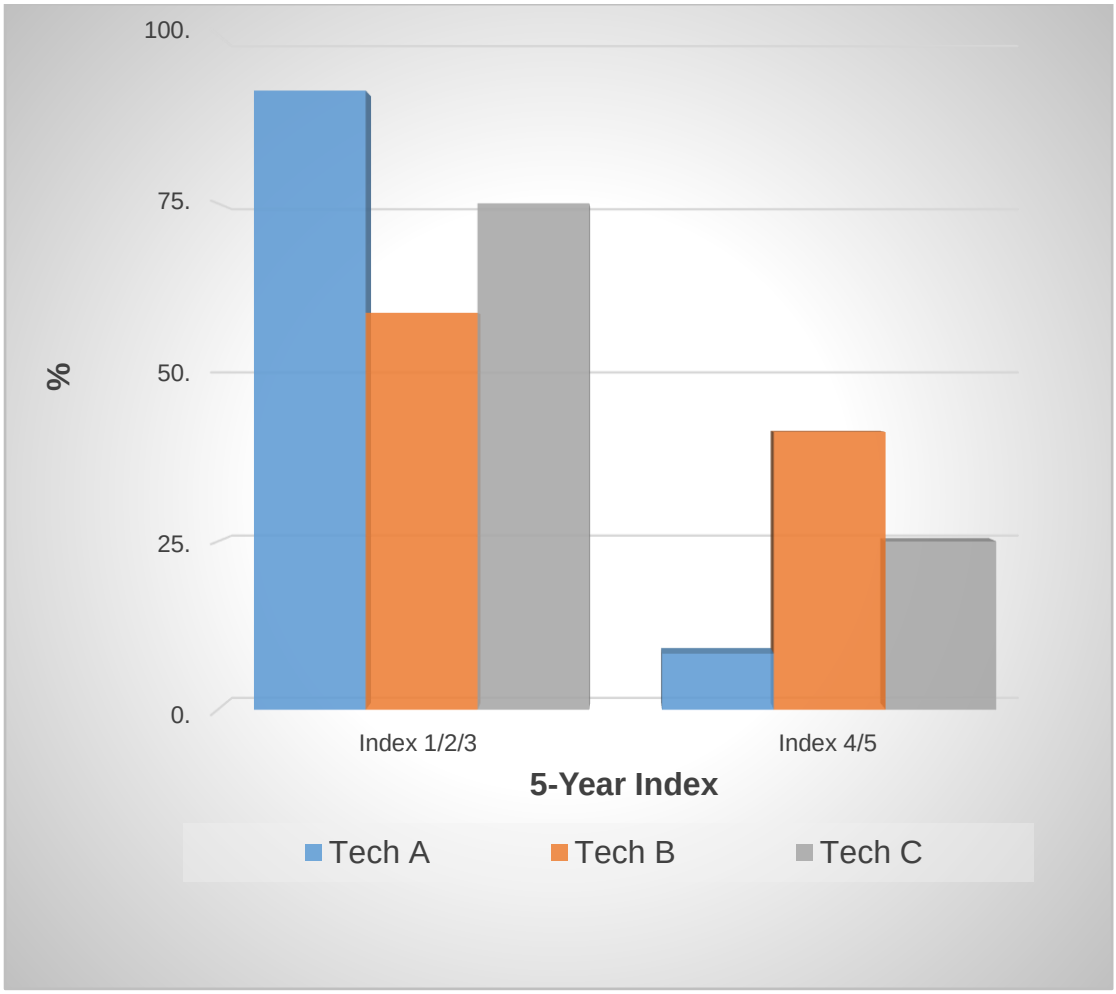
Table 3.2.7: Bilateral cleft lip and palate – Age of patient (days) at time of palate closure

Technique	N	Mean (Days)	Min (Days)	Max (Days)
A	24	263.3	169	936
B	17	95	62	126
C	8	225.4	191	302

Table 3.2.8: Bilateral cleft lip and palate – Effect of technique on facial growth

Outcome	Tech A	Tech B	Tech C
Index 1/2/3 (Freq.)	22	10	6
Index 1/2/3 (%)	**91.67**	**58.82**	**75.00**
Index 4/5 (Freq.)	2	7	2
Index 4/5 (%)	**8.33**	**41.18**	**25.00**

Figure 3.2.8: Bilateral cleft lip and palate – Effect of technique on facial growth



A Pearson chi-squared test gave a p value of 0.045 and a Fisher's exact test gave a p value of 0.030. This revealed that technique B has worse 5-year index scores compared to technique A and technique C. This is statistically significant.

Table 3.2.9: Bilateral cleft lip and palate – Effect of gender on facial growth

Outcome	**Male**	**Female**
Index 1/2/3 (Freq.)	32	6
Index 1/2/3 (%)	**82.05**	**60**
Index 4/5 (Freq.)	7	4
Index 4/5 (%)	**17.95**	**40**

A Pearson chi-squared test showed a p value of 0.14 and a Fisher's exact test showed a p value of 0.20. The effect of gender on the 5-year index is not statistically significant.

Table 3.2.10: Bilateral cleft lip and palate – Effect of anomalies of the deciduous lateral incisors on facial growth

Outcome	No Anomaly	Hypodontia	Supernumerary
Index 1/2/3 (Freq.)	19	10	9
Index 1/2/3 (%)	**76.00**	**71.43**	**90.00**
Index 4/5 (Freq.)	6	4	1
Index 4/5 (%)	**24.00**	**28.57**	**10.00**

A Pearson chi-squared test showed a p value of 0.542 and a Fisher's exact test showed a p value of 0.605. This demonstrated that the presence of an anomaly of the deciduous lateral incisor did not have a statistically significant effect on the 5-year index.

A logistic regression was carried out on the 49 bilateral cleft lip and palate subjects. This showed an odds ratio of technique B being 7.7 times more likely to have a worse 5-year index score. Technique C had an odds ratio of 3.7 times more likely to have a worse 5-year index score.

Once the confounding factors of gender and anomalies of the deciduous lateral incisors have been accounted for, technique B had an odds ratio of 9.1 times more likely to have a worse 5-year index score. Technique C had an odds ratio of 4.6 times more likely to have a worse 5-year index score.

Table 3.2.11: Bilateral cleft lip and palate – Effect of technique on the presence of bone in the cleft

Bone	**Tech A**	**Tech B**	**Tech C**
Yes (Freq.)	3	8	0
Yes (%)	**15**	**61.54**	**0**
No (Freq.)	17	5	5
No (%)	**85**	**38.46**	**100**

A Pearson chi-squared test showed a p value of 0.005 and a Fisher's exact test showed a p value of 0.007. This demonstrated that technique B is more likely to result with bone in the cleft, prior to alveolar bone grafting, compared to technique A and technique C. This was statistically significant.

A logistic regression was carried out on 33 bilateral cleft lip and palate subjects, who had radiographs to distinguish the absence or presence of bone in the cleft prior to alveolar bone grafting. This showed technique B as being 9.1 times more likely to have bone in the cleft, prior to alveolar bone grafting. Once the confounding factors of gender and anomalies of the lateral incisor have been accounted for, this increased to technique B being 20.8 times more likely to have bone in cleft prior to alveolar bone grafting.

Table 3.2.12: Bilateral cleft lip and palate – Side of treatment Vs. side bone is present

Treatment Side	Side Bone Present
Left	Left
Left	Right
Left	Right
Right	Right
Right	Right
Left	Right
Right	Both
Left	Both

Data was collected for technique B to ascertain if there is a link between the side which is operated on initially and if bone is more likely to be present on the same side. These results were random therefore there is no association between the side of the cleft that has been treated first and the side where bone is found in the cleft, prior to alveolar bone grafting.

Table 3.2.13: Bilateral cleft lip and palate – Effect of the presence of bone in the cleft and facial growth

Bone	**5 Yr Index 1**	**5 Yr Index 2**	**5 Yr Index 3**	**5 Yr Index 4**	**5 Yr Index 5**
Yes (Freq.)	4	4	0	1	2
Yes (%)	**23.53**	**40**	**0**	**33.33**	**33.33**
No (Freq.)	13	6	2	2	4
No (%)	**76.47**	**60**	**100**	**66.67**	**66.67**

A Pearson chi-squared test showed a p value of 0.784 and a Fisher's exact test showed a p value of 0.845. This shows that the presence of bone in the cleft is not statistically significantly associated with the 5-year index.

Chapter 4

Discussion

4.1 Discussion

Following a national audit of treatment outcome using the 5-year index (Atack et al, 1997) there was a perceived significant difference between the two techniques used, at [redacted]. This research was carried out to explore the possible causes for this difference in the 5-year index results between the two techniques, that have both been used for 13 years. The factors explored were the surgical technique used, severity of the initial cleft, dental anomalies of primary lateral incisors and presence of bone in the cleft prior to alveolar bone grafting.

Technique B involves closing the cleft earlier than technique A. The mean number of days that subjects had their clefts repaired was 231.6 for technique A and 103.8 for technique B (Table 3.1.7). The range of days for palate closure for technique A was 184-365 days, whereas for technique B the range was 81-200 days. Technique A involves the lip being repaired at approximately 3 months and the hard and soft palate being repaired together at approximately 6-8 months. This is carried out using a vomer flap. In technique B, the lip and the hard palate have been repaired simultaneously using a vomer flap at 3 months, including a bi-lobed flap from the pro-labium in the lip repair and an anteriorly based inferior turbinate flap laterally. This facilitates complete closure of the alveolar flap with soft tissue at the time of the lip repair. A soft palate repair is carried out at 6 months. Studies have been carried out to assess the effect timing of palate repair on maxillary growth. Jolleys, (1954) looked at subjects that were operated on at 2 years and compared them to those that had been operated between 3 to 5 years. It was reported that there was no difference in maxillary growth between these two groups. Robertson and Jolleys,

(1974) assessed subjects who had received early hard palate closure between 12 to 15 months and compared them to subjects who had undergone palatal closure at 5 years. The authors found that there was no difference between occlusion and facial profile between these two groups by 4 years of age. After reporting no significant difference in facial growth, Robertson and Jolleys (1983) made a move to early closure of the hard palate. The Oxford Cleft Palate Study (Rohrich et al, 1996., Rohrich and Byrd, 1990., Grieg et al, 1984) compared early closure at 10 months to late closure at 48 months. There was no statistical difference between dental arch width and facial growth. It was also reported that there was a greater statistical difference in the proportion of patients with a persistent palatal fistula. Five percent of patients with early palatal closure had a palatal fistula, compared to 35% of patients with delayed palatal closure.

Table 3.1.8 and Figure 3.1.9 demonstrates the effect of technique on mid-facial growth, using the 5-year index scores, for technique A and technique B on unilateral cleft lip and palate patients. Of the patients who received technique A, 86.7% had a favourable 5 –year index score of 1 (excellent), 2 (good) or 3 (fair). The remaining subjects who had been operated on using technique A, had a 5-year index score of 4 (poor) and 5 (very poor). There was a reduced proportion of patients, 60.3%, with a favourable 5-year index score who had received technique B. The percentage of patients who had an index score of 4 or 5 was increased compared to technique A at 39.7%. A Pearson chi-squared test was carried out which had a p value < 0.001 and a Fisher's exact test resulted in a p value of 0.001. These results demonstrate that technique B is more likely to have worse 5-year index scores and this is statistically significant. This demonstrates an association between technique B and greater

maxillary growth inhibition. Patients who receive technique B are more likely to require orthognathic surgery in the future compared to those patients who receive technique A. This is statistically significant.

The severity of the initial cleft was a factor that was assessed as part of this research, to determine if there was an association with midfacial growth using the 5-year index. Delestan et al, (2013) had reported a neonatal classification system for unilateral cleft lip and palate patients, with the aim of correlating this with dental anomalies of the primary and permanent lateral incisor and the sagittal growth of the maxilla. There were 4 classes as follows:

- Class 1: maxillary arch with a very narrow alveolar cleft. The two cleft margins are sometimes in closed contact with a tiny bridge.
- Class 2: a balanced form in which the shape of the maxillary arch is close to the controls. The cleft is narrow and the small segment is not displaced, presenting a harmonious curve without a sagittal shift compared with the large segment.
- Class 3: a wide cleft and short maxilla. The transverse distance of the maxillary arch is more important than the sagittal length when compared with the controls. The nasal septum is significantly deviated anteriorly with a torque effect.
- Class 4: a wide cleft and long maxilla. The transverse distance is close to class 3, but the sagittal length of the arch is increased when compared with the controls. The septum is rectilinear.

The authors reported that these four classes can give information on the distribution of the primary lateral incisor. Subjects which were categorized into class 1, would usually have a supernumerary of the lateral deciduous incisor. Subjects which were in the class 3 category, had hypodontia of the deciduous lateral incisor. Class 2 and class 3 subjects had a correlation with a deciduous lateral incisor being located on the lateral palatal segment. These results were statistically significant. Doucet et al, (2014) used lateral cephalograms to measure maxillary growth after the age of 10. The authors found maxillary growth to be most severe in the class 3 category. This was similar to the finding in this research where Table 3.1.12 demonstrates that subjects with a wider cleft on a shorter arch, have worse 5 year index results.

The method described by Peltomaki et al, (2001) was used to measure the severity of the cleft, by measuring recognised landmarks using digital calipers. Peltomaki et al, (2001) had carried out a retrospective study in New York, on 24 consecutive non-syndromic UCLP babies. Measurements on the infant maxillary study casts were taken and compared to maxillary cephalometric variables, taken at age 5. Peltomaki et al, (2001) worked out the cleft gap to arch circumference ratio and the cleft gap to arch length ratio. A lateral cephalogram of each of the 24 subjects was used to measure the maxillary growth. The length of the maxilla was measured, as was the relationship of the maxilla and the mandible to the cranial base. Peltomaki et al, (2001) found that the neonatal maxillary study cast measurements correlated in a statistically significant manner with maxillary cephalometric measurements, at age 5 to 6. Patients with larger cleft gaps and a smaller arch circumference, arch length, or both demonstrated less favourable maxillary growth than those with smaller cleft gaps and a larger arch circumference or arch length at birth.

Rather than using lateral cephalograms as a way to measure mid-facial growth, the 5-year index was used instead in this research. There were 138 UCLP patients in total, of which 44 had neonatal study models. This was almost double the number of patients which had been included in the study conducted by Peltomaki et al, (2001). Table 3.1.11 demonstrates the effect of the cleft width to arch circumference ratio on the 5-year index, for unilateral cleft lip and palate patients. The mean cleft width to arch circumference ratio is 0.15 for subjects which had a 5-year index score of 1 (excellent), 2 (good) and 3 (fair). This ratio was increased to 0.20 for subjects with a 5-year index score of 4 (poor) or 5 (very poor). This finding coincided with that of Peltomaki et al, (2001) who had reported that patients with larger cleft gaps and a smaller arch circumference had demonstrated less favourable maxillary growth. Table 3.1.12 demonstrates the effect of the cleft width to arch length ratio on the 5-year index, for unilateral cleft lip and palate patients. The mean cleft width to arch length ratio was 0.37 for subjects which had a 5-year index score of 1 (excellent), 2 (good) and 3 (fair). This ratio is increased to 0.46 for subjects with a 5-year index score of 4 (poor) or 5 (very poor). This agreed with the finding reported by Peltomaki et al, (2001) which demonstrated that subjects with larger cleft gaps on a shorter arch had less favourable maxillary growth. Patients with larger cleft gaps on a shorter arch circumference or shorter arch length, are more likely to have a worse 5-year index due to unfavourable mid-facial growth. Therefore, they would be more likely to require orthognathic surgery to correct the class III skeletal and occlusal relationship.

4.2 Limitations of the study

A greater number of subjects would be beneficial to assess the effect anomalies of the deciduous lateral incisor would have on the 5-year index, as a trend was visible however this was not statistically significant. As this was a retrospective study, it was only possible to use what was available. Only 44 of the unilateral cleft lip and palate subjects had neonatal study models, as they were not always taken for each patient from the year 2000.

Chapter 5

Conclusions

5.1 Conclusions

The following are the conclusions formed through this study for unilateral cleft lip and palate patients:

1. Subjects receiving technique B have statistically significant worse mid-facial growth.
2. There was no statistical significance of gender on mid-facial growth.
3. The severity of the initial cleft had a statistically significant effect on the mid-facial growth.
4. There was no statistical significance of anomalies of the deciduous lateral incisor on the mid-facial growth.
5. Subjects who had their cleft lip and palate repaired using technique B, were more likely to have bone in the cleft prior to alveolar bone grafting. This was statistically significant.
6. There is a trend present between worse mid-facial growth & bone being present in the cleft prior to alveolar bone grafting, however this was not statistically significant.

The following are the conclusions formed through this study for bilateral cleft lip and palate patients:

1. Subjects receiving technique B had statistically significant worse mid-facial growth.
2. There was no statistical significance of gender on mid-facial growth.

3. There was no statistical significance of anomalies of the deciduous lateral incisors on mid-facial growth.
4. Subjects who had their cleft lip and palate repaired using technique B, were more likely to have bone in the cleft prior to alveolar bone grafting. This was statistically significant.
5. There was no trend present between bone being present in the cleft prior to alveolar bone grafting and worse mid-facial growth.

5.2 Hypothesis

1. The surgical technique is a determinant of mid-facial growth of unilateral and bilateral cleft lip and palate patients.
    - Accepted

2. The severity of the cleft is a determinant of mid-facial growth of unilateral cleft lip and palate patients.
    - Accepted

3. Dental anomalies and agenesis of the dentition are determinants of mid-facial growth of unilateral and bilateral cleft lip and palate patients.
    - Rejected

4. Presence of bone in the cleft is a determinant of mid-facial growth of unilateral cleft lip and palate patients.

- Trend present

5. Presence of bone in the cleft is a determinant of mid-facial growth of bilateral cleft lip and palate patients.
    - Rejected

5.3 Clinical significance

This study has recognised that there is an association between the surgical technique used and mid-facial growth, assessed using the 5-year index. The surgical technique used can have an effect on the mid-facial growth of a patient and could increase the likelihood of the patient requiring orthognathic surgery in the future. It was also recognized, that the more severe the initial cleft is, the more likely a patient will have a poor 5-year index score, indicating that they are predicted to require orthognathic surgery in the future. This study had found that technique B is more likely to result with bone in the cleft, in unilateral and bilateral cleft lip and palate patients. Bone in the cleft was associated with a poor 5-year index score, in unilateral cleft lip and palate patients. This has a clinical significance as by recognising the effect of technique B, this can be adjusted to reduce the number of patients which have a poor 5-year index score and reduce the likelihood for the patient requiring orthognathic surgery in the future. Also by making changes to the techniques being used, would not only remove the liklihood for the patient having to undergo orthognathic surgery in the future, but would also have the effect of

potentially improving the patient's self-esteem and quality of life as they would have not had a significant noticeable discrepancy, in their malocclusion and facial profile.

5.4 Suggestions for further study

The next step to continue from this study would involve collecting data nationally, as increasing the numbers of subjects further would help recognise and establish results. Collecting data from other surgeons who are using the techniques analysed in this study, would help to identify the particulars of the techniques which are associated with the poor 5-year index results. Assessing the severity of a neonatal models using 3D morphology would be a way to develop this further. The neonatal models would be scanned using a 3D scanner. This would allow the measurement of the volume of the palate, along with additional measurements of the neonatal models, to further establish the relationship between severity of the initial cleft and the 5-year index score.

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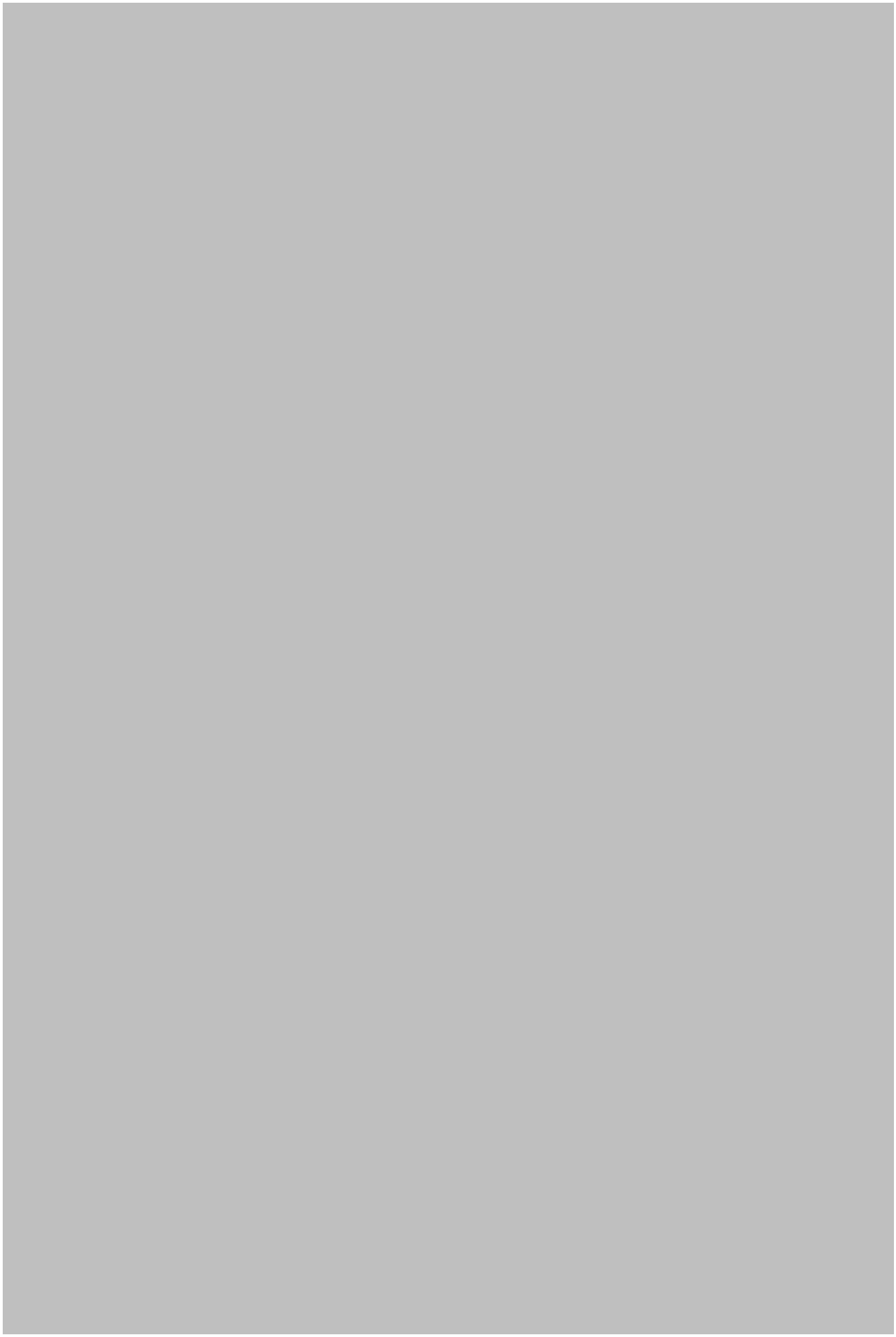

Appendix 2: Raw Data – Unilateral Cleft Lip and Palate

Unilateral Cleft Lip and Palate												
Subject Num	Gender	Ethnicity	Surgical Technique	Date Lip	Time	Date Palate	Time	Side of Cleft	Lateral Incisor (Hypodontia, Supernumerary, Microdont, Transposition, No anomaly)	Dental anomalies of other teeth	5 Year Index (Group 1,2,3,4 or 5)	Presence of Bone in Cleft (Yes/No/Too early to assess)
1	2	Caucasian	B	4/3/00	13	8/24/00	33 (3 days)	L	Missing ULB	Hypodontia UL2	3	Yes
2	1	Caucasian	A	4/28/00	13 (4 days)	7/28/00	26 (4 days)	R	No anomaly	Hypodontia UR2	2	Yes
3	2	Asian/Asian Brit - Pakistani	B	5/11/00	14 (5 days)	10/16/00	37 (2 days)	L	No anomaly	Nil	5	No
4	1	Caucasian	A	6/9/00	13 (1 day)	11/3/00	34 (1 day)	L	$ ULB	Nil	1	No
5	2	Asian/Asian Brit - Indian	A	20/7/20000	13 (6 days)	1/12/01	39	L	Hypodontia ULB	Hypodontia UL2	3	No
6	1	Caucasian	A	8/21/00	14	12/15/00	30 (4 days)	L	No anomaly	Nil	4	No
7	Male	Caucasian	A	8/10/00	12	12/21/00	31	L	$ ULB	Nil	1	No
8	Male	Caucasian	A	10/19/00	16 (5 days)	2/16/01	33 (6 days)	L	No anomaly	Nil	3	Transferred to Salisbury age 6 yrs
9	Female	Caucasian	A	11/2/00	14 (1 day)	5/4/01	40 (2 days)	L	$ ULB	Microdont UL2	1	No
10	Male	Caucasian	B	12/14/00	20 (1 day)	4/12/01	37 (1 day)	R	Missing URB	Missing LRD, LLD, UR2	3	No
11	Female	Asian/Asian Brit - Indian	A	11/10/00	14 (3 days)	4/5/01	35 (2 days)	L	No anomaly	Hypodontia UL2	2	Yes
12	Male	Caucasian	A	11/17/00	15 (2 days)	3/9/01	31 (2 days)	L	No anomaly	Hypodontia UL2	1	No
13	Male	Caucasian	A	11/3/00	13 (1 day)	3/16/01	32 (1 day)	L	No anomaly	Nil	3	No
14	Male	Caucasian	B	11/30/00	14 (1 day)	3/26/01	30 (5 days)	L	Missing ULB	Misssing UR2, UL2	2	No
15	Male	Caucasian	B	1/4/01	14 (3 days)	5/17/01	33 (3 days)	L	No anomaly	N/A	3	Pre-op occlusal not present/notes not present
16	Female	Caucasian	A	3/1/01	16 (2 days)	6/12/01	31	R	$ URB	Nil	2	No
17	Female	Caucasian	A	6/1/01	14 (4 days)	11/13/01	38 (1 day)	R	Hypodontia URB	Hypodontia UR5,2; UL5	3	No
18	Female	Caucasian	A	12/7/01	13	4/16/02	31 (4 days)	L	No anomaly	No anomaly	3	No
19	Female	Caucasian	B	4/25/02	12 (6 days)	10/18/02	39 (1 day)	L	No anomaly	No anomaly	1	No
20	Male	Caucasian	A	4/30/02	14 (4 days)	9/3/02	32 (4 days)	L	Hypodontia ULB	Hypodontia UL2	2	No
21	Male	Mixed-White & Black Caribbean	A	4/26/02	13 (5 days)	9/17/02	34 (2 days)	L	No anomaly	Microdont UL2	1	Yes
22	Male	Caucasian	A	6/11/02	15 (3 days)	11/12/02	37 (3 days)	L	No anomaly	Hypodontia UR5, UL5	2	No
23	Female	Caucasian	A	6/14/02	12	11/5/02	32 (4 days)	L	ULB missing	Missing UR5, LL5. UL2 diminutive	2	No

24	Male	Caucasian	A	7/13/02	14 (2 days)	11/8/02	31 (1 day)	L	No anomaly	Nil	1	No
25	Male	Caucasian	A	8/23/02	17 (4 days)	1/7/03	37 (1 day)	L	No anomaly	Hypodontia UL2	2	No
26	Male	Caucasian	B	12/16/02	13 (3 days)	4/28/03	32 (3 days)	L	No anomaly	Microdont UL2	1	No
27	Female	Caucasian	B	2/14/03	21	7/14/03	42 (3 days)	R	No anomaly	UR2 missing	2	Yes
28	Male	Caucasian	B	1/7/03	15	4/25/03	30 (3 days)	R	No anomaly	Missing URA	4	No
29	Male	Caucasian	A	1/17/03	13 (2 days)	4/29/03	27 (6 days)	L	ULB microdont	Missing LRA, LLA UR5, UR4, UR2, UL2, UL4, UL5, LL5, LL1, LR1, LR5	1	No
30	Male	Caucasian	A	3/27/03	18 (6 days)	7/3/03	32 (4 days)	L	Missing ULB	Microdont UL2	1	No
31	Female	Asian/Asian Brit - Pakistani	A	3/18/03	15 (6 days)	6/24/03	29 (1 day)	L	No anomaly	Missing UL2	2	Yes
32	Male	Caucasian	A	4/5/03	14 (4 days)	8/5/03	31 (5 days)	L	Missing ULB	$ ULQ	1	No
33	Male	Caucasian	A	3/20/03	11 (6 days)	8/12/03	32 (1 day)	L	No anomaly	Microdont UL2	2	No
34	Male	Asian/Asian Brit - Bangladeshi	B	6/19/03	13 (4 days)	9/18/03	26 (2 days)	L	No anomaly	$ ULQ	5	Yes
35	Male	Caucasian	B	8/1/03	13 (4 days)	12/5/03	31 (2 days)	L	No anomaly	No anomaly	3	No
36	Male	Caucasian	A	11/24/03	16 (4 days)	3/2/04	30 (4 days)	L	Missing ULB	No anomaly	2	No
37	Female	Caucasian	B	12/16/03	17 (4 days)	2/5/04	24 (4 days)	L	No anomaly	No anomaly	4	Yes
38	Male	Caucasian	B	11/11/03	12	2/19/04	26	L	Hypodontia ULB	Hypodontia UL2	1	Yes
39	Female	Caucasian	B	12/12/03	12 (6 days)	5/10/04	34	L	No anomaly	Missing UR5, UL5	2	No
40	Female	Caucasian	A	12/12/03	12 (3 days)	5/4/04	32 (5 days)	L	No anomaly	Missing UL2	1	No
41	Female	Caucasian	A	2/10/04	18 (5 days)	6/15/04	36 (4 days)	R	Missing URB	Missing UR2	4	No
42	Male	Caucasian	B	1/15/04	13 (3 days)	5/27/04	32 (2 days)	L	Missing ULB	Microdont UL2	5	No
43	Male	Caucasian	B	5/20/04	11 (6 days)	9/2/04	26 (3 days)	L	No anomaly	Microdont UL2	2	No
44	Male	Caucasian	A	7/15/04	15	12/16/04	36 (4 days)	L	Missing	Microdont UL2	4	No
45	Male	Caucasian	A	7/27/04	12 (6 days)	11/16/04	28 (3 days)	L	ULB missing	Missing UL2	2	No
46	Male	Caucasian	A	8/10/04	14 (3 days)	11/12/04	27 (4 days)	L	No anomaly	UL2 microdont	3	No
47	Male	Caucasian	B	9/2/04	16 (6 days)	12/17/04	31 (6 days)	R	No anomaly	Nil	4	No
48	Male	Caucasian	A	8/19/04	13 (6 days)	1/24/05	36	R	No anomaly	No anomaly	2	No
49	Female	Caucasian	B	9/17/04	16	11/19/04	24 (6 days)	L	Missing ULB	Missing UL2	5	Yes
50	Female	Asian/Asian Brit - Pakistani	A	10/21/04	15	4/7/05	38 (5 days)	L	No anomaly	Nil	3	Yes
51	Male	Caucasian	A	11/23/04	15 (1 day)	4/29/05	37 (3 days)	L	No anomaly	Missing UL2	1	Yes

52	Male	Caucasian	A	1/6/05	19 (4 days)	4/11/05	33 (1 day)	R	Hypodontia URB	Hypodontia UL2	4	Yes
53	Male	Black/Blk Brit-African	A	1/4/05	15	5/9/05	32 (6 days)	R	No anomaly	Missing UR2	2	No
54	Female	Caucasian	A	1/28/05	15 (5 days)	6/13/05	35	L	Supernumerary ULB	Hypodontia LL5	2	No
55	Male	Caucasian	B	1/28/05	12 (5 days)	4/22/05	24 (5 days)	R	No anomaly	UR2 microdont	3	Yes
56	Male	Other Ethnic Group - Chinese	A	3/29/05	17 (5 days)	7/12/05	32 (3 days)	L	No anomaly	Hypodontia UR2	1	No
57	Male	Black/Blk Brit-African	A	5/23/05	16 (1 day)	9/15/05	32 (1 day)	L	No anomaly	Supernumarary UL2	3	No
58	Male	Caucasian	B	5/19/05	12 (3 days)	8/26/05	26 (2 days)	L	ULB missing	Microdont UL2, $ ULQ	3	No
59	Male	Caucasian	A	6/16/05	13 (4 days)	10/10/05	29 (6 days)	L	No anomaly	Nil	3	No
60	Female	Asian/Asian Brit - Pakistani	A	7/21/05	13	11/22/05	30 (2 days)	R	URB missing	Missing UR2, UL2	3	No
61	Female	Caucasian	A	9/13/05	15 (1 day)	1/9/06	31 (5 days)	L	No anomaly	Supernumerary UL2	2	Yes
62	Male	Caucasian	B	9/1/05	11 (4 days)	12/15/05	26 (3 days)	L	ULB missing	Microdont UL2	2	Yes
63	Male	Caucasian	A	11/3/05	13 (1 day)	2/21/06	28 (4 days)	L	No anomaly	Nil	2	No
64	Male	Caucasian	B	11/17/05	12 (6 days)	2/10/06	24 (5 days)	R	2 x URB	Nil	5	Yes
65	Female	Asian/Asian Brit - Pakistani	B	12/15/05	15 (1 day)	3/16/06	28 (1 day)	L	No anomaly	Hypodontia UL2	2	No
66	Male	Caucasian	A	1/5/06	14 (4 days)	5/30/06	35(2 days)	R	No anomaly	Hypodontia UR2	2	Yes
67	Male	Caucasian	B	1/5/06	14 (2 days)	5/4/06	31 (2 days)	L	2 x ULB	Nil	2	Yes
68	Female	Caucasian	B	2/2/06	12 (2 days)	5/5/06	25 (4 days)	R	URB missing	Nil	2	No
69	Male	Caucasian	A	2/16/06	13 (2 days)	6/15/06	30 (2 days)	L	No anomaly	Hypodontia UR2	2	No
70	Male	Asian/Asian Brit - Pakistani	B	3/16/06	13 (6 days)	6/15/06	26 (4 days)	R	URB missing	Missing UR6,5,4,2; UL2,5,6; LL1,2,4,5,6; LR1,2,3,4,5,6,7	5	Yes
71	Male	Caucasian	B	6/30/06	25 (3 days)	10/13/06	40 (1 day)	R	URB missing	Microdont UR2	3	Yes
72	Female	Caucasian	A	5/2/06	17	9/12/06	35 (4 days)	R	No anomaly	N/A	1	No radiographs present/notes checked
73	Female	Caucasian	A	5/2/06	16 (6 days)	8/29/06	33 (4 days)	L	No anomaly	Hypodontia UL2	3	Yes
74	Male	Caucasian	A	6/12/06	20 (5 days)	1/22/07	52 (1 day)	R	Supernumerary URB	Hypodontia UR2	1	No radiographs present/notes checked
75	Female	Asian/Asian Brit - Bangladeshi	A	5/4/06	15 (2 days)	9/12/06	33 (4 days)	L	No anomaly	Missing UL2	4	Yes
76	Female	Any Other Ethnic Group	A	5/26/06	16 (2 days)	10/9/06	35 (2 days)	L	No anomaly	Microdont UL2	1	Yes

77	Female	Caucasian	A	8/1/06	24	12/5/06	41 (5 days)	R	No anomaly	Nil	1	No
78	Male	Caucasian	B	5/12/06	7	8/17/06	26 (2 days)	L	No anomaly	$ ULQ, Missing UL1, UL2. Microdont UR2	2	Yes
79	Female	Caucasian	A	7/31/06	24	12/8/06	42 (1 day)	R	No anomaly	Hypodontia UR2	2	No
80	Female	Asian/Asian Brit - Pakistani	B	5/26/06	14 (3 days)	9/8/06	29	R	No anomaly	Missing URA, ULA	5	No
81	Female	Caucasian	A	6/12/06	15 (1 day)	9/25/06	29 (6 days)	L	No anomaly	Nil	3	No
82	Female	Caucasian	B	10/20/06	18 (4 days)	1/18/07	31 (1 day)	L	Microdont ULB	Missing UL2	3	Yes
83	Female	Caucasian	B	11/2/06	13	2/15/07	27 (5 days)	R	Missing URB	Missing UR2	3	No
84	Female	Black/Blk Brit-African	B	11/30/06	14 (1 day)	3/1/07	27 (1 day)	L	Missing ULB	Missing UL2, ULC	4	Yes
85	Female	Caucasian	B	12/8/06	13 (4 days)	3/2/07	25 (4 days)	L	Missing ULB	Dilacerated UL1, Missing UL2	5	Yes
86	Male	Caucasian	A	1/16/07	14 (4 days)	5/14/07	31 (3 days)	L	No anomaly	Nil	1	No
87	Female	Caucasian	A	2/6/07	14 (5 days)	6/12/07	32 (5 days)	L	No anomaly	Nil	4	Yes
88	Male	Caucasian	B	1/25/07	12 (6 days)	5/11/07	28	L	Missing ULB	Missing UR5,4; UL1,2,4,5; LL1,2,5; LR1,2,5	4	Yes
89	Male	Caucasian	A	3/13/07	13	6/19/07	26 (5 days)	R	No anomaly	Hypodontia UR2	2	No
90	Male	Other Ethnic Group - Chinese	A	4/17/07	16	7/6/07	27 (2 days)	L	No anomaly	Nil	5	No
91	Female	Caucasian	A	3/24/07	11 (4 days)	7/12/07	27	L	No anomaly	Nil	4	No
92	Male	Caucasian	A	5/8/07	14 (1 day)	9/6/07	31	L	$ ULB	Nil	2	Yes
93	Female	Caucasian	B	5/17/07	15	8/16/07	27 (5 days)	L	Microdont UL2	N/A	3	Yes
94	Male	Caucasian	A	7/17/07	13 (1 day)	10/22/07	26 (5 days)	R	No anomaly	Hypodontia UR2	3	No
95	Female	Caucasian	B	9/6/07	15 (4 days)	11/16/07	25 (4 days)	L	Missing ULB	Missing UL2	4	No
96	Male	Caucasian	A	8/31/07	14 (5 days)	1/25/08	35 (2 days)	L	No anomaly	Nil	2	Yes
97	Male	Caucasian	B	9/20/07	15	12/14/07	27	R	No anomaly	N/A	3	No radiographs present/notes checked
98	Female	Caucasian	A	11/1/07	15 (2 days)	2/19/08	30 (5 days)	L	No anomaly	Missing UL2	3	Yes
99	Male	Caucasian	A	1/3/08	18 (1 day)	3/18/08	28 (6 days)	L	ULB supernumerary	Microdont UL2 and $ ULQ	2	No
100	Male	Asian/Asian Brit - Indian	A	1/4/08	15 (3 days)	4/14/08	29 (5 days)	L	No anomaly	Hypodontia UL2	3	Yes
101	Male	Asian/Asian Brit - Indian	B	2/15/08	12 (2 days)	5/15/08	25 (1 day)	R	No anomaly	N/A	2	No radiographs present/notes checked
102	Male	Caucasian	A	3/11/08	14 (3 days)	9/15/08	40 (5 days)	L	Hypodontia ULB	N/A	3	No radiographs

												present/notes checked
103	Female	Mixed - any other mixed background	A	5/6/08	17 (4 days)	9/16/08	36 (1 day)	L	Hypodontia ULB	N/A	2	No
104	Male	Caucasian	B	6/19/08	21 (6 days)	9/18/08	34 (4 days)	L	$ ULB	ULA & ULB fused	2	Yes
105	Male	Caucasian	A	6/3/08	14 (4 days)	9/30/08	31 (2 days)	L	Peg shaped ULB & $ULB	N/A	1	No radiographs present
106	Male	Caucasian	B	10/16/08	28 (4 days)	1/30/09	43 (3 days)	L	No anomaly	N/A	2	No radiographs present
107	Male	Caucasian	B	9/5/08	13 (6 days)	12/5/08	26 (5 days)	L	No anomaly	N/A	3	No radiographs present
108	Female	Caucasian	B	10/2/08	16 (5 days)	1/16/09	31 (4 days)	R	Hypodontia URB	N/A	3	No radiographs present
109	Female	Caucasian	B	9/18/08	13 (2 days)	1/23/09	31 (1 day)	L	Nil	N/A	4	No radiographs present
110	Male	Caucasian	B	11/6/08	15 (5 days)	1/29/09	27 (4 days)	R	Hypodontia URB	N/A	4	Occlusal radiograph not present
111	Male	Caucasian	B	11/7/08	15 (1 day)	2/5/09	27 (5 days)	L	Hypodontia ULB	LRA & LRB fused	4	No radiographs present
112	Male	Caucasian	B	11/28/08	16 (6 days)	2/5/09	26 (3 days)	R	Hypodontia URB	Hypodontia URA	3	No radiographs present
113	Female	Caucasian	B	12/18/08	15 (3 days)	3/18/09	28 (2 days)	L	Hypodontia ULB	N/A	3	No radiographs present
114	Male	Caucasian	B	12/5/08	12	4/14/09	30 (3 days)	L	No anomaly	N/A	3	No radiographs present
115	Male	Asian/Asian Brit - Pakistani	B	12/4/08	11 (4 days)	4/17/09	30 (4 days)	L	Hypodontia ULB	N/A	3	No radiographs present
116	Female	Asian/Asian Brit - Pakistani	A	1/20/09	14 (5 days)	5/19/09	31 (5 days)	R	No anomaly	N/A	2	No radiographs present
117	Male	Caucasian	B	2/17/09	15 (4 days)	7/28/09	38 (4 days)	L	Hypodontia ULB	N/A	4	No radiographs present
118	Female	Asian/Asian Brit - Indian	A	3/2/09	14 (5 days)	6/30/09	31 (4 days)	L	$ ULB	N/A	3	No radiographs present
119	Male	Caucasian	B	5/1/09	13 (1 day)	9/4/09	30 (5 days)	L	No anomaly	N/A	4	No radiographs present
120	Female	Caucasian	A	7/9/09	12 (2 days)	11/9/09	29 (3 days)	L	Hypodontia ULB	N/A	1	No radiographs present
121	Male	Caucasian	B	8/20/09	16 (4 days)	10/15/09	24 (3 days)	R	No anomaly	N/A	4	No radiographs present
122	Male	Caucasian	A	9/8/09	18	3/19/10	45 (2 days)	R	No anomaly	N/A	2	No radiographs present
123	Male	Caucasian	B	9/15/09	14 (6 days)	1/12/10	31 (4 days)	L	No anomaly	N/A	4	No radiographs present

124	Female	Caucasian	B	9/15/09	13 (5 days)	2/19/10	35 (5 days)	L	$ ULB	N/A	2	No radiographs present
125	Male	Caucasian	B	10/13/09	11 (4 days)	2/9/10	28 (1 day)	L	No anomaly	N/A	3	No radiographs present
126	Male	Caucasian	B	11/5/09	14 (1 day)	1/21/10	25	R	Hypodontia URB	N/A	4	No radiographs present
127	Male	Caucasian	B	11/13/09	14 (2 days)	2/4/10	25 (6 days)	L	No anomaly	N/A	2	No radiographs present
128	Male	Caucasian	A	11/23/09	13 (5 days)	3/12/10	29 (2 days)	R	No anomaly	N/A	4	No radiographs present
129	Female	Caucasian	A	3/2/10	25 (4 days)	6/14/10	40 (1 day)	L	$ ULB	N/A	2	No radiographs present
130	Female	Caucasian	B	2/19/10	15 (2 days)	8/20/10	41 (1 day)	R	$ URB	N/A	4	No radiographs present
131	Male	Caucasian	A	2/19/10	14 (2 days)	6/1/10	28 (6 days)	R	No anomaly	Hypodontia UR2	2	No occlusal radiograph
132	Male	Caucasian	B	2/18/10	12 (6 days)	5/21/10	26 (1 day)	R	$URB & $ULB	N/A	2	No radiographs present
133	Female	Asian Brit - Pakistani	B	3/9/10	15 (3 days)	6/22/10	30 (1 day)	R	$ URB	N/A	4	No radiographs present

Appendix 3: Raw data – Bilateral Cleft Lip and Palate

Subject Num	Gender	Ethnicity	Surgical Technique (A or B or C)	Date 1st Procedure	Time (weeks)	Date 2nd Procedure	Time (weeks)	Date 3rd Procedure (weeks)	Time (weeks)	Date 4th Procedure	Time (weeks)
134	1	Caucasian	A	7/28/00	14 (4 days)	12/8/00	33 (1 day)	9/18/01	73 (1 day)	4/1/03	152 (1 day)
135	1	Asian Brit - Pakistani	C	1/11/01	27 (1 day)	5/3/01	43 (1 day)				
136	2	Caucasian	B - R vomer	9/28/00	8 (6 days)	11/30/00	17 (5 days)	3/12/01	32 (2 days)		
137	1	Caucasian	A	11/16/00	12 (4 days)	3/23/01	30 (5 days)	9/30/03	160 (2 days)		
138	1	Caucasian	A	12/8/00	13 (6 days)	5/3/01	34 (4 days)	8/27/02	102 (2 days)		
139	1	Caucasian	A	2/23/01	16 (2 days)	6/19/01	32 (6 days)	1/9/04	164 (2 days)		
140	1	Caucasian	A	2/15/01	12 (4 days)	7/2/01	32 (1 day)	6/6/02	79 (6 days)		
141	1	Caucasian	A	4/17/01	11 (3 days)	9/11/01	32	1/10/03	100 (3 days)		
142	1	Caucasian	B - L vomer	7/26/01	11 (5 days)	1/14/02	35 (5 days)				
143	1	Caucasian	A	8/7/01	12 (2 days)	1/15/02	34 (2 days)	3/11/03	94 (2 days)	8/20/04	168 (3 days)
144	1	Caucasian	A	11/6/01	17 (2 days)	8/20/02	57 (6 days)	7/27/04	157 (3 days)		
145	2	Caucasian	A	11/9/01	14 (5 days)	4/9/02	36 (1 day)	2/27/04	133	9/28/04	163 (1 day)
146	2	Caucasian	A	2/1/02	13 (1 day)	6/18/02	32 (5 days)	11/16/04	156 (5 days)		
147	2	Caucasian	A	3/19/02	12 (3 days)	8/20/02	34	8/31/04	138 (3 days)		
148	1	Caucasian	B - L vomer	4/8/02	11 (6 days)	7/16/02	25 (6 days)	3/25/03	61 (3 days)		
149	1	Asian Brit - Pakistani	C	7/9/02	15 (1 day)	10/22/02	29 (6 days)				
150	1	Caucasian	A	8/23/02	16 (2 days)	1/28/03	38 (3 days)	5/25/08	312 (2 days)		
151	1	Caucasian	C	11/26/02	12 (4 days)	4/8/03	31 (3 days)				
152	2	Caucasian	B - R vomer	3/20/03	15 (3 days)	8/21/03	37				
153	1	Asian Brit - Pakistani	A	6/5/03	13 (1 day)	10/2/03	29 (6 days)				
154	1	Caucasian	A	8/19/03	13 (6 days)	12/2/03	28 (4 days)	11/28/05	130 (6 days)		
155	1	Caucasian	A	12/12/03	12 (3 days)	3/4/04	24 (1 day)				
156	1	Caucasian	B - L vomer	12/18/03	11 (6 days)	3/25/04	25 (5 days)				
157	1	Caucasian	A	1/29/04	16 (4 days)	6/8/04	35	5/9/06	133 (5 days)	9/21/06	152 (4 days)
158	1	Caucasian	A	3/9/04	14 (3 days)	8/17/04	37	2/13/07	165		
159	2	Black/Brit-Caribbean	B - L vomer	5/6/04	16 (4 days)	7/22/04	27 (3 days)				

160	2	Caucasian	B - R vomer	6/17/04	14 (4 days)	9/16/04	27 (2 days)				
161	1	Caucasian	B - L vomer	8/27/04	14	11/19/04	25 (5 days)				
162	2	Caucasian	C	8/31/04	14 (1 day)	2/8/05	36 (4 days)				
163	1	Caucasian	B - R vomer	11/26/04	12 (4 days)	3/4/05	26 (4 days)				
164	1	Caucasian	B - R vomer	1/20/05	12 (5 days)	4/21/05	25 (5 days)				
166	1	Mixed	B. L vomer	4/1/05	13	7/1/05	25 (6 days)				
167	1	Caucasian	B - R vomer	11/25/05	12 (4 days)	2/24/06	25 (2 days)				
168	2	Caucasian	A	3/27/06	12 (6 days)	8/1/06	30 (4 days)	5/23/08	123 (5 days)		
169	2	Caucasian	A	5/8/06	12 (5 days)	9/29/06	32 (6 days)	7/8/08	124 (1 day)		
170	1	Caucasian	C	3/12/07	14 (4 days)	7/3/07	30 (3 days)				
171	1	Caucasian	B - L vomer	5/4/07	16 (3 days)	9/21/07	36				
172	1	Other	C	3/4/08	13 (5 days)	6/9/08	27 (2 days)				
173	1	Caucasian	B - R vomer	3/14/08	14 (1 day)	7/3/08	29 (5 days)				
174	1	Caucasian	A	4/22/08	14	7/28/08	27 (5 days)	5/24/08	18 (4 days)	9/28/09	87 (5 days)
175	1	Caucasian	C	12/2/08	13 (1 day)	3/31/09	30				
176	1	Asian Brit - Pakistani	A	1/13/09	16 (3 days)	4/28/09	31 (3 days)				
177	1	Caucasian	B - R vomer	3/5/09	13 (3 days)	6/12/09	27 (2 days)				
178	1	Caucasian	C	3/17/09	13 (1 day)	7/7/09	28 (6 days)				
179	1	Asian Brit - Pakistani	A	3/24/09	13 (5 days)	6/23/09	26 (3 days)	12/13/11	153 (4 days)		
180	1	Caucasian	A	5/29/09	11 (6 days)	9/22/09	28	1/4/11	94		
181	1	Asian Brit - Pakistani	B - L vomer	7/31/09	18	10/23/09	29 (5 days)				
182	1	Caucasian	A	2/9/10	26	6/8/10	43				

Lateral Incisor (Hypodontia, Supernumerary, Microdont, Transposition, No anomaly)	Dental anomalies of other teeth	5 Year Index (Group 1,2,3,4 or 5)	5 Year Index Repeated	Presence of Bone in Cleft (Yes/No/Too early to assess)
No anomaly	Supernumerary UR2. Microdont UR2, UL2	2	2	No
No anomaly	Nil	4	4	No
Hypodontia URB, ULB	Hypodontia UR5,4,3,2; UL2,3,4,5; LR5 to LL5	1	1	No
Supernumerary URB	Hypodontia UL2, LL2	1	1	No
$ ULB	Hypodontia UL1, UL2	2	2	No
Supernumerary URB & ULB	Nil	2	2	No
No anomaly	Hypodontia UR5,2; UL1,2,5; LL5, LR5	1	1	No
No anomaly	Hypodontia LR5, LL5	1	1	No
No anomaly	Nil	1	1	No
No anomaly	Hypodontia UR2, UL2	2	2	No
No anomaly	Hypodontia UR2, UL2	1	1	No
Hypodontia URB, ULB	Hypodontia UR2, UL2, LL5	1	1	No
Hypodontia URB, ULB	Hypodontia UR2, UL2	1	1	No
$ URB & ULB	Hypodontia UR2	1	1	No
Supernumerary URB	Supernumerary UR2 & UL2	1	1	Yes - left
Hypodontia URB	Hypodontia UR2	2	1	Yes - right
No anomaly	Hypodontia UR2, UL2, LR5, LRE, LLE, LL5	1	1	Yes - left
No anomaly	Missing UL2	3	3	No
No anomaly	$ LRA. Hypodontia UR5, UR2, UR1, UL2 UL5, LR5, LL4, LL5.	5	5	No
Hypodontia URB, ULB	Hypodontia UR2	5	5	No
No anomaly	Microdont UR2, UL2. $ URQ	2	2	No
Hypodontia URB. ULB	Hypodontia UR1, UL5, LL5, LR5	2	2	Yes - right
No anomaly	Hypodontia UR2	5	5	No
No anomaly	Hypodontia UR2, UL2	1	1	No
No anomaly	No anomaly	1	1	No
No anomaly	Hypodontia UR2, UL2	4	4	Yes - left
No anomaly	Hypodontia UR2,1; UL2	1	1	No
No anomaly	Hypodontia UR5,E,2,1; UL2,E,5; LLE,5; LRE,5	5	5	No
Supernumerary URB	Hypodontia UL2	4	4	No
Hypodontia URB	Nil	1	1	Yes - right
$ URB & $ ULB	Nil	2	2	No
Supernumerary URB	Nil	3	3	Yes - right
Hypodontia URB, ULB	Hypodontia UR2, UL2	5	5	Yes - left
No anomaly	Hypodontia URD, UR2, UL2, ULD,	5	5	No
No anomaly	Hypodontia UR2, UL2	1	1	No
Hypodontia URB, ULB	Hypodontia UR2, UL2	2	1	No
No anomaly	Hypodontia UR2, UL2, UL5	2	2	Yes - right
No anomaly	N/A	3	3	No radiographs present
Hypodontia URB	N/A	4	4	No radiographs present
Hypodontia URB & ULB	Hypodontia UR2, UL2	1	1	Yes - right
Microdont URB	Hypodontia URD	2	2	No radiographs present
Hypodontia ULB	Hypodontia URD, URA, ULA, ULB, ULD. N/A permanent	2	2	No radiographs present
Hypodontia URB & ULB	N/A	4	4	No radiographs present
Hypodontia/extracted URB; ULA,B,C	Hypodontia UR5,4,2,1; UL1,2; LL5; LR5. Macrodont LRE,LLE. Microdont LRB,A; LLA,B	3	3	No occlusal radiograph present. OPG present
No anomaly	N/A	1	1	No radiographs present

Hypodontia URB, ULB	N/A	1	1	No radiographs present
No anomaly	N/A	1	1	No occlusal radiograph present. OPG present
No anomaly	Hypodontia ULA	1	1	No radiographs present

Appendix 4: Neonatal Measurements

Subject	cw	archc	antw	postw	archl
1	10.72	58.84	31.22	31.04	24.39
10	3.33	74.65	28.19	29.49	24.29
21	14.5	67.49	36.04	27.78	29.38
24	11.08	65.63	29.75	28.56	29.83
27	16.97	68.53	36.87	27.11	31.81
30	9.49	67.62	30.81	33.53	28.27
31	13.62	64.81	31.67	33.59	27.93
33	10.25	69.25	37.63	39.11	28.25
32	5.2	65.53	23.72	27.24	27.95
34	9.58	71.87	33.42	29.59	25.79
35	11.42	69.07	30.03	32.02	27.75
36	10.45	68.43	30.56	34.5	30.68
37	10.91	80.75	35.93	39.74	33.01
39	10.94	63.07	34.2	28.89	25.66
40	6.25	73.67	31.97	31.8	28.75
42	12.86	82.28	42.56	31.53	32.54
41	14.34	49.11	35.73	32.41	18.54
43	10.8	74.16	38.36	36.4	30.81
44	15.19	63.5	31.53	30.31	31.08
45	13.85	69.49	33.59	36.91	28.56
47	12.58	76.22	37.76	28.79	31.41
49	17.12	67.72	35.98	32.52	33.7
50	11.62	65.17	31.19	33.25	26.01
55	15.98	79.45	41.69	31.12	31.45
58	8.83	79.51	29.85	33.6	33.65
62	1.1	78.43	28.24	28.02	26.22
64	12.56	76.3	42.98	37	32.87
67	10.59	73.7	37.59	38.82	31.78
68	2.77	76.89	35.53	36.14	23.91
70	16.54	62.11	38.78	32.79	26.74
71	14.29	71.49	37.27	31.53	34.09
75	18.07	62.92	36.1	35.55	28
80	7.64	62.67	26.45	26.27	27.73
78	16.89	66.15	40.9	37.15	29.61
82	12.65	71.54	34.3	30.03	30.92

83	15.44	71.81	40.38	32.7	28.84
84	14.33	75.06	34.8	28.18	36.47
85	18.58	65.86	37.31	35.35	29.42
88	17.65	64.51	40.31	39.42	30.68
93	14.52	73.68	36.66	29.61	31.97
95	10.83	64.87	34.69	30.61	26.21
97	12.61	71.67	35.16	34.32	26.89
99	2.32	60.47	27.3	38.97	20.74
101	14.11	68.39	38.62	31.4	26.14

Subject	cw2	archc2	antw2	postw2	archl2
1	8.92	62.68	30.91	31.12	22.92
10	4.13	76.21	34.43	32.44	24.76
21	15.86	66.59	33.11	27.75	30.74
24	12.13	66.41	29.63	32.65	29.43
27	17.47	66.51	36.59	29.79	29.88
30	10.26	72.44	35.34	32.96	32.75
31	14.01	65.55	32.55	33.45	31.51
33	9.16	70.51	37.19	38.88	23.91
32	5.49	64.15	19.24	27.54	27.51
34	8.87	73.42	31.09	29.11	26.82
35	11.2	68.13	34.03	33.5	27.52
36	11.15	70.52	32.36	33.52	29.47
37	10.16	80.67	36.7	38.01	29.04
39	9.75	69.08	36.06	29.73	27.72
40	5.69	75.05	31.84	31.84	28.27
42	11.78	83.84	36.76	33.75	31.53
41	14.6	52.43	35.93	33.27	28.33
43	11.29	74.7	37.79	34.64	31.09
44	16.68	66.57	33.86	29.77	31.29
45	12.48	70.7	33.35	36.72	31.45
47	11.84	77.59	36.87	33.52	31.26
49	16.37	69.39	36.47	31.98	34.52
50	11.5	66.04	31.04	33.3	28.86
55	15.78	71.09	40.81	36.51	30.43
58	8.9	79.33	30.04	33.9	32.3
62	1.64	79.49	31.67	28.97	26.35
64	12.44	80.16	40.05	35.16	33.69
67	10.17	72.07	31.91	37.93	29
68	2.91	82.16	35.41	32.7	27.02
70	16.47	61.54	38.43	32.44	26.94
71	13.67	77.02	36.8	30.75	32.01

75	17.82	63.71	36.32	35.53	26.28
80	5.64	65.62	26.27	24.76	27.04
78	15.14	69.63	39.5	35.82	30.41
82	13.02	71.14	37.98	33.46	31.45
83	14.66	74.2	40.16	31.5	29.6
84	14.26	74.71	34.42	29.28	36.34
85	18.86	64.57	39.11	32.88	29.33
88	16.36	72.29	40.04	36.96	32.42
93	14.43	73.29	36.53	32.89	29.81
95	10.71	64.52	35	31.97	25.33
97	12.58	71.62	32.95	34.22	28.57
99	1.98	64.78	32.25	38.77	21.09
101	13.89	70.73	36.99	30.96	27.46

Appendix 5: Excluded subjects

Subject	Gender	Type of cleft	Reason for exclusion
1	Male	UCLP	TRANSFERRED TO [redacted] AT 3 YEARS OLD
2	Male	BCLP	NO 5 YEAR MODEL PRESENT, ONLY NEONATAL MODEL PRESENT.
3	Female	UCLP	HAD SURGERY ELSEWHERE
4	Female	BCLP	TRANSFERRED TO [redacted] AT 6 YEARS
5	Female	UCLP - L	UNKNOWN CLEFT TYPE
6	Male	BCLP	TRANSFERRED TO [redacted] AGE 9 MONTHS
7	Female	BCLP	DECEASED ON DAY OF BIRTH
8	Male	UCLP	INCOMPLETE UCLP
9	Male	BCLP	ONLY NEONATAL MODEL PRESENT
10	Male	UCLP	PT HAD SURGERY BEFORE COMING TO [redacted]
11	Male	UCLP - R	SIMONARTS BAND 10+MM - NOT TRUE UCLP
12	Male	BCLP	HAD SURGERY ELSEWHERE
13	Male	BCLP	HAD SURGERY ELSEWHERE
14	Female	BCLP	PASSED AWAY
15	Female	UCLP - R	TRANSFERRED FROM [redacted] 2013
16	Female	BCLP	HAD SURGERY ELSEWHERE
17	Male	UCLP	TRANSEFRRED TO [redacted] AT 4 & 1/2 YEARS OLD
18	Female	BCLP	HAD SUREGRY IN [redacted]
19	Male	UCLP	TRANSFERRED TO [redacted] AT 1 & 1/2 YEARS OLD
20	Female	BCLP	HAD SURGERY ELSEWHERE & HAS LEFT COUNTRY
21	Female	UCLP -	INCOMPLETE UCLP
22	Female	UCLP - R	SIMONARTS BAND PRESENT
23	Female	BCLP	MAJOR REDO
24	Female	UCLP - R	PT MOVED TO [redacted] AGE 1
25	Female	BCLP	PASSED AWAY AT 1-2 YRS OLD
26	Female	BCLP	PT TRANSFERRED TO [redacted] AFTER 1 YEAR
27	Female	BCLP	ONLY NEONATAL MODEL PRESENT
28	Aden	BCLP	HAD SURGERY ELSEWHERE. PASSED AWAY
29	Male	BCLP	REFERRED TO [redacted] AGE 4 YEARS

Appendix 6: Codes for Statistical Analysis

Description	Code
Male	1
Female	2
UCLP tech A	1
UCLP tech B	2
BCLP tech A	1
BCLP tech B	2
BCLP tech C	3
Caucasian	1
Pakistani	2
Indian	3
Bangladeshi	4
Afro-Carribean	5
Chinese	6
Mixed	7
Other	8
bone - yes	1
bone - no	2
bone - left	1
bone - right	2
bone - both sides	3
no anomaly	1
hyp	2
$	3
no anomaly	1
hyp R & L	2
hyp R	3
hyp L	4
$ R & L	5
$ R	6
$ L	7