Assessment of the correlation between patients with a unilateral cleft lip and palate (UCLP) and non-cleft individuals regarding the duration and speed of maximum smile using 4d imaging

By

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Abstract

In a cleft lip and palate (CLP), the upper lip and palate fail to develop correctly during embryological development. CLP is managed by surgical interventions; cleft lip repairs, nasal reconstruction and revision procedures. Asymmetry is noted in the nasolabial region (Hallac et al., 2017), due to scarring, muscular pull and underdeveloped muscles around the cleft causing weakness or muscular imbalance which can cause profound psychosocial impact (Yezioro-Rubinsky et al., 2020).

Scar revision during childhood can minimise the psychosocial impact (Tan and Pigott, 1993) and restore function to facial muscles. The decision for revision surgery is currently based on subjective evaluation of limitations by a surgeon. Objective quantification of dynamic motion with 4D imaging could allow comparison of different treatments, monitor patients for worsening and guide future intervention. Each expression has specific muscle groups that undergo contraction and relaxation during different phases of movement. Some of these muscles are surgically corrected during repair and others are relatively untouched.

This study aims to objectively assess dynamic dysmorphology from rest to maximum smile with 4D imaging for individuals with a unilateral cleft lip and palate (UCLP) and unaffected individuals, to improve quality of care and treatment for patients with UCLP. The impact that residual scarring has on expression speed during the maximum smile was also investigated. Maximum smile for the two groups were compared, 31 UCLP patients (13-17yrs) and 34 control participants. Nine landmarks were used; 6 paired landmarks to analyse lip motion, cheilion, crista philtri and lower lip and 3 landmarks to minimize head motion. Different phases of the smile were assessed; onset, apex and offset and the speed for the individuals to reach maximum smile. Comparison allows differences between groups and intrapersonal differences between right and left to be identified.

Results show UCLP participants have longer onset and offset (contraction and relaxation) phases and a longer smile duration (2.02 secs) than unaffected individuals (1.33 secs). There was measurable asymmetry in philtrum magnitude and speeds between the two sides in UCLP participants with the cleft side significantly slower (7.24mm/s) than the unaffected side (8.22mm/s). Although the same pattern was seen for cheilion magnitude and speed, this did

not reach statistical significance (cleft side 28.69 mm/s, non-cleft side 32.05 mm/s). In contrast the cleft side had significantly greater magnitude and speeds at the lower lip (20.98mm/s) than the non-affected side (19.22mm/s). Asymmetric movement on the lower lip is due to distorted muscle dynamics, secondary to the asymmetric upper lip muscles during expression phases. Less muscular development on the cleft side causes weakness, reduced control and tension from scarring limits upper lip movement, causing the lower lip to compensate for the deficit. Control participants had no significant speed or magnitude differences for the landmarks on opposing sides, indicating no discernible asymmetry.

During maximum smile, all landmarks on the cleft side exhibited slower speeds than control participants (cheilion 34.89 mm/s slower, philtrum 14.53 mm/s slower, lower lip 18.1 mm/s slower). This was also reflected for the UCLP participant's unaffected side (Cheilion 37.71 mm/s slower, philtrum 12.21 mm/s slower, lower lip 21.14 mm/s slower) when compared to individuals without a cleft. Indicating restriction in muscular activity on both sides regardless of which side is affected by the cleft.

The odds of having reduced speeds at the cheilion are 87% higher when a cleft is present and it is 3 times more likely to have slower speeds at the philtrum on the cleft side than in an unaffected individual. Unlike other landmarks, the lower lip is faster on the side affected by the cleft than the unaffected individuals.

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Authors declaration

I declare that this thesis has been composed solely by myself and that it has not been submitted, in whole or in part, for any other degree or professional qualification except as specified.

Except where stated otherwise by reference or acknowledgment, the work presented is entirely my own.

Abbreviations

- AU - Action units
- AI – Artificial intelligence
- CBCT - Cone beam computed tomography
- CCPA - California consumer Privacy Act
- chR - Cheilion right, the most lateral point located on the right corner of the mouth
- chL - Cheilion left, the most lateral point located on the left corner of the mouth
- cphR - Crista philtri right- the point on the right elevated margins of the philtrum above the vermillion line
- cphL - Crista philtri left- the point on the left elevated margins of the philtrum above the vermillion line
- CLP - Cleft lip and palate
- COHIP - Child Oral Health Impact Profile
- CPO - Cleft palate only
- CN - Cranial nerve
- CT - Computed tomography scan
- DMFT - Decayed, missing, and filled teeth
- ecL - Left endocanthion, the point on the left side of the face at which the inner ends of the upper and lower eyelid meet, a stabilising landmark to account for head motion
- ecR - Right endocanthion, the point on the right side of the face at which the inner ends of the upper and lower eyelid meet, a stabilising landmark to account for head motion
- FACs - Facial action coding system
- FASD - Foetal Alcohol Spectrum Disorder
- FIPS - Federal Information Processing Standards
- GDPR - General Data Protection Regulation
- HIPAA - Health Insurance Portability and Accountability Act
- IOS - Intraoral optical Scan
- llL - Lower lip left, the point below the vermillion line opposite cphL
- llR - Lower lip right, the point below the vermillion line opposite cphR
- LLS - Levator Labii Superioris
- MRI - Magnetic resonance imaging

- NAS - Neonatal Abstinence Syndrome
- NAM - Nasoalveolar moulding
- NATO - North Atlantic Treaty Organisation
- NCSC CPA - National cyber security centre commercial product assurance
- NIPE - Newborn physical examination
- NLNCSA BSPA - Netherlands National Communications Security agency, baseline security product assessment
- NOSE - Nasal Obstruction Symptom Evaluation
- OHRQoL - On health related quality of life
- Pn - Pronasale the most anterior midpoint of the nasal tip
- SD - Standard deviation
- SOX - Sarbanes Oxley Act is the compliance in cyber security
- TB - Terrabyte
- TIA – Transient ischaemic attack
- UCLP - Unilateral cleft lip and palate
- US - Ultrasound
- WHO - World health organisation
- 2D - 2-Dimensional
- 3D - 3-dimensional
- 4D - 4-dimensional

Glossary

- Agenesis - lack or failure of development
- Anthropometry - scientific study of the measurements and proportions of the human body
- Autogenic - self generating, produced within, from the same subject
- Bifid uvula - a uvula that is split in two
- Craniofacial microsomia - part of the face is smaller as it is underdeveloped and does not grow normally
- Diastasis - separation of parts of the body that are normally joined
- Duchenne smile - a smile that signals true enjoyment. It is characterized by lifting the corners of the mouth while the orbicularis oculi muscles lift your cheeks and crinkle the eyes
- Ectoderm - a germ layer, the outermost layer of cells or tissues of an embryo in early development, gives rise to the skin, nervous system and sense organs
- Ectopic - abnormal place or position
- Endoderm - the innermost germ later that forms the linings of the respiratory and gastrointestinal tracts
- Eustachian tube - opening that connects the middle ear and the nasal sinus cavity, it helps to balance pressure in the middle ear
- Facial morphogenesis - shaping of the face by an embryological process of differentiation of cells, tissues and organs
- Fibromuscular mass - both fibrous and muscular tissues in one composition
- Frontonasal prominence – establishes the facial midline, composed of the forehead, bridge and tip of nose, philtrum and primary palate
- Hypoplasia - incomplete development or underdevelopment of an organ/tissue
- Iliac crest - superior border (curved part at the top) of the ilium which is the largest bone of the pelvis
- Incisive foramen - oral opening of the nasopalatine canal located in the midline of the maxilla, posterior to the central incisors

- Inferior turbinate – a bone in the nasal cavity responsible for the majority of airflow direction, humidification, heating and filtering of air inhaled through the nose
- Lacrimal groove - deep groove in front of the opening of the maxillary sinus on the nasal surface of the maxilla
- Malrotated - improper rotation of a body part
- Mandibular prominence – embryological structure giving rise to the lower portion of the face
- Maxillary prominence - embryological structure that forms the lateral wall and floor of the orbit, the greater maxilla and zygomatic bone are ossified here
- Medial crura - the posterior parts of the cartilage that form the nasal tip and are important for nose shape and appearance
- Medial palpebral ligament - a ligament of the face, attaches to the frontal process of maxilla, the lacrimal groove and the connective tissue of each eyelid
- Mentolabial sulcus - or labiomental fold, is the indistinct line separating the lower lip from the chin
- Mesoderm – another one of the three primary germ layers, forms structures such as neural tube, skeletal muscles smooth muscles, bone, cartilage, blood vessels and connective tissue
- Microdeletion - chromosomal deletions too small to be detected by usual testing methods and specialised tests are required to detect these
- Modiolus - small fibromuscular structure at the corner of the mouth where fibres from multiple facial muscles converge and helps to coordinate the action of these muscles
- Nasal placodes - thickened ectoderm from frontonasal prominence and give rise to the olfactory epithelium
- Nasal regurgitation - when nasopharynx doesn’t close properly and swallowed fluid or food backtracks into the nose
- Nasolabial folds - creases in your skin extending from both side of the nose to the corners of the mouth
- Neuroectoderm - region of the ectoderm which develops into the central nervous system and other nervous tissue
- Oropharyngeal membrane - where masses of ectoderm and endoderm come into direct contact with each other and form a thin membrane, which creates a septum between the mouth and pharynx

- Palatine aponeurosis - is a thin, firm, fibrous lamella that supports the soft palate
- Palatal shelves - wedge shaped and commence development as processes, that grow downwards from the maxillary processes each side of the tongue
- Pharyngeal arches - paired structures that grow on either side of the developing head and neck of the embryo, and they fuse at the midline, there are 5 pairs
- Phenotype - observable physical properties of an organism
- Piriform aperture - or anterior nasal aperture, is a pear-shaped opening in the human skull
- Primary palate - anterior to the incisive foramen
- Pterygo-mandibular raphe - ligament which gives attachment to the central portion of the buccinator muscle anteriorly and superior pharyngeal constrictor muscle posteriorly
- Pyriform rim - pear shaped bony inlet of the nose formed by the nasal and maxillary bones, it forms a boundary between the anterior and posterior nasal cavity
- Quad helix - orthodontic appliance applied to upper teeth by 2-4 bands and 2-4 active helix springs to widen the upper arch, to create additional room
- Redline – junction between the non-keratinised intraoral mucosa (wet) and keratinised mucosa (dry) of the vermillion
- Rhinoplasty - plastic surgery performed on the nose
- Secondary hard palate - posterior to the incisive foramen
- Stereophotogrammetry - estimates the 3d coordinates of points on an object employing measurements made in 2 or more photographic images taken from different positions. It allows us to create or enhance the illusion of depth in an image.
- Superior constrictor muscle - originates from the pterygoid process and its main function is the constriction of the upper part of the pharynx which aids deglutition
- Supernumerary - present in excess of the normal number
- White roll – the pale convexity outlining the vermillion borders of the upper and lower lips
- Velopharyngeal mechanism - comprised of a complex group of structures that act in unison to control airflow through the nose and mouth by elevating the soft palate and constriction of the pharyngeal walls
- Velum - the soft palate
- Vermillion border - the sharp demarcation between the lip and the adjacent normal skin

- Vomer - the bony part of the nasal septum
- Zona pellucida- a thick transparent membrane surrounding a mammalian ovum before implantation
- Zygomaticotemporal suture- the cranial suture between the zygomatic bone and the temporal bone

Chapter 1. Introduction and Literature review

1. Introduction

I. Background

Cleft lip and palate (CLP) is one of the most common congenital conditions, affecting the formation of the upper lip and the palate during foetal development (Vanderas, 1987). In layman terms it is when the lip and/or palate fail to develop correctly resulting in a gap or channel being left. This can either occur in isolation, a unilateral cleft lip and/or palate or bilaterally.

The extent of this gap varies among cases, ranging from an incomplete cleft lip which may be in the form of a small defect to a complete cleft which extends all the way to the nasal floor. A cleft palate can be either a partial palatal cleft which only affects the soft palate or a complete cleft which affects the hard and soft palates. Cleft palates may also be submucous; meaning that the overlying mucosa is intact while the underlying palate muscles have failed to fuse at the midline. This anomaly occurs when the nasal and maxillary processes fail to fuse during embryological development, in turn leading to an asymmetric muscle pull on the nasal septum during development of the mid face (Hall and Precious, 2013). Development of oral structures commence at around week four of pregnancy, a lack of fusion of the primary palate manifests as cleft of the lip and alveolus whereas the secondary palate failing to fuse during the eighth week causes cleft of the palate (Sperber et al., 2010). Having a cleft may cause problems with feeding, swallowing, speaking clearly, hearing problems and affect dental development.

II. Clinical Management

CLP is managed by surgical interventions such as cleft lip repairs, nasal reconstruction and in some cases revision procedures. Greater asymmetry was noted in the nasolabial region in children treated for cleft lip and palate (Bugaighis et al., 2014). Even with the surgical intervention by highly skilled surgeons, some asymmetry persists (Hallac et al., 2017). This is due to scar tissue, muscular pull and the muscles around the lip and palate being underdeveloped, weaker, or imbalanced (Yezioro-Rubinsky et al., 2020). Causing reduced co-ordination, asymmetry, compensatory movements or a limitation in facial movement, which can have a profound psychosocial impact on patients (Shaw et al., 1985). Not only do these patients experience static asymmetry but they also can have impairments during dynamic movement. Daily function and interaction involve dynamic movements, so to fully assess asymmetries and limitations we need to explore these. Some revision procedures of lip scarring are carried out during childhood to try and minimise the psychosocial impact caused from the scarring and consequent nasolabial asymmetry (Tan and Pigott, 1993).

III. Population cohort

Directly comparing patients with cleft lip and palate and non-cleft subjects could be misleading, due to large variations in the mean (Trotman et al., 2007). So if studying two separate groups, it can be appropriate to look at a normal scale of movement and how this may differ. In 2017, Hallac used 4D imaging to assess facial expressions during smiling and pouting (Hallac et al., 2017). These results showed asymmetry in the path and magnitude of motion. However it would be beneficial to know at what stage of the expression asymmetry and variation occurs so we can refine surgical techniques to improve outcomes.

IV. Assessment of Treatment Outcome

The aim of primary and secondary cleft lip surgery is to minimise post-surgical scarring, achieve optimal facial aesthetics and restore function to the orbicularis oris muscle. The decision for lip revision surgery is currently based on subjective evaluation of lip limitations by a surgeon. It has been hypothesised that lip revision surgery would cause more scarring, making any impairments worse. However, in 2010, (Trotman et al., 2010) there was reported improvement in movement after lip revision. Objective evaluation would be beneficial during assessment of the initial cleft repair to establish if there is a need for future corrective surgery.

V. Facial Expression

Human beings communicate together by a variety of verbal and non-verbal expressions which are of equal importance for day-to-day social interaction (de Gelder, 2009). Facial expression can be one of the richest banks of emotional information (Ekman, 2009) in humans, making it an important form of non-verbal communication. Non-verbal expressions are crucial in understanding emotion, social context and mood. There are many ways our facial expressions can be distorted; craniofacial anomaly, trauma, facial paralysis, Bell's palsy, stoke/TIA and some psychiatric conditions. Ekman described that key information from the expressed emotion can be seen by looking at the muscle movement phases in more detail, such as contraction from rest to maximum and relaxation of the muscles back to rest (Ekman, 2009). Research on measurement of facial expressions includes the facial action coding system (FACS), with 23 facial motion units (Ekman and Friesen, 1978). FACS analyses facial expressions in real time, to determine the person's emotion, breaking down expressions into individual components of muscle movement, called action units.

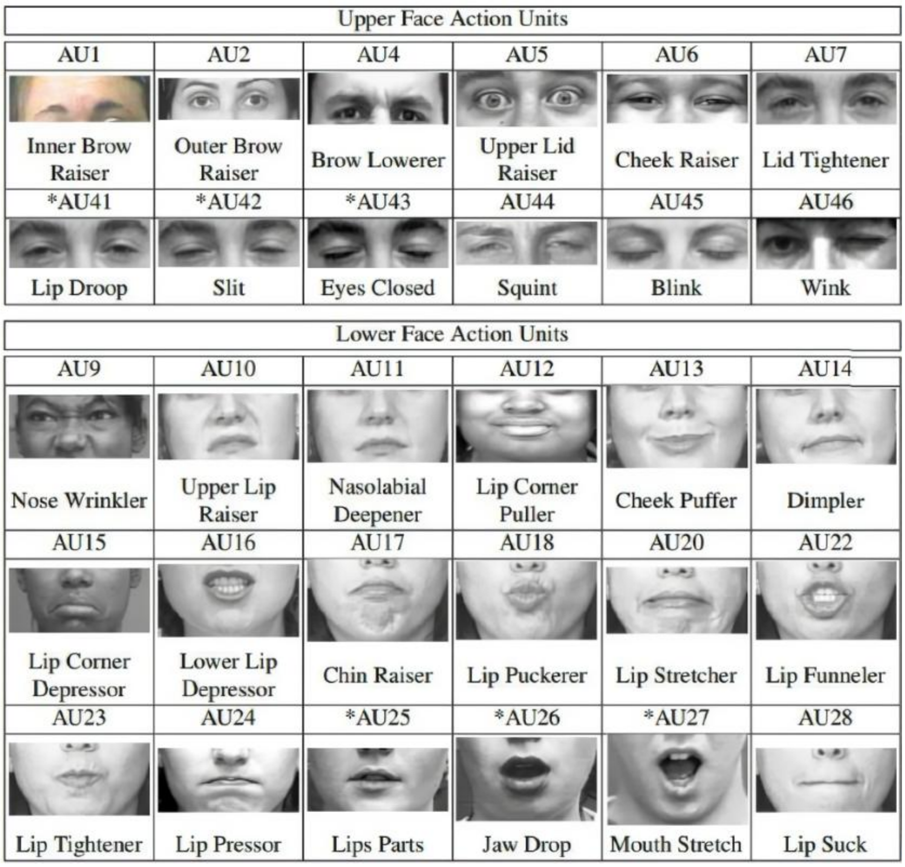

Figure 1 - Examples from different facial Action Units (AUs) (Ekman and Friesen, 1978) for upper and the lower face.

Facial motion can be captured with 2D,3D or 4D imaging, and can be known as "expression tracking". Two-dimensional capture is less sophisticated, using a single camera and capture software. Three-dimensional capture is more expensive, more complicated and more time consuming. It uses multi-cameras or a laser system with either a marker or marker-less tracking system.

2. Cleft lip and palate

Orofacial clefts can be classified as; syndromic or non-syndromic clefts. Syndromic clefts occur due to a genetic deformity e.g. Van der Voude's syndrome or Pierre-Robin syndrome. Non-syndromic clefts do not involve genetic abnormalities.

Clefts of the lip and palate can be subdivided into the following categories:

- isolated cleft lip
- cleft lip and alveolus
- cleft palate only
- unilateral incomplete cleft lip and palate
- unilateral complete cleft lip and palate
- incomplete bilateral cleft lip and palate
- bilateral complete cleft lip and palate

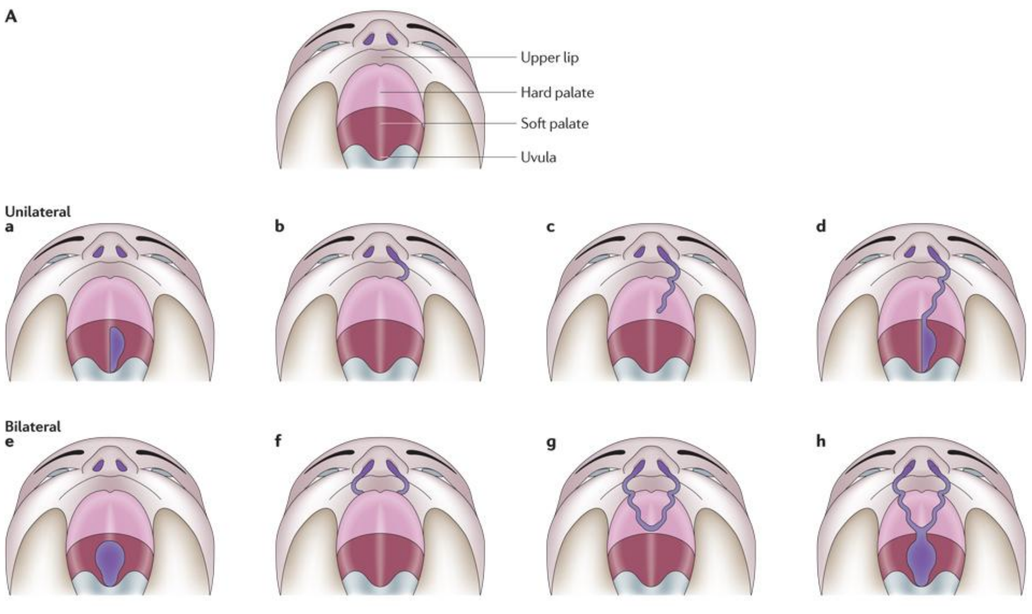

Figure 2 - A set of illustrative drawings of CLP types (with kind permission springer nature (Dixon et al., 2011))

I. Classification

i. Classification of cleft lip

When classifying the cleft lip, clefting of the lip may be complete, incomplete or lesser form. Lesser-form clefts can be further subdivided into minor-form, microform and mini-microform.

A bilateral cleft lip may feature the same degree of clefting on each side known as symmetric bilateral cleft lip or may differ from side-to-side, asymmetric bilateral cleft lip.

ii. Classification of cleft palate

Palatal clefts can be overt; meaning the cleft is open and can be visualised intraorally or submucous when the cleft is not visibly open and not obvious during intraoral inspection. For the submucous cleft, the oral mucosa is intact, but the underlying musculature has failed to attach at midline.

There are three signs of an Submucous cleft:

I. zona pellucida—a blue discoloration due to levator veli palatini muscle diastasis
II. a bifid uvula
III. a palpable bony notch at the edge of the hard palate

In some cases, there can be an occult submucous cleft palate, which has no visual signs intraorally. Only diagnosed by direct observation i.e.: during surgery or by magnetic resonance imaging (MRI).

Figure 3 - The zona pellucida (with kind permissions © 2019 Ulster Medical Society)

Figure 4 - A bifid uvula (Martin et al., 2019) with kind permissions © 2019 Ulster Medical Society)

II. Morphology

The clefting of the *palate* is most usefully described by the Veau classification:

- Veau-I cleft palate: A midline cleft of the velum (soft palate), with the intact hard palate.
- Veau-II cleft palate: A midline cleft of the soft palate and secondary hard palate (posterior to the incisive foramen) but an intact primary palate (anterior to the incisive foramen)
- Veau-III cleft palate: A cleft of the soft palate, extending *unilaterally* through the primary and secondary hard palate and alveolus. The vomer (the bony part of the nasal septum) remains attached to the palatal shelf on the greater segment (non-cleft side).
- Veau-IV cleft palate: A cleft of the soft palate, extending in the midline through the secondary hard palate and then *bilaterally* through the primary hard palate and alveolus on each side.

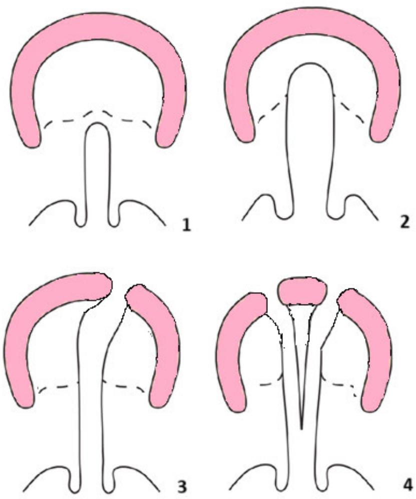

Figure 5 - Veau classification of cleft palate. (1) Veau I (2) Veau II (3) Veau III (4) Veau IV

III. Notation of Cleft lip and palate

i. Kernahan's notation

Kernahan's classification classifies cleft lip and palate as a striped Y with the incisive foramen as a reference point (Smarius et al., 2017). The anatomical region affected by the cleft is numbered 1 to 9. The system of classification is based on the ideology that the intra-oral view of the mouth is the shape of an inverted Y.

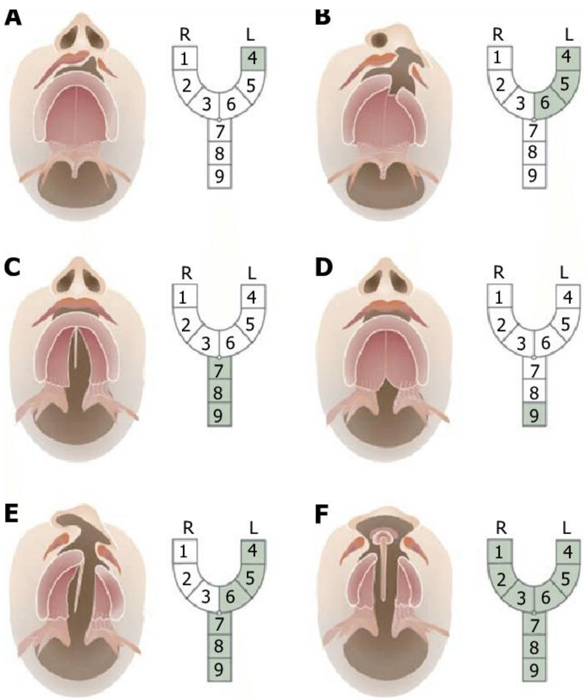

Figure 6 - Kernahan's classification. The area affected by the cleft is labelled from 1-9, each of which represents a different anatomical structure: 1: Right lip; 2: Right alveolus; 3: Right premaxilla; 4: Left lip; 5: Left alveolus; 6: Left premaxilla; 7 (Smarius et al., 2017) (with kind permissions The Author(s) 2017. Published by Baishideng Publishing Group Inc.)

ii. LAHSHAL notation

Surgeons most commonly use LAHSHAL (Houkes et al., 2023) classification. The Houkes et al 2023, study states that it's the most suited universal classification system, due to its extensiveness, high implementation rate, convenient to use and easier for computer-based coding.

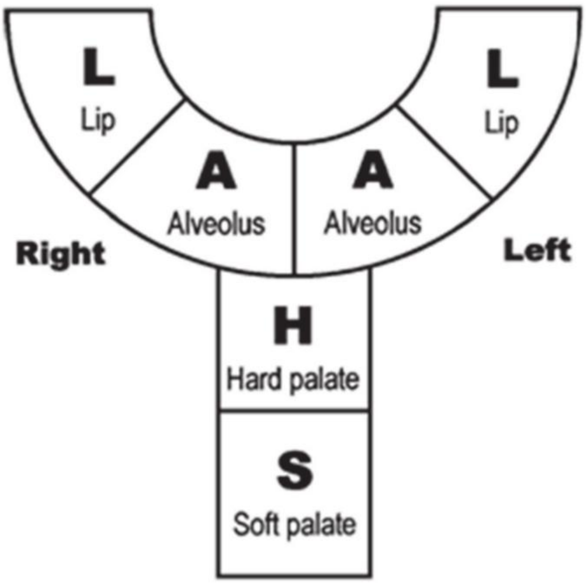

Figure 7 - LAHSAL system for the classification of cleft lip and palate – with kind permissions BDJ (Martin and Swan, 2023)

In the LAHSHAL system, each column of the acronym is filled by a letter or symbol that confirms involvement of that part of the anatomy as well as the severity of the clefting:

- A capital letter means that anatomic feature was completely clefted;
- A lowercase letter means incomplete clefting;
- An asterisk (*) means minimal clefting (e.g., lesser-form cleft lip, notched alveolus, submucous cleft palate);
- A period (.) or dot (•) means that anatomic feature is normally developed

iii. CLAP notation

The CLAP notation was developed to be read more easily and relay clinical information of the cleft phenotype. It consists of the capital letters *L*, *A*, and *P*, denoting involvement of the lip, alveolus and palate, respectively. A capital letter signifies clefting of that part of the anatomy and absence of that letter signifies that part of the anatomy is normal.

A lowercase prefix composed of two letters is used to describe laterality; *u* denotes unilateral, and *b* denotes bilateral. Severity is notated by a *c* for complete, *i* for incomplete and *m* signifies the lesser-forms.

The morphology is denoted by a suffix, lowercase *v1* signifies Veau-I, *v2* for Veau-II, *v3* for Veau-III, *v4* for Veau-IV. The suffix *sm* indicates occult submucous cleft palate, and *bu* for overt submucous cleft palate with bifid uvula.

Prefix (describing cleft lip)		CLAP (anatomic involvement)		Suffix (describing cleft palate)
Laterality	Severity			
u (unilateral)	c (complete)	C	L (lip)	v1 (Veau-I)
b (bilateral)	i (incomplete)		A (alveolus)	v2 (Veau-II)
	m (lesser form)		P (palate)	v3 (Veau-III)
				v4 (Veau-IV)
				sm (occult submucous)
				bu (overt submucous with bifid uvula)

Figure 8 - Phenotypic description by CLAP notation (Allori et al., 2017b)

IV. Coding

Diagnostic codes exist to describe the various forms of CL/P. The two most common coding systems used for description of the type of cleft include ICD-9 and ICD-10.

Modifications to these coding systems were developed for use in epidemiologic surveillance and research to now include information about laterality, severity, and specific anatomic involvement.

3. Embryology

Facial morphogenesis occurs during embryological development and craniofacial anomalies result when elements fail to fuse or do not develop and grow harmoniously. During cleft lip and palate this anomaly occurs when the nasal and maxillary processes fail to fuse during embryological development.

I. Normal development of the face

The external human face and palate form during embryonic development. During week 3 of embryonic development, an oropharyngeal membrane, comprised of ectoderm and endoderm appears where the face will eventually form.

During the 4th week of development, this oropharyngeal membrane breaks down to allow it to become the oral cavity and the mesoderm on both sides of the pharynx will create pocketings which then become the pharyngeal arches. Each of these pharyngeal arches have their own branch of the aorta, cranial nerve and cartilage. The neural crest cells originate from the neuroectoderm. As the neural tube develops, cells from the neuroectoderm are displaced into the mesoderm and into the pharyngeal arches which helps form the head and neck.

The nose and face are developed from the pharyngeal arches and neural crest cells. The external human face forms from the 4th week of embryonic development up until completion at week 6. The first pharyngeal arch allows formation of the mandibular and maxillary prominences. The maxillary and nasal prominences fuse creating a continuous structure at the midline. The oropharyngeal membrane that lies between the maxillary prominences goes on to become the mouth and pituitary gland.

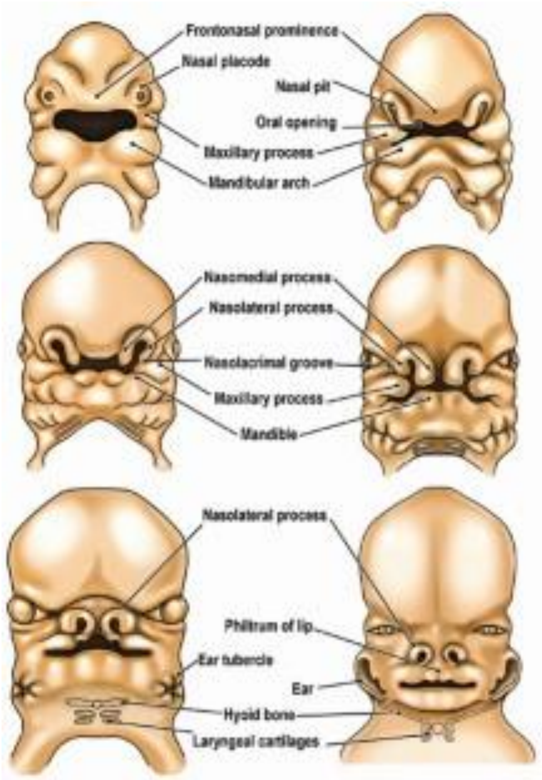

Figure 9 - Normal embryological development of the human face (with kind permissions Cleft palate craniofacial journal (Houkes et al., 2023))

II. Normal Development of the lip and nose

Lip development occurs during weeks 5-6. A cleft lip can form when the nasal prominences and maxillary prominences fail to properly fuse. This can cause a unilateral or bilateral cleft lip depending if fusion fails to occur on one side or both. The frontonasal prominence develops from proliferating mesenchymal neural crest cells and creates raised bumps known as nasal placodes, which invaginate to form nasal pits and help form the nose. (Houkes et al., 2023)

III. Normal development of the palate

Palate devolvement happens from week 5 until week 12. Which causes a distinction between the nasal and oral cavities.

The primary palate is created by the fusion of the medial nasal prominence at the midline which creates the intermaxillary segment and goes on to become the anterior third of the hard palate, this begins around week 5 of gestation. It also contributes to the labial component of the philtrum, incisive foramen and the upper incisors. The maxillary prominences expand medially creating palatal shelves and fuse superior to the tongue. During this time the mandible expands which helps increase in the size of the oral cavity and allows the tongue to move out of the way of the palatal shelves (Yu and Ornitz, 2011).

The secondary palate forms slightly later, gestation week 6, by fusion of the bilateral palatal shelves and the nasal septum. They fuse at the midline, anterior to posterior, and will become the remaining hard palate and the soft palate. A cleft occurs if these palatal shelves don’t fuse in the midline. Fusion of shelves begins around week 9 of gestation and is complete by week 12.

Tooth development begins around week 6 of gestation from the ectoderm which forms enamel and neural crest mesenchymal cells which form all other tooth structures (Martin and Swan, 2023). Tooth development occurs over 4 complex stages in both jaws; the initial bud stage during week 8 of gestation, then cap stage and followed by the early and late bell stages. If there is any interruption during these stages, individuals may experience dental anomalies such as variation in tooth size, shape form or number. Of particular relevance to patients with a cleft lip and palate is the upper lateral incisor, as this has dual origin from both the medial nasal process and maxillary process, which is the area disrupted in CLAP. This tooth is also more likely to experience dental anomalies (Martin and Swan, 2023).

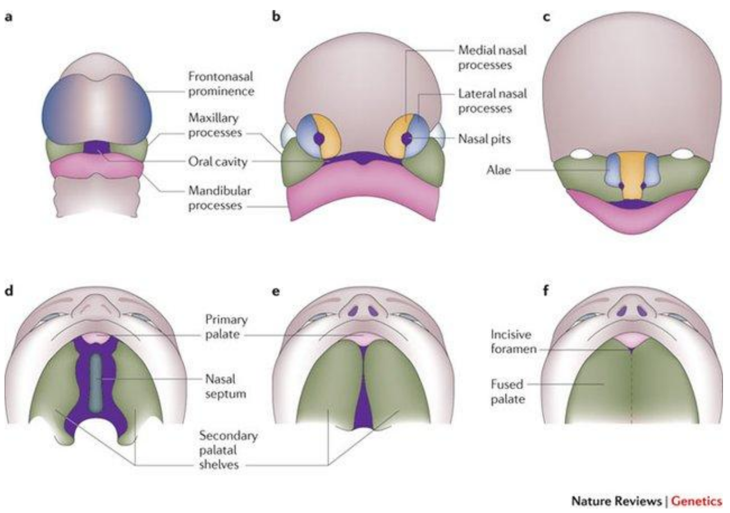

Figure 10 - Development of the Lip and Palate in Humans (with kind permissions Nature Reviews Genetics, Springer Nature 2011 (Dixon et al., 2011))

4. Aetiology

Despite it being one of the most common birth defects, surprisingly little is understood about the underlying causes of cleft lip and palate. There isn't one specific cause of cleft lip and palate and it is likely to be a combination of genetic predisposition and specific environmental factors (Dixon et al., 2011). One known cause of clefting is the tongue preventing the two halves of the palate from joining but in most cases there is no obvious explanation.

I. Environmental or lifestyle factors

Environmental or lifestyle factors such as; things that the mother encounters during her pregnancy, what she eats or drinks, or certain medications she uses during pregnancy have been considered a cause. Exposure to certain environmental substances during pregnancy such as tobacco, illegal drugs, alcohol, or presence of heavy metals in food/water can also increase the risk (van Gelder et al., 2009, Little et al., 2004, Mbuyi-Musanzayi et al., 2018). The baby's position in the womb may increase the likelihood of having a cleft (Muller et al., 1977). Women with diabetes diagnosed before pregnancy have an increased risk of having a child with a cleft lip with or without cleft palate (Correa et al., 2008) and maternal obesity has also been associated with higher risk of congenital anomalies (Lee et al., 2021), such as clefting of the lip or palate.

i. Smoking

Women who smoke during pregnancy are more likely to have a baby with an orofacial cleft (Mossey et al., 2009). This is most significant during the first trimester as it can cause hypoxia of the embryo in utero (Lie et al., 2008). Transforming growth factor alpha (TGFA) gene has been linked with increased genetic susceptibility to maternal smoking in the causation of orofacial clefts. If a mother smokes 20+ cigarettes a day, it can have 3-11 times greater risk in having a baby with an orofacial cleft (Shaw et al., 1996). This does not seem to apply to paternal smoking, however there is limited evidence.

ii. Alcohol consumption

Maternal intake of alcohol is documented to have a teratogenic effect to the foetus (DeRoo et al., 2016). There is an increasing risk of infant clefts with moderate-high levels of alcohol consumed during pregnancy, this has been described in the literature as more than 5 drinks per drinking occasion/binge drinking (DeRoo et al., 2016). The odds also seem to increase depending on the type of alcohol consumed; spirit>wine> beer, and the risk was further increased if there was no folic acid intake.

iii. Folic acid intake

Low folic acid during pregnancy increases the incidence (Ahmed Sakran et al., 2022). Certain supplements such as folic acid have been shown to provide protective effects on pregnant mothers with regards birthing healthy babies. The lowest incidence of cleft was found in women with high folate diets and those taking satisfactory levels of folic acid supplements and multivitamins. An intake of up to 400 microgram of folic acid a day, reduces the incidence of cleft lip by one third (Correa et al., 2008).

iv. Prescription Medication

Using prescription medications for epilepsy, such as topiramate or valproic acid during the first trimester of pregnancy have an increased risk of having a baby with a cleft lip (with or without cleft palate) compared to women who didn’t take these medicines (Kallen, 2003). There also seems to be a moderately increased risk if the mother is taking corticosteroids during the first trimester (Carmichael et al., 2007), odds ratio 1.7 for cleft lip and palate and 0.5 for cleft palate only.

v. Advanced maternal or paternal age

Mothers who are 35 years or older have a higher prevalence of orofacial clefts. For cleft palate alone, the prevalence increases with advanced maternal age, mothers 40 years and above are 2/3 more likely to have a baby with an orofacial cleft than mothers 20 years or younger. This may also be due to the higher rate of certain chromosomal birth defects among older women, such as trisomy 18 and trisomy 13, which are often associated with cleft palate (Mai et al., 2014).

II. Sex

Males are more likely to have cleft lip with or without cleft palate; females are more likely to have cleft palate without cleft lip (Martelli et al., 2012).

The sexual difference variations might be due to the different development of important phases of the craniofacial structure between male and female embryos. Failure of fusion of the primary palate occurs early involving; the lip, premaxilla/maxilla, alveolus (extending to the incisive foramen). Whereas failure in fusion of the secondary palate happens later involving; the uvula, hard palate, and soft palate (Putri and Pattamatta, 2024). The reason females were more likely to exhibit secondary palate maldevelopment or cleft palate is likely due to the fact palatal development is slower than males (Yow et al., 2021).

III. Socioeconomic status

Socioeconomic status, including income, has been proposed as one of the risk factors of orofacial cleft. Some studies have found a connection between a lower socioeconomic status and a higher incidence of orofacial clefts (Vu et al., 2022, Alfwaress et al., 2017). However there are also many studies that have found no link between the likelihood of orofacial clefts and a lower socioeconomic class. This may be because the socioeconomic status of a population can be difficult to quantify and define (Mossey et al., 2009). However studies looking at the Scottish population have shown a positive correlation between a low socioeconomic status and the incidence of cleft lip and palate (Clark et al., 2003).

Possible reasons for the link between socioeconomic class and clefting may be due to the limited availability of nutrient-dense food, or these families may come into contact with heavy metals through tainted food or contaminated water, which has been connected to cleft lip and palate (Mbuyi-Musanzayi et al., 2018). Due to the limited access to healthcare, mothers with a low socioeconomic status are less likely to obtain advice regarding healthy eating during pregnancy.

A low socioeconomic status may result in a lower standard of education that can cause a lack of knowledge or awareness about environmental risk factors that may affect the pregnancy (Kruppa et al., 2022). A systematic review (Inchingolo et al., 2022) also found a link between low paternal educational level and the occurrence of non-syndromic orofacial clefts.

IV. Genetics

There seems to be increased risk of CLP with a family history of cleft lip and palate (Grosen et al., 2010). An isolated cleft palate is believed to have a different cause to cleft lip and palate. Therefore a family affected by a cleft palate only, may only pass on the cleft palate. Based on UK statistics, 15-30% of clefts are secondary to a genetic syndrome, where a genetic mutation results in a wide range of birth defects. Infants with CPO are more likely to have related congenital abnormalities (52.5%) than CLP (26.5%) (Worley et al., 2018). Common anomalies seen in patients with cleft lip only are; congenital heart defects, hydrocephalus and urinary tract defects. There are over 400 conditions and syndromes that list cleft as a symptom. For some of these conditions having a cleft is very rare but others have a 50% chance of being passed on.

i. Syndromic clefts

Some of these conditions include:

- DiGeorge Syndrome - 22q11.2 microdeletion
- Pierre-Robin sequence
- Treacher-Collins syndrome
- The gene involved in Van de Woude syndrome
- Stickler syndrome
- Craniofacial microsomia (spectrum of disorders, including Goldenhar syndrome)
- Neonatal Abstinence Syndrome (NAS), which includes Foetal Alcohol Spectrum Disorder (FASD)

ii. Non Syndromic clefts

The genetic sequence could be important for the patient in terms of future reproductive plans, aiding pregnancy planning and assisting with prenatal diagnosis. Knowing the genetics of the individuals could help doctors to predict the accompanying problems of the patient and find the best option for their care.

The most common genes found in non-syndromic clefts:

- CDH1 (l16q22.1)
- COL2A1 (12q13.11)
- CRISPLD2 (16q24.1)
- FOXE1 (9q22.33)
- GRHL3 (1p36.11)
- IRF6 (1q32.2)
- JAG2 (14q32.33)
- MSX1 (4p16.2)
- PAX7 (1p36.13)
- ROCK1 (18q11.1)
- SUMO1 (2q33.1)
- TBX22 (Xq21.1)
- TCOF1 (5q32-q33.1)
- TGFA (2p13.3) (Paradowska-Stolarz et al., 2022)

5. Epidemiology

I. Prevalence/incidence

CLP is relatively common, approx. 1/700 births worldwide, or 0.14% of the population (WHO 2001). Occurrence rate of clefts varies by population with higher rates reported in Asians and American Indians, 1 in 500 births and lower rates have been reported in African-derived populations, 1 in 2,500 births (Dixon et al., 2011). Some studies have shown for Native Americans it can be as high as 3 in 1000 births (Lowry et al., 2009, Mullen et al., 2023).

Similar figures are seen for the UK (1 in 700), making it the most common craniofacial condition. This means that around 1200 babies are born every year with a cleft in the UK. About 31% of these babies will have a cleft lip and palate, 45% will have an isolated cleft palate and 24% will have an isolated cleft lip. In only 8% of babies born with a cleft in the UK does this happen bilaterally.

II. Gender

An isolated cleft palate (CPO) is more frequently found in females than males, with a ratio of 2:1 (Mossey et al., 2009). Females also have a slightly higher incidence of an isolated cleft lip, a ratio of 0.8:1 (Male/Female) (Impellizzeri et al., 2023). However research has found that males are twice as likely as females to be born with a cleft lip and palate (CLAP) (Asher-McDade, 1991).

III. Laterality

A cleft lip and palate can be either bilateral or unilateral. Unilateral clefts are more common than bilateral clefts with a ratio of 4:1. For unilateral clefts, about 70% occur on the left side of the face (Vyas et al., 2020).

IV. Ethnicity

There have been multiple studies which show that the incidence of a cleft lip and palate can depend on the individuals ethnicity. There is a high prevalence of orofacial clefts in individuals with Asian ethnicity (1 in 500 live births) and the lowest prevalence in individuals of African descent (1 in 2500 live births). In contrast approximately 1 in 1000 European live births are affected (Dixon et al., 2011).

Although both genetics and environmental factors likely play a role in the incidence of having a cleft lip and palate, ethnic variation seems to be linked to genetic differential. This is because the incidence remains similar for these individuals independent of their residing location (Mossey et al., 2009).

6. Diagnosis

A cleft lip is usually picked up during the mid-pregnancy anomaly scan done between 18 and 21 weeks pregnant. However not all cleft lips will be obvious on this scan. There is a sensitivity level of about 88% for detection of a cleft lip on an ultrasound but there is a very low detection rate of a cleft palate from an ultrasound, as the palate is often not visualised during the scan. Although, signs of micrognathia on a scan could be associated with a CP (Smarius et al., 2017). If a cleft diagnosis is confirmed on an USS it is often possible to perform amniocentesis to test for any associated inherited genetic syndromes (Stock et al., 2019).

In the UK, 46% or orofacial clefts are diagnosed before birth (CRANE, 2021). If it is not diagnosed prior to birth, it should be picked up immediately after birth or during the newborn physical examination (NIPE), which happens within 72 hours of birth. Approximately 41% are diagnosed at birth, the remainder are diagnosed later. Early diagnosis is continuing to improve and for the best outcomes a cleft should be diagnosed within the first 24 hours (CRANE, 2021). During this examination there is direct visualisation of the hard and soft palate using a torch and a tongue depressor.

Once a cleft lip or palate is diagnosed, the patient is referred to a specialist multidisciplinary cleft team who will discuss any treatments required and will be seen by a cleft specialist nurse within 24 hours.

I. Cleft sequelae

Cleft lip and palate conditions can vary in severity and sequelae can depend on the severity. A cleft lip and palate can have a visible impact on facial appearance and can affect functions such as feeding, speech, hearing, and their quality of life (Rumsey and Harcourt, 2004). Children affected by cleft lip and palate can present with low self-esteem, body dysmorphia, depression, anxiety and a lack of satisfaction with their speech (Hunt et al., 2005). Previous studies have shown that children affected by cleft lip and palate had fewer friends when compared to patients without a cleft lip and palate, which shows reduced socializing skills in CLP patients (Ramstad et al., 1995).

i. Feeding

Infants affected by cleft lip and palate may experience difficulty making the sucking action or creating a good seal which can affect normal feeding, due to part or the whole of the roof of the mouth not being developed completely. This can then result in fatigue, poor weight gain, excessive air intake, choking and nasal regurgitation. Due to this a special feeding bottle and advice from the cleft specialist nurse are essential.

ii. Audiology

Patients with cleft lip and palate may have dysfunction of the eustachian tube which can cause recurring ear infections or conductive hearing loss. If the middle ear fills with fluid it can interfere with the transmission of sound causing reduced hearing. Patients may also experience a sensation of ear fullness, popping or clicking sounds and notice changes in hearing sensitivity. If a patient has an unrepaired cleft, up to 90% can develop glue ear which is secondary to the eustachian tube dysfunction.

iii. Speech

Failure during the fusion of the palate and lip may result in the muscle function of the mouth being compromised, bringing about a speech delay or abnormal speech. The opening in the palate from the cleft can lead to nasal air escaping during speech, resulting in hypernasality which creates muffled or unclear speech (Smarius et al., 2021). If the Child has Pierre-Robin sequence they may experience airway problems and children that have an associated syndrome are more likely to experience severe speech difficulties than children without a syndrome, due to general developmental delays (Hardin-Jones and Chapman, 2011).

iv. Dental

Due to the deformities associated with the intra-oral mucosa and the alveolus, normal dental development is affected. There is delay in tooth development both in the upper and lower jaw and not only around the cleft. Developmental tooth abnormalities, such as enamel hypoplasia, agenesis of teeth, malrotated teeth and ectopic teeth are frequently seen in cleft patients (Van Dyck et al., 2021). It is also common to have missing lateral incisors or microdontic maxillary lateral and central incisors and 25% of cleft patients have the presence of supernumerary teeth, which is likely caused by the division of the dental lamina (Menezes et al., 2018). These patients may also experience hypodontia, anterior and/or posterior crossbites, have rotated or retroclined incisors and may have a marked centreline shift to the cleft side (Gillgrass, 2023b). The central incisor on the cleft side is commonly tipped as there is no distal bone and so may be more markedly displaced.

Presence of teeth in a new born is rare with an incidence ranging from 1:1000 to 1:30000. Teeth present at birth are called natal teeth and teeth that emerge in the oral cavity within the first 30 days of life are defined as neonatal teeth. However 7% of patients with a cleft lip and palate have been found to have neonatal teeth but none were found in patients with CPO (Yilmaz et al., 2016). Neonatal teeth in infants with CLP are located to the cleft region. If possible immediate extraction of the neonatal teeth is advised as they may interfere with a presurgical intraoral plate if it is required.

They may also present with malocclusions such as increased overjet, anterior crossbite, open bites and lateral crossbites especially on the cleft side. Using angles classification the most common incisor relationship for these patients is class 1, however there is a larger number of this population that have a pseudomesioclusion, class 3 than unaffected individuals (Raghavan et al., 2018). This is because of maxillary hypoplasia which is a visible stigmata of the cleft. Orthognathic surgery can help reduce visibility of this.

Patients with an orofacial cleft are at a higher predisposition to dental caries due to demarcated teeth and enamel hypoplasia. They should have regular visits with their dentist and topical fluoride application at least twice a year and fissure sealants should be considered (Luzzi et al., 2021).

v. Psychological

Having a cleft lip and palate can impact the individual's psychological and social well-being. Facial appearance and attractiveness are compromised due to varying levels of facial asymmetry. Symmetrical faces are seen as more attractive (Perrett et al., 1998) and even babies have been noted to stare longer at an attractive face (Quinn et al., 2008). Historically symmetry was seen as a sign of reproductive advantage, health and fertility and absence of disease (Livshits and Kobyliansky, 1989). Psychosocial issues can stem from the realization of their facial differences and the reactions or from the judgment of others and may even have difficulty maintaining friendships (Turner et al., 1997).

The facial deformation, pain and need for repair procedures may influence a patient’s life. Improvement to their smile and occlusion can provide the same satisfaction as with healthy individuals; to improve their life quality (Kaczorowska. N and Mikulewicz. M, 2022).

7. Anatomy of Muscles affected in a cleft lip and palate

A histological sign of a cleft lip and palate is inappropriate orientation and abnormal insertion of the levator veli palatini muscle and the orbicularis oris muscle. This abnormality to muscle formation is even found in patients with microform cleft lip or those with a submucosal cleft palate. For successful cleft lip and or palate repair, there needs to be closure of these muscular diastases (Kim et al., 2021).

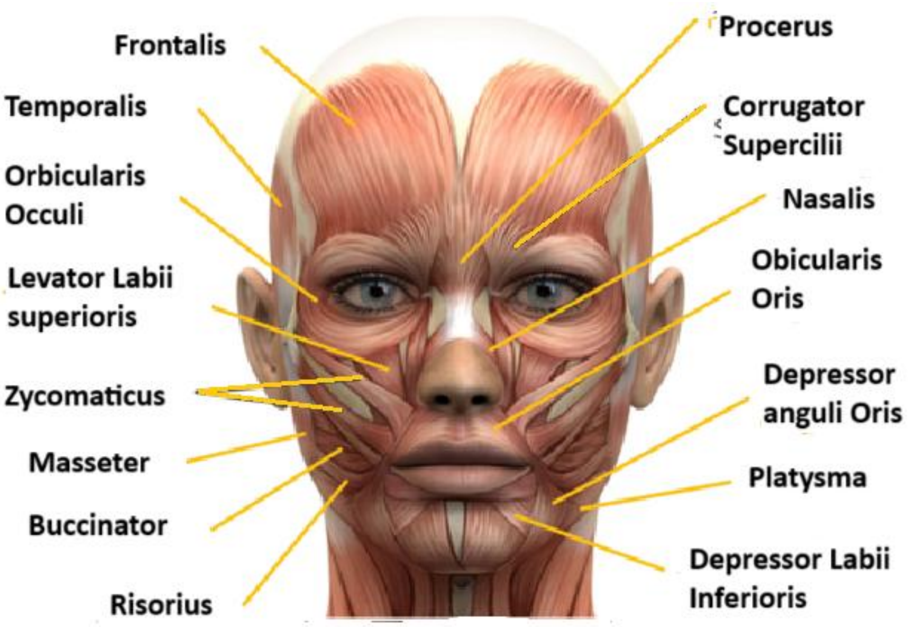

Figure 11 - Muscles involved in facial expression (edited from an unknown online source)

Motor neurons enable the brain to innervate muscles and sensory neurons transmit sensory information to the brain. The lower motor neuron that innervates muscles of facial expressions is the facial nerve or the trigeminal nerve.

I. Main muscles of the nasolabial area involved during smiling

i. Zygomatic Major

During a genuine smile, the zygomatic major muscle contracts, raising the corners of the mouth and causing upward movement of the lips, it also deepens and raises the nasolabial fold. The zygomatic major works in conjunction with other muscles to produce expressions such as smiling, disdain, contempt, or smugness. This muscle may develop in a bifid form, which is thought to cause cheek dimples.

The zygomatic major muscle originates from the superior margin of the lateral surface of the temporal process of zygomatic bone, just anterior to the zygomaticotemporal suture and it inserts at the corner of the mouth by blending with the levator anguli oris muscle, the orbicularis oris muscle and deeper muscular structures.

Motor innervation is from the buccal and zygomatic branch of the facial nerve (CN VII) and arterial supply is from the superior labial artery (Palastanga and Soames, 2012).

ii. Zygomatic Minor

The zygomaticus minor is a thin paired facial muscle extending horizontally over the cheeks and works to draw the upper lip back, up, and outward during smiling. It is a direct tractor of the upper lip, alongside levator labii superioris alaeque nasi and levator labii superioris. Due to the fact it inserts to the upper lip directly, it does not require an intermediary. Working with the other muscles, zygomaticus minor elevates the upper lip, exposes the teeth and deepens the nasolabial lines. The function of zygomaticus minor is to contribute to facial expressions; smiling, smugness and contempt and it also aids speech, particularly certain sounds, such as the letter “E” (Moore et al.).

The Zygomaticus minor muscle originates from the zygomatic bone, lateral to the rest of the levator labii superioris muscle, and inserts into the outer part of the upper lip, blending distally with levator labii superioris muscle.

Vascular supply to zygomaticus minor comes from the superior labial branch of facial artery and it receives motor innervation from the zygomatic branches and buccal branches of the facial nerve (CN VII).

iii. Levator anguli oris

The main function of the levator anguli oris is to elevate the corner of the mouth, in coordination with the zygomaticus major muscle, which raises and lateralizes the oral commissure. It is not a major muscle involved in creating the smile, but it plays a supporting role in shaping the smile.

The levator anguli oris arises from the canine fossa located on the anterior surface of the maxilla right below the infraorbital foramen. The fibres of the Levator Anguli Oris and Depressor Anguli Oris decussate at the corner of the mouth. Levator Anguli oris muscle fibres continue into the lower lip, and the Depressor Anguli Oris fibres continue into the upper lip.

Innervation is from a terminal buccal branch of the facial nerve (CNVII).Various small branches of the facial, internal maxillary and superficial temporal arteries, supply blood to the levator anguli oris.

iv. Levator Labii Superioris

The Levator Labii Superioris (LLS) muscle elevates the upper lip, particularly during smiling. It also provides eversion and can help convey expressions such as disgust, sadness, distain and has a role during vomiting. During smiling, the levator labii superioris contracts raising the upper lip, exposing the upper teeth and contributes to the curvature of the mouth. It works in tandem with the zygomatic major and orbicularis oris.

These muscles begin to develop from the mesoderm layer of the second brachial arch between weeks 3 and 8 of embryonic development. The muscle consists of three heads; angular, infraorbital and the zygomatic head. The angular head originates from the frontal process of the maxilla below the infraorbital foramen. These divide into two sections of muscles, the first attaching to the greater alar cartilage and ala of the nose and the second blends with the Orbicularis Oris in the upper lip. The infraorbital head of the LLS arises from below the orbit and attaches to the maxilla and a part of the zygomatic bone. The zygomatic head arises in the malar process of the zygomatic bone and inserts near the corner of the mouth and upper lip (Bloom et al., 2023).

The levator labii superioris is innervated by the zygomatic branch of the facial nerve (CNVII) and receives its blood supply from terminal branches of the facial artery and the infraorbital branch of the maxillary artery.

v. Levator labii superioris alaeque nasi

A facial muscle that dilates the nostril and elevates the wing of the nose and upper lip, this muscle allows the facial expression of snarling. The levator labii superioris alaeque nasi muscle originates from the frontal process of the maxilla and inserts into the skin of the ala of the nose and upper lip. It is innervated by the zygomatic branches of the facial nerve (CN VII) and the blood supply comes from the facial artery and the infraorbital branch of the maxillary artery.

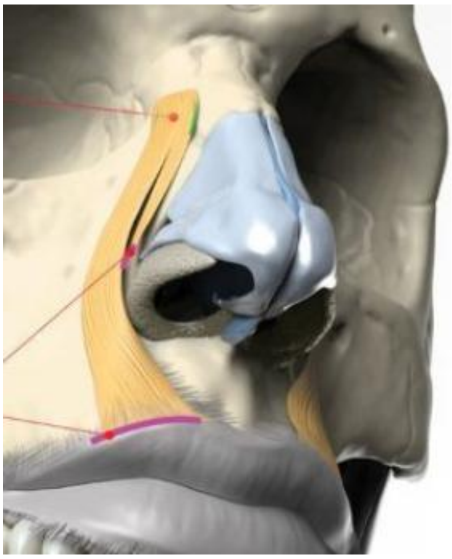

Figure 12 - Origin and insertion of levator labii superioris alaeque nasi (image from unknown online source)

vi. Orbicularis Oris

The orbicularis oris muscle is affected in a cleft lip due to its role in orofacial movement and the contour of the lip. Ensuring correct orientation during repair will be critical to correcting upper lip anatomy and allow normal function. This muscle works in association with the buccinator muscles to create contact between the teeth and lips, by pressurizing the dental arches and in the production of speech sounds (Green et al., 2000). It plays a vital role in forming and shaping the mouth during various facial expressions and is crucial for swallowing, mastication, sucking and puckering the lips.

The muscle is derived from the mesoderm of the second branchial arch. It develops from two embryonic laminae; mandibular (lower fibres) and infraorbital lamina (upper fibres) during the 6-8th weeks in utero (Jain and Rathee, 2023). It consists of superficial and deep layers.

The deep fibres of the orbicularis oris muscle are primarily used to create a sphincter and originate from the modiolus bilaterally. The fibres pass continuously, across the midline, from one commissure to another and they run circumferentially creating this sphincteric motion which is responsible for holding food in the mouth. The lower border of these fibres' curls upon themselves, forming the vermilion by everting the mucous membrane. The facial expression and the precise movements of lips, needed in speech, arise from the superficial fibres. The superficial orbicularis oris muscle fibres are divided into a nasal bundle (upper) and nasolabial (lower) bundle. The superficial fibres originate from the modiolus on each side. They insert in the skin and the decussation of fibres results in the formation of the philtral columns. A lack of insertion at the midline causes the philtral depression.

The orbicularis oris muscle is innervated by the buccal and mandibular branches of the facial nerve (CNVII). The main blood supply of this muscle is from two branches of the facial artery, superior labial branch and inferior labial branch. However, it also receives some blood supply from the maxillary artery and superficial temporal artery via its transverse facial branch.

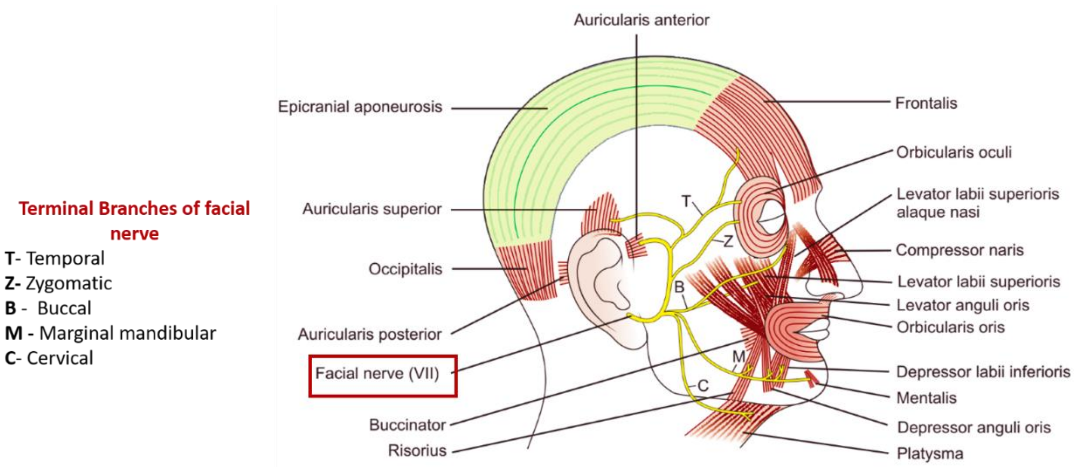

Figure 13 - Innervation of facial muscles by facial nerve (image from unknown source)

vii. Risorius

The risorius muscle is known as the *'smiling muscle'* as its bilateral contraction pulls the angles of the mouth laterally and slightly superiorly to produce a smile. The risorius muscle can be variable across the population, ranging from one or more slender bundles to a thin wide fan. It is absent in some people and can be asymmetrical in others. If it is present, it is found in the superficial layer of the facial muscles on either side of the lips, overlying the buccinator muscle.

It originates from the zygomatic arch, parotid fascia, the fascia over the masseter, the fascia enclosing the platysma and the fascia over the mastoid process. It inserts at a fibromuscular mass called the modiolus.

The risorius receives motor innervation from the buccal branch of the facial nerve (CN VII) and receives arterial supply mostly from the superior labial artery.

viii. Depressor Anguli Oris

The main function of the depressor anguli oris is to depress the angle of the mouth, acting as an antagonist to the levator anguli oris muscle and the zygomaticus major muscle. It's role during smiling is to counteract the action of other muscles and prevent the smile from becoming overly forced or awkward.

This muscle originates from the oblique line of the mandible anteriorly, below the canines and the premolars, and inserts in to the modiolus after its fibres are directed medially. Some fibres from each side may pass below the mental tubercle and cross the midline and interlace, forming the Transversus Menti.

The depressor anguli oris is innervated by the buccal and the mandibular branch of the facial nerve (CNVII).The blood supply for the depressor anguli oris is from the inferior labial branch of the facial artery and the mental branch of the maxillary artery.

ix. Depressor labii inferioris

The depressor labii inferioris muscle helps to depress and evert the lower lip exposing the lower teeth when smiling. It acts as an antagonist of the orbicularis oris muscle. The depressor Labii Inferioris muscle pulls the lower lip inferomedially when contracting which can help express facial expressions associated with sadness and doubt.

It originates from the oblique line of mandible, between the symphysis menti and mental foramen before passing superomedially and inserting into the skin and submucosa of lower lip. The mandibular end of depressor labii inferioris is continuous with platysma and the labial attachment fuses with inferior fibres of the orbicularis oris muscle.

The depressor labii inferioris muscle is supplied by the mandibular branch of the facial nerve (CN VII). Vascular supply to this muscle comes from the inferior labial branch of facial artery and mental branch of maxillary artery (Moore et al.).

x. Mentalis

The mentalis muscle causes a weak upward-inward movement of the soft tissue complex of the chin and raises the central portion of the lower lip. When the lips are incompetent, mentalis muscle contraction can bring temporary but strained oral competence. It can cause wrinkling and dimpling of the chin when displaying displeasure and works alongside the orbicularis oris during pouting. Mentalis muscle originates from the incisive fossa of mandible before inserting to the skin of the chin, at the level of mentolabial sulcus. It is innervated by the mandibular branch of the facial nerve (CNVII) and gets its blood supply from the Inferior labial branch of the facial artery and mental branch of the maxillary artery.

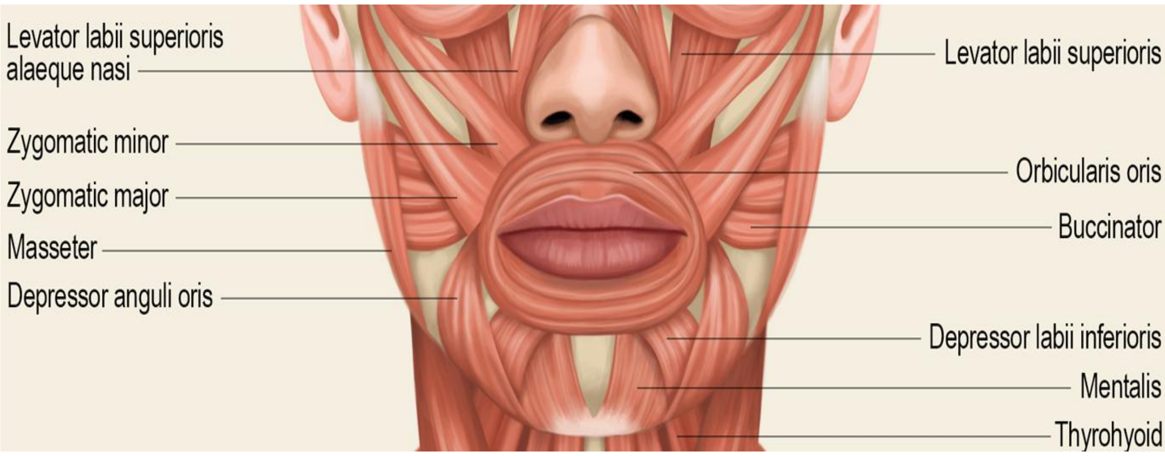

Figure 14 - Lower facial muscles used to produce facial expressions - with permission [Jeff Searle: Muscles of the head and neck]

II. Other muscles which may be used during smiling

xi. Orbicularis oculi

Orbicularis oculi acts to close the eye and is the only muscle capable of doing so. Loss of function for any reason results in an inability to close the eye. It closes the eyelids during smiling, particularly during a genuine smile. There are 3 sections of the orbicularis oculi muscle; orbital orbicularis which works by conscious control to close eyelids tightly, palpebral orbicularis which closes the eyelids gently i.e. sleeping or blinking and lacrimal orbicularis which compresses the lacrimal sac. When the entire muscle is activated, the eyelids are firmly closed.

The muscle arises from the frontal bone, the frontal process of the maxilla in front of the lacrimal groove, and from the medial palpebral ligament.

This muscle is innervated by the temporal and zygomatic branches of the facial nerve (CN VII), and the blood supply is from ophthalmic, zygomatico-orbital, angular artery (Palastanga and Soames, 2012).

xii. Buccinator

The Buccinator works along with the orbicularis oris muscle during swallowing, mastication, blowing, and sucking. It compresses the cheeks inwards towards the molars and is an accessory muscle used during mastication to prevent food accumulation in the buccal sulci and is involved in puffing out the cheeks (Rathee and Jain, 2023). During smiling it acts primarily by flattening the cheeks and creating a broader smile. It contributes to the overall movement and positioning of the lips, enhancing the shape of the smile.

Buccinator is derived from the second pharyngeal arch (hyoid arch) and originates from three different locations; the alveolar process of the maxilla, the buccal part of the alveolar process of the mandible and from the pterygo-mandibular raphe (Yadav et al., 2020). From its origin, it extends and inserts into the Orbicularis Oris muscle.

The posterior part of buccinator is supplied by the buccal artery and the facial artery supplies the inferior and anterior parts of the muscle. Buccinator has both motor and sensory innervations. Sensory innervation from the long buccal nerve of maxillary division of the trigeminal (CNV) and motor innervation via temporal and cervical divisions of the facial nerve (CNVII).

xiii. Platysma

Platysma is a broad superficial muscle covering most of the anterior and lateral aspect of the neck, it has a subtle involvement during smiling. The platysma has a minor role in lip depressor function, alongside the depressor anguli oris and the depressor labii inferioris, conveying surprise, horror, or disgust (Hoerter and Patel, 2023).

Development of platysma begins in gestation weeks 9 and 10 from the cervical lamina. The platysma arises from fascia at upper segments of the deltoid and pectoralis muscles and the muscle fibres thin out anteriorly and attach behind the symphysis menti. Most of the platysma muscle fibres start to thin as they reach the lower face and merge with the muscles around the angle and lower part of the oral cavity.

It is primarily innervated by the cervical branch of the facial nerve (CN VII). However, some muscle fibres are innervated by the mandibular branch (CN VII). The blood supply to the platysma is from branches of the external carotid artery.

8. Muscles of the palate

i. Levator Veli palatini

The main function of the levator veli palatini is to elevate the soft palate alongside other muscles of the soft palate, which contributes to the act of swallowing. The levator veli palatini muscle originates from the temporal bone and the medial rim of the eustachian tube and inserts onto the superior aspect of palatine aponeurosis where it interlaces with the fibres of the opposing side. This muscle is innervated by branches from the glossopharyngeal (CN IX) and Vagus nerves (CN X) and blood supply comes from the ascending palatine artery and descending palatine artery.

ii. Tensor Veli Palatini

The main function of the tensor veli palatini is contribution to the act of swallowing, by tensing the palatine aponeurosis and opening the pharyngeal opening of auditory tube. This muscle originates from the pterygoid process, spine of sphenoid bone and wall of auditory tube and inserts into the palatine aponeurosis. This muscle is innervated by the medial pterygoid branch of the mandibular nerve (CN V) and blood supply comes from the greater palatine artery and ascending palatine artery.

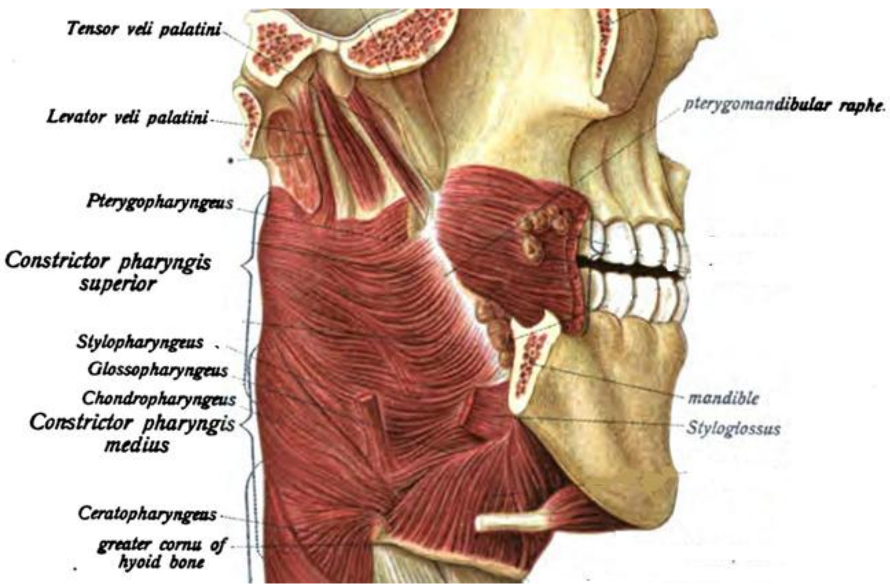

Figure 15 - A lateral view of head and neck from the midline Palatoglossal and palatopharyngeal muscles form anterior and posterior pillars, respectively (with permission public domain - Atlas and Textbook of Human Anatomy)

iii. Palatoglossus muscle

The palatoglossus muscle function is to elevate the posterior portion of the tongue and draw the soft palate inferiorly, narrowing the diameter of the oropharyngeal opening. It has a significant role during swallowing to propel the food bolus toward the oesophagus and occlude the oral cavity, preventing a retrograde flow of the food. It also prevents the spillage of saliva by maintaining the palatoglossal arch. The right and left palatoglossus muscles create ridges in the lateral pharyngeal wall which separate the oral cavity and the oropharynx. It works as an antagonist to the levator veli palatini muscle.

The palatoglossus muscle is innervated by the pharyngeal branch of the vagus nerve (CN X) and arterial supply is from the lingual artery, a branch of the external carotid artery. Some circulation also comes from the tonsillar artery, a branch of the facial artery.

iv. Palatopharyngeus muscle

The palatopharyngeus muscle plays a role during swallowing. It originates from the posterior border of hard palate and palatine aponeurosis. The muscle then descends posterolaterally along the pharyngeal wall, forming the palatopharyngeal arch. In the oropharynx, the muscle fibres fan out and insert to the posterior border of thyroid cartilage and some cross the midline and blend with its counterpart.

The palatopharyngeus muscle is innervated by branches of pharyngeal plexus from the vagus nerve (CN X). The blood supply is from the ascending palatine branch of facial artery, greater palatine branch of maxillary artery and the pharyngeal branch of ascending pharyngeal artery.

9. How are these muscles affected in a patient with a Cleft

I. The effect on the lip

A Complete Unilateral Cleft Lip (UCL) can have varied involvement with hard and soft tissues. It may range from minor notching of the vermillion border of the upper lip or extend beyond into the nasal floor and alveolus. In a UCL the fibres of the Orbicularis Oris muscle are interrupted. These muscles fibres move horizontally from the commissures towards the midline and then turn upwards along the cleft margins, where they may partly insert, or may extend up to the anterior nasal spine medially and alar base laterally. The vessels of the upper lip also move along the margins of the cleft.

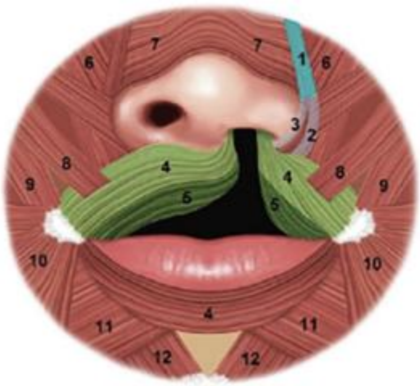

Figure 16 - UCLP abnormal muscle insertion: 1. LLSAN, 2&3. labial & nasal division LLSAN, 4&5. orbicularis oris, 6. levator labii superioris, 7. nasalis, 8&9. zygomaticus minor & major, 10. depressor anguli oris, 11. depressor labii inferioris, 12. mentalis (With kind permissions BDJ (Houkes et al., 2023))

For incomplete clefts, the fibres of orbicularis oris above the cleft remain intact. Muscle fibres can accumulate on the lateral aspect of the cleft due to poor or incomplete development of muscle fibres. There is muscle thinning near the philtrum on the cleft side, due to underdeveloped fibres and this may cause shortening of the philtrum and lip (Ayoub et al., 2003). Acceptable lip closure and correction of the deficits are important not just for regaining aesthetics and facial expression symmetry but also for appropriate optimal speech and function. Inadequate approximation of the orbicularis oris muscle fibres during primary surgery can cause tension on the skin, and scar tissue formed during healing can pull the lip toward the cleft side.

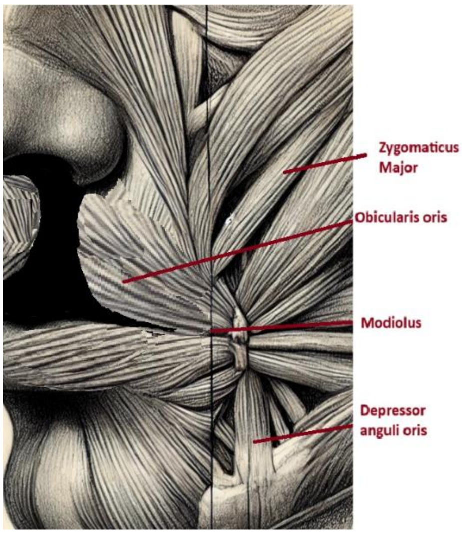

Figure 17 - The orbicularis oris muscle's abnormal insertions into the soft tissues under the alar base and piriform aperture (image created)

A cleft lip can disrupt the normal alignment and function of the zygomatic major and minor muscles (Hallac et al., 2017). The attachment points of these muscles may be affected which can lead to an imbalance in muscle function of one or both sides of the face. This may cause an uneven or asymmetric smile (Yezioro-Rubinsky et al., 2020). While surgical procedures to repair the cleft lip are carried out, scarring can occur as a natural part of the healing process. Scar tissue can affect the flexibility and function of the zygomatic major and minor muscles, which may limit their ability to produce a symmetrical smile (Hallac et al., 2017).

The presence of a cleft lip can also lead to problems with the normal function of the levator labii superioris (Bloom et al., 2023), meaning individuals with a cleft lip may have difficulty raising the upper lip symmetrically, impacting their ability to smile/ form other facial expressions, and affect the aesthetics.

The depressor anguli oris muscle normally functions to pull the corners of the mouth downward. However presence of a cleft lip can lead to weakness or asymmetry of the depressor anguli oris muscle on the affected side (Moore K. L and F, 2018). This can result in uneven positioning of the corners of the mouth, affecting facial symmetry and smile aesthetics and can impact functional movements such as lip closure and speech articulation. In some cases, individuals with a cleft lip may develop compensatory movements to overcome the weakness or asymmetry of the depressor anguli oris muscle. These compensations may involve altered patterns of facial expression or speech articulation, which can cause some muscles to over stimulate.

II. The effect on the Nose

Nasal deformity varies and may occur along with the upper lip dysmorphology. In unilateral clefts, the nasal septum deviates away from the midline, the nasal tip can also deviate towards the cleft side and the columella base deviates to the noncleft side.

In a cleft lip, the Levator Labii Superioris Alaeque Nasi muscle may not fully develop or may be disrupted by the cleft (Moore K. L and F, 2018). This muscle controls elevation of the upper lip and nostril dilation, so if affected, it can impact on the overall aesthetics of the nose causing uneven elevation of the upper lip and dilation of the nostril on one or both sides. This can be more pronounced in individuals where the cleft extends into the nose.

Abnormal orbicularis oris attachment causes an unopposed pull and deviation of the anterior nasal septum and columella base toward the noncleft side. The lateral cleft of orbicularis oris pulls the alar base away from the cleft which affects nostril orientation. If there is a complete unilateral cleft lip, it will have an unstable nasal base, no nasal sill and abnormal muscle attachments, which cause a malformed and asymmetric alar cartilage (Roussel et al., 2015).

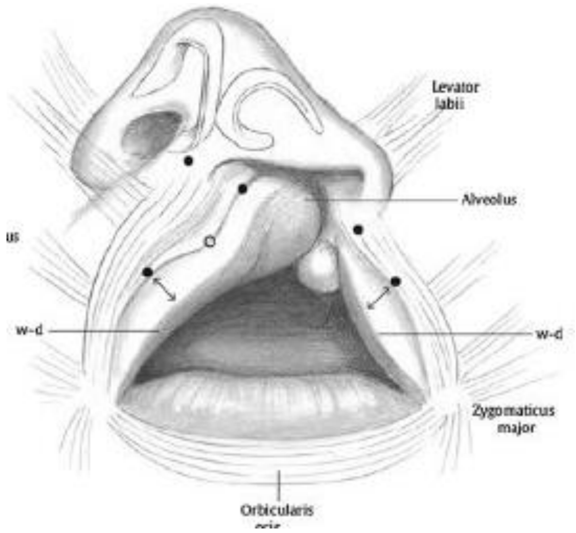

Figure 18 - Illustration depicting the alveolus of the premaxilla, perioral muscles, and typical cleft nasal deformity. The arrows show the vermilion height, which should be made symmetric and the red line of Noordhoff (wet-dry junction) of the lip. (with kind permissions (Shaye et al., 2015))

10. Management of cleft lip and palate

An untreated cleft lip or palate could cause problems with the airway, feeding, glue ear or hyper nasal/unclear speech. It can also have a psychosocial impact and the child may be a target for bullying or discrimination. An untreated cleft can affect tooth development resulting in misaligned teeth. A multidisciplinary team is involved in cleft care (Hodgkinsin et al., 2005) with care commencing at birth. Treatment procedures begin in early childhood, when the child is 3-6 months of age and continues until adolescence. These patients with CLP undergo multiple surgeries, to restore facial symmetry and function.

I. Initial management - multidisciplinary approach (0-3 months)

- Airway assessment and management
- Specialist feeding - they may need special feeding bottles or teats and some babies may need a nasogastric tube or anti-reflux medication
- Newborn hearing test
- Psychological support
- Dental health education
- Monitoring for genetic syndromes associated with a cleft

II. Non-surgical techniques

The long-term emotional impact of a child born with a developmental condition has been well documented. It is important these patients receive emotional support and guidance, counselling and psychological evaluation (Barr and McConkey, 2007). There can be problems maintaining the child's weight and growth due to challenges with feeding and this can emotionally impact the parents as well as the child (Endriga and Kapp-Simon, 1999). Reducing the severity of clefts pre-operatively can help achieve better post-operative results.

i. Adhesive Tape

Adhesive Tape pre-surgically was suggested by (Pool and Farnworth, 1994). They found that placing adhesive tape 6 weeks prior to surgery could reduce alveolar gaps by 53% and narrow the lip segments by a range of 40% to complete apposition.

Figure 19 - A child with a complete unilateral cleft lip, with adhesive tape therapy in place(with kind permission Chopan M,. Surgical Techniques for Treatment of Unilateral Cleft Lip. IntechOpen; 2017. DOI: 10.5772/67124. (Chopan et al., 2017))

ii. Naso-Alveolar moulding (NAM)

This technique can be carried out by using an intra-oral device to align the alveolar segments and narrow cleft defects. The appliance fits over the maxillary arch and circular elastics are attached to the face bilaterally. It is adjusted once a week by an orthodontist by adding and removing acrylic from the palate and the alveolar gap is regularly measured. Once the gap is less than 5mm, a nasal stent can be added to the appliance. Tissue expansion from the stent expands soft tissue and helps shape the alar cartilage and can lengthen the columella and nasal tip which moulds the nose before cleft repair (Shaye et al., 2015).

Figure 20 - Naso-alveolar moulding appliance in place, also patient being fed with a Haberman feeder which allows control of formula flow (with kind permission Facial Plast Surg Clin North America (Shaye et al., 2015))

iii. Lip adhesion

The first surgical stage of a two-stage reconstruction is lip adhesion. This not only moulds the alveolar segments, but also improves nasal contour and vertical lip height of both medial and lateral segments. The disadvantages of a two-stage surgical repair include an additional procedure and potential for additional scarring, which could make future dissection more challenging. Repair involves incisions on the vermillion of medial and lateral lip elements (Randall, 1965) and mattress sutures are passed through the medial cleft incision and through orbicularis oris and buccal mucosa. The mucosal flaps are then closed in layered fashion (Chopan et al., 2017).

III. Cleft lip Repair

Initial cleft lip surgery is usually performed under GA between three and six months old. The aim of cleft lip surgery is to reduce scarring, create a symmetrical cupid's bow and nasal area and restore optimal form and function. Management of a cleft lip continues as the infant's face develops, instead of just one surgical procedure.

There are some complications associated with the surgery, such as; anaesthetic risks, post-operative bleeding, infection, airway obstruction, damage to deeper structures, hypertrophic or keloid scarring, wound dehiscence or notching at the lip vermillion.

Surgical repair alters the orientation of facial muscles from scarring, muscle pull and may have a negative effect on craniofacial growth (Kuijpers and Long, 2000). This can cause asymmetry and reduce optimal muscle function therefore affecting the patient's ability to create facial expressions.

Initially cleft lip repair was performed as a straight-line repair. William Rose in 1979 closed a cleft lip using curved incisions which lengthened the union of the two cleft margins (Chopan et al., 2017). Since then new techniques have been developed to improve surgical outcomes of cleft repair.

IV. Surgical techniques

i. Millard or rotation advancement technique

Millard recognized that in a UCLP the majority of the Cupid's bow (one philtral column and the philtral dimple) were intact on the medial aspect but required rotation to shift the tissue into a normal anatomic position (Millard, 1964a). These principles can also be modified for use in a bilateral cleft lip repair. The repair involves incisions made in the lip to create a rotational flap from the medial segment of the cleft and an advancement flap from the cleft's lateral segment. These flaps are then brought together and sutured to correct the cleft in the muscle, subcutaneous tissue and skin. A limitation with Millard's technique is that the incisions are positioned such that a scar forms across the upper third of the philtral column and does not re-create the philtrum on the cleft side (Oh and Kim, 2023).

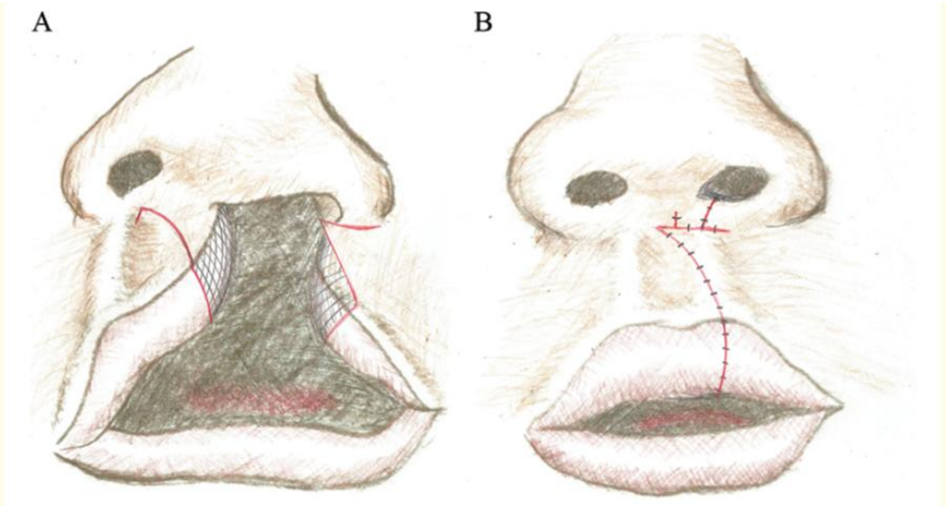

Figure 21 - Millard Rotation advancement technique. A) schematic representation of the incisions and B) representation of closure (with kind permission Chopan M. Surgical Techniques for Treatment of Unilateral Cleft Lip. IntechOpen; 2017. DOI: 10.5772/67124.)

ii. Mohler's technique

In 1987 Mohler modified Millard's technique, in an aim to reduce external scarring by placing the rotational incision in a position that mirrors the philtral column. The raised Cupid's bow point medial to the cleft is brought down level with its noncleft side counterpart by a rotation incision, which extends to the base of the columella and ends with a back cut. The resulting defect beneath the base of the columella is filled with an advancement flap from the cleft side (Roussel et al., 2015).

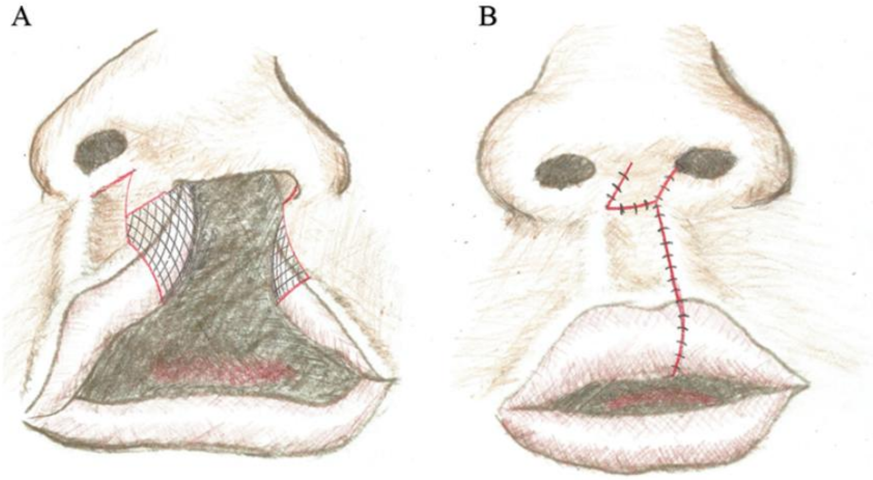

Figure 22 - Mohler's technique A) schematic representation of the incisions and B) representation of closure (with kind permission Chopan M. Surgical Techniques for Treatment of Unilateral Cleft Lip. IntechOpen; 2017. DOI: 10.5772/67124.)

iii. Fisher Repair

The Fisher repair is a blend of traditional techniques from the Tennison triangle repair with the rotation advancement of Millard. This method involves a small triangle above the cutaneous roll at the outset. The width of the small triangular flap is determined by the deficiency in philtral height minus 1 mm. This triangular flap avoids the use of a rotation incision and allows most of the scar to be placed from the cleft-side peak of Cupid's bow to the base of the nose, along a line that mirrors the noncleft-side philtral column, then superolaterally to the point of closure in the nostril sill while bordering the lip-columellar crease (Roussel et al., 2015).

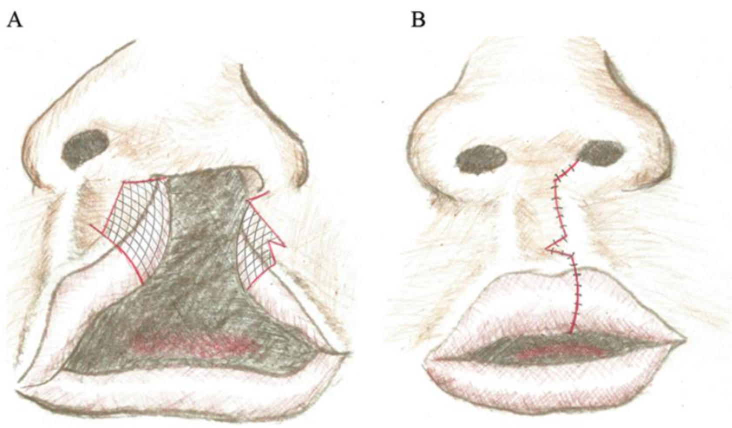

Figure 23 - Fisher's Technique A) schematic representation of the incisions and B) representation of closure (with kind permission Chopan M. Surgical Techniques for Treatment of Unilateral Cleft Lip. IntechOpen; 2017. DOI: 10.5772/67124.)

V. Methods of Vermillion repair

i. Millard vermillion repair

Originally Millard used a lateral vermilion mucosal flap to strengthen the thinned medial vermilion (Millard, 1958a). However this caused vermillion notching and a linear scar from the straight line closure at the vermillion. It was then adapted to interdigitate the lateral vermillion flap posteriorly with the medial vermillion. To improve symmetry, he introduced a back cut at the superior end of the rotational incision which allowed rotation in the horizontal plane.

ii. Noordhoff vermillion flap

Noordhoff's vermilion flap consisted of a triangular flap of lateral vermilion and orbicularis muscle from the lateral lip to help balance the thickness of the vermilion on both sides of the cleft. A back cut on the medial cleft element below the white roll to the redline of Noordhoff allows downward rotation of the medial lip and can avoid a scar at the base of the nose (Fisher, 2005). A defect is created by the downward rotation of the medial lip and this is filled with the triangular lateral lip flap (Cheema et al., 2012). To help enhance the natural pout of the lip some tension is placed above the white roll (Fisher, 2005).

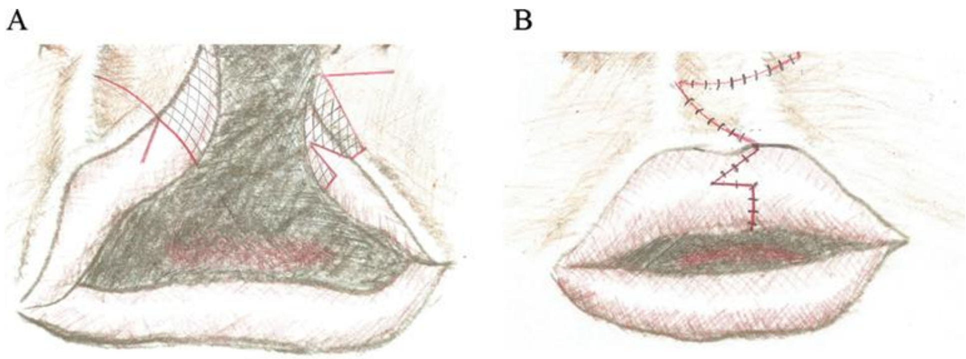

Figure 24 - (A) Schematic representation of the incisions for a Noordhoff flap (B) Schematic representation of the closure of a Noordhoff flap (with kind permission Chopan M. Surgical Techniques for Treatment of Unilateral Cleft Lip. IntechOpen; 2017. DOI: 10.5772/67124.)

iii. Fisher's vermillion repair

This technique uses concave excisions at cleft margins to provide length when closing in a straight line to achieve lip length (Rose, 1891). A back cut above the white roll allows augmentation of lip height and a back cut along the medial red line of Noordhoff allows augmentation of the vermilion. On the lateral lip, an incision is made perpendicular to the white roll and into the vermillion at a point that matches the medial lip vermilion height. One potential disadvantage of Fisher’s technique is that you may get flattening of Cupid's bow (Fisher, 2005).

VI. Muscle repair

Orbicularis oris normally inserts into the skin, creating paired philtral columns and it is used during function for oral competence and lip animation. In unilateral cleft lip, the orbicularis oris attaches to the anterior nasal spine, the foot plates of the medial crura and the anterior nasal septum on the noncleft side. However, on the cleft side the orbicularis oris attaches to the nostril sill and periosteum of the piriform aperture on the cleft side (Mulliken et al., 1993).

Repairing abnormal muscle attachments of the orbicularis oris in cleft lip repair is essential to reestablish the philtral columns and improve function and lip movement. Millard's rotational flap reorientates the orbicularis oris muscle bundle from an abnormal vertical position to a more horizontal position. Millard thought that interrupted sutures starting superiorly would help reapproximate the orbicularis, but Mulliken proposed an end-to-end muscle repair with vertical mattress sutures to evert the orbicularis and help form a philtral ridge on the cleft side (Stal et al., 2009). Fisher dissected less than 1mm of the overlying skin from the orbicularis along the medial lip but maintained the non-cleft side philtrum column. By dissecting the lateral lip to the alar base, this eliminates the orbicularis muscle bulge and frees the orbicularis muscle allowing it to be reapproximated posteriorly (Fisher, 2005).

VII. Repair of palate

Palatoplasty happens at 6-12 months old, to reattach the soft palate muscles and ensure a normal functioning velopharyngeal mechanism, which separates the oral and nasal cavities preventing nasal reflux during swallowing and hypernasal speech. The five palate muscles reconstructed during a palatoplasty are; tensor veli palatini, levator veli palatini, palatoglossus, palatopharyngeus, musculus uvulae. There are different palatoplasty techniques; straight line repair with intravelar veloplasty, furlow/double Z plasty or Veau-Wardill-Kilner V-Y Pushback (Agrawal et al., 2019).

The intravelar veloplasty technique involves elevation of nasal mucosal and oral mucosal flaps anteriorly from the maxillary alveolus toward the soft palate. The medial mucosal attachments of the flap are left intact over the soft palate only and the flaps are then rotated medially and closed in a layered fashion. However this technique does not lengthen a short palate (Agrawal et al., 2019).

The Furlow palatoplasty involves Z-plasty or transposition of soft palatal muscle flaps in one layer to re-create the levator sling and transposition of mucosal flaps in a second layer to recreate the uvula. The Z-plasty technique allows for lengthening of the palate. Straight-line mucoperiosteal flaps are elevated for the closure of the hard palate cleft.

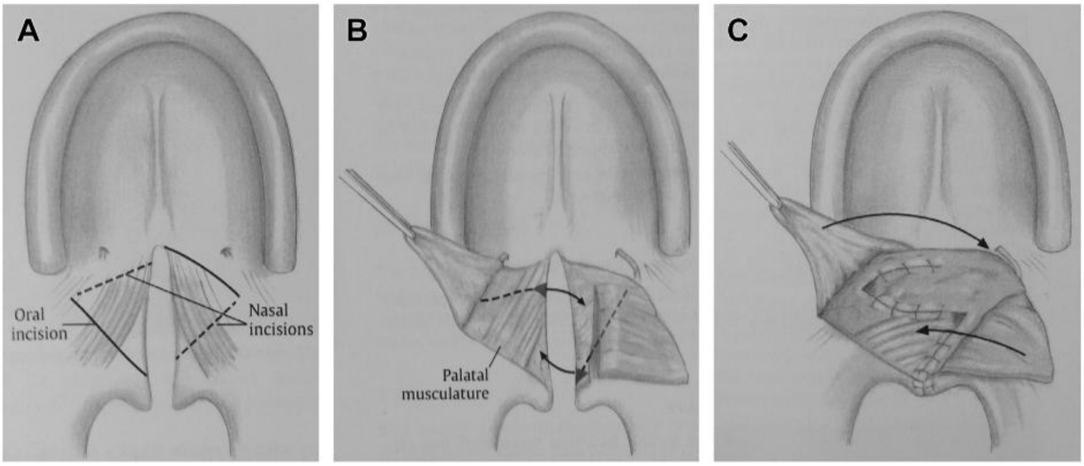

Figure 25 - Double-opposing Z-plasty technique A) left palate posteriorly based oral myomucosal layer rotated posteriorly and left nasal mucosal layer rotated anteriorly. B) right anteriorly based mucosal layer rotated anteriorly and nasal myomucosal layer rotated posteriorly. C)Recreation of levator sling and extends palate posteriorly (with kind permission Facial Plast Surg Clin North America (Shaye et al., 2015))

Veau Wardill Kilner V-Y pushback involves elevation of bilateral mucoperiosteal flaps in an anterior to posterior direction. The posterior attachments of the flaps remain intact and the mucoperiosteal flaps are then pushed back and reapproximated at the midline to allow palatal lengthening. The nasal mucosal layer is closed primarily in its position and is thereby exposed on its inferior or oral aspect, to close by secondary intent.

Potential complications during cleft palate repair are similar to those for lip repair above but there is also risk of flap necrosis, oronasal fistula formation, hanging palate, poor speech outcomes or the need for further surgery (Agrawal et al., 2019).

VIII. Nasal repair

Early nasal reconstruction can help a patient's self-esteem from a young age and eliminates the need for correcting worsening nasal deformities during growth. Success of a nasal repair is dependent on dissection that frees the alar cartilage and repositioning it into normal position. Primary rhinoplasty at the time of lip repair has become an adjunct procedure in patients with unilateral cleft lip (Sitzman et al., 2008).

Millard's technique uses a columella flap to form the nostril sill and straighten the posterior nasal septum and columella (Millard, 1958b). For better nasal symmetry the lower lateral cartilage on the cleft side is sutured higher on the nasal septum.

McComb's technique lifts the alar cartilage to shorten the nose on cleft-side. Dissection in a subcutaneous plane from the upper buccal sulcus and through the columella releases the medial and lateral crura. The dissection extends from the nostril rim to the tip, dorsum and nasion. Using 1 or 2 mattress sutures through the nasal lining can achieve an alar lift, raising the cleft side alar cartilages into a symmetrical position (Roussel et al., 2015).

11. Follow Up

After the initial repair of their cleft lip and/or palate, patients will require regular follow-up until they are around 20 years of age.

This may include:

- Regular audiology assessment at age 7-10 months and then annually until age 5
- Speech and language therapy takes place at 18 months, again at age 3 and treatment may be offered if necessary. The aim is for all children to have good quality, intelligible speech by age 5/6.
- Ongoing psychological support
- Advice and treatment from paediatric dentistry
- Orthodontic assessment and treatment if required around 10 years old

Patients will have full assessment by the cleft team at age 5, age 10, 15 and 20 to ensure that any ongoing or emerging issues are being dealt with appropriately and to review previous surgical sites. Further surgery may be required such as; palatal fistulae closure or palatal lengthening, restorative surgery, lip or cleft revision surgery, alveolar bone graft and orthognathic surgery (CLAPA, 2024). If revision surgery is required this commonly occurs between the ages of 16 and 20.

I. Palatal fistulae closure

Following a palatoplasty, the tissues may heal so that an oronasal fistula through the palate is created. This may cause nasal regurgitation during swallowing and speech problems. This can be closed in a palate revision surgery known as secondary palatoplasty.

II. Restorative dentistry

If a patient has missing or malformed teeth, a restorative dentist may replace these with fixed or removable prosthetics or use restorations to reshape teeth to improve how they look. This treatment can often not be completed until all the patient’s orthodontic treatment has been completed and all their adult teeth have erupted.

III. Cleft rhinoplasty

They may also need lip and/or cleft rhinoplasty which is often delayed until around age 16 when a patient has finished growing, this may be later for males.

IV. Alveolar bone graft

Patient's may also need an alveolar bone graft, to restore the shape of the bone for the permanent dentition and prosthetic restoration. Assessment happens around age 7-9 years and treatment is usually completed between 9-11 years but the stage of dental development and not the child's age will be the deciding factor. The procedure is performed when there is insufficient bone around the alveolar defect which could affect normal eruption of the permanent teeth. Grafting this area aids orthodontic treatment which can align the teeth in the cleft area.

For this procedure, autogenic cancellous bone is taken from the iliac crest, which is found in the patient's hip and it's grafted into the cleft defect. This should be placed gently as crushing the bone can increase resorption which can result in reduced volume and quantity. Prior to surgery the patient will have 3D planning to ensure the bone graft is the correct size and fit. In some cases the 3D scan can be used to print a bio glass scaffold for the bone graft (Paradowska-Stolarz et al., 2022).

V. Orthodontic treatment

These children come with additional dental and skeletal challenges; tooth form and number may be affected, they will have an alveolar bone graft site which may need managed and their growth pattern may be affected. These patients commonly have hypodontia, anterior and posterior crossbites, incisor rotation and retroclination (Gillgrass, 2023b). Patients with a CLP commonly have a centreline shift to the cleft side, or may have supernumerary teeth near the cleft. These patients are commonly missing the lateral incisor on the cleft side and may have a smaller central incisor which may have enamel defects present (Gillgrass, 2023b). Prior to alveolar bone grafting the patient may need orthodontic treatment to widen the area around the cleft to improve access for the surgeon. This commonly involves placing a quadhelix about 6-9 months before the surgery takes place. Patients may require extraction of some primary teeth to create space for the permanent dentition and aid the subsequent surgery.

The alveolar bone graft can help minimise disruption to the permanent dentition but most patients will still require further orthodontic treatment. Timing is crucial as grafting before tooth eruption can encourage mesial migration and good positional eruption of the canine adjacent to the incisor. The bone seen after tooth eruption is not the bone from the graft but bone that is brought by the emerging canine tooth (Gillgrass, 2023b). Grafts performed after canine eruption show more recession, periodontal pathology and poorer crown root ratios. Once patients are in the permanent dentition they may then need a course of fixed appliances. The presence of a cleft can affect the eruption sequence, prevent the eruption of some teeth or cause rotated or crowded anterior teeth. Definitive orthodontic treatment usually occurs age 12-15 years.

VI. Orthognathic surgery

Some patients develop a retrusive maxilla, whereby it is underdeveloped in relation to the mandible. This can affect the patients profile making the upper lip and nose look flatter and affect the occlusion, where the upper teeth sit behind the lower teeth in a class 3 incisor relationship, creating a reverse overjet. This is more common in a cohort of patients with CLP than the general population which may be due to genetics and restriction of maxillary growth.

If the patients malocclusion can't be managed by orthodontics alone, some patients may be offered Orthognathic surgery. This occurs in combination with orthodontic treatment by repositioning their jaws, to functionally improve their bite and/or change the appearance of their side profile which can reducing the flat appearance of the mid face.

It is a multidisciplinary procedure between a maxillofacial surgeon and orthodontist. The surgery is not completed until the face has finished growing, for females this is usually around the age of 16-18 years and 17-21 years for males.

VII. Cleft Services in the UK

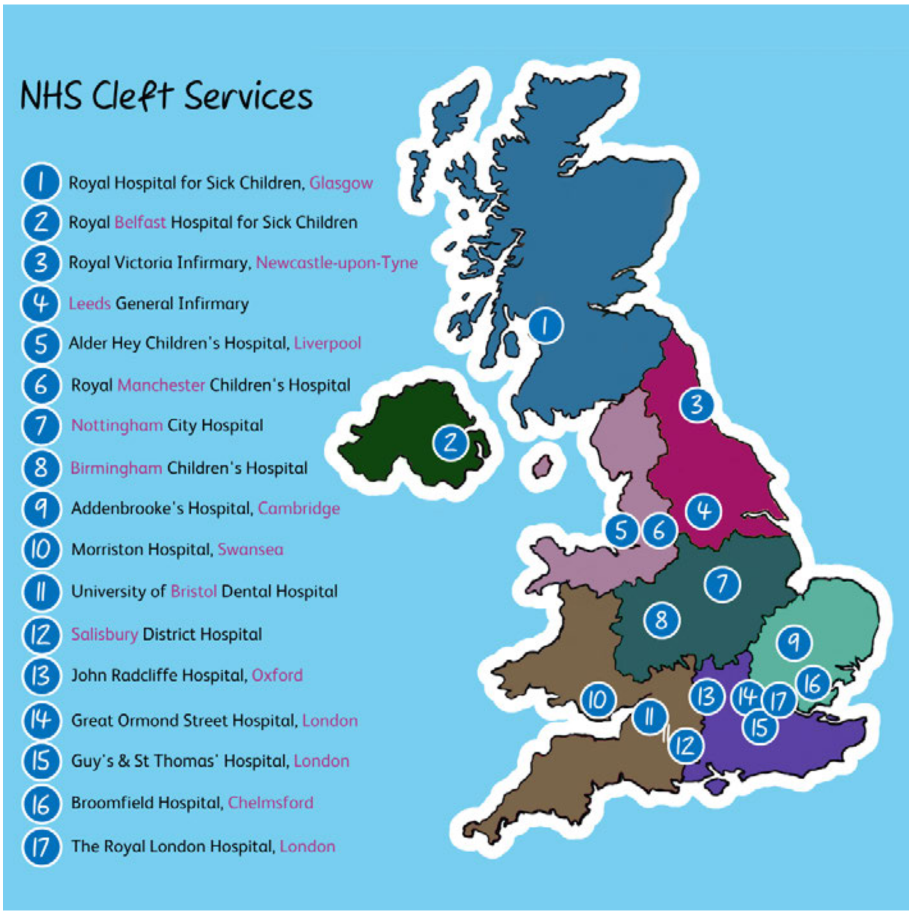

Figure 26 - The NHS cleft teams and services available across the UK (CLAPA, 2024)

A patient is discharged from Child Cleft Services between 16-20 years but some patients will be referred on to adult services to continue their treatment if necessary (CLEFT, 2024).

A survey conducted in 2014 by CLAPA showed that 97% of adults with a cleft lip said they thought they had a visible difference from others due to the presence of a scar (CLAPA, 2024). For this reason it is important that patients are aware of services available to them even as an adult. It also highlights the need to assess surgical outcomes and whether revision surgery is required, to improve patient satisfaction in a timely manner.

12. Assessment of outcomes

I. Gestational age and weight

Body weight is an important measurable outcome reflecting the nutritional status and well-being of the child. It also portrays the effectiveness or downfalls of feeding education and support received. This involves looking at the clinician-reported body weight (kg) at different time points, as well as change in weight percentile since birth, and 3 months is a common time point selected for infants (Allori et al., 2017a). Eating and drinking can have a psychological and sociological impact for older children. This can be assessed with the CLEFT-Q Eating-and Drinking subscale (Wong et al., 2014).

The CLEFT-Q is a rigorously developed patient reported outcome (PRO) measure that can be used internationally to collect and compare evidence based outcome data from patients aged 8-29 years with a cleft lip and or palate. It looks at measuring 3 overarching domains; appearance, facial function and health related quality of life (Michael and Olusanya, 2022).

II. Child growth

Normal facial growth can be affected in children with a cleft lip and/or palate and scarring following surgical repair may also adversely affect downward and forward growth of the upper jaw. For this reason it is important to assess growth outcome in patients with a cleft to allow the cleft team, and especially the surgeons, to get an early indication of how treatment should progress.

Assessment of the malocclusion in a 5 year old unilateral cleft lip and palate patient involves examining the position of the upper teeth in relation to the lower teeth. A favourable outcome is indicated by upper teeth that bite in front of the lower teeth and upper teeth that bite behind lower teeth, may require further intervention. The cleft team may need to consider further surgery for the patient when they are a young adult.

III. Dental health

For patients with a CLP it is important to look at how dental health, periodontal health, mastication and occlusion are affected. The ‘decayed, missing, and filled teeth’ (DMFT) index simply counts the number of decayed, missing (due to caries only) and restored teeth for both dentitions. The Child Oral Health Impact Profile (COHIP) subscale was chosen as a patient-reported reflection of periodontal health, including gingivitis. The COHIP was developed to assess on health-related quality of life (OHRQoL) in terms of oral health, functional well-being, social-emotional well-being, school environment, and self-image in children. It has excellent reliability and validity. Mastication is the functional capability due to the occlusion and is assessed in part of the patient-reported CLEFT-Q Eating-and-Drinking scale at time points, these are usually assessed later than the assessment of occlusion as patient-reported outcome measures cannot be used until 8 years of age or older.

Occlusion is assessed at various time points by using an index to grade the severity of the malocclusion. This is usually assessed at age 5, 12 and approx. 16-20 years. Some of the Indices used to assess occlusion can be seen below.

i. 5-year-old Index

The “5 year old Index” can be used to assess dental relationships in patients with UCLP, primarily developed for 5 year old patients. Dental models are compared to the ‘Atack 5 year index’ (Atack et al., 1997) and ranked from 1 (good growth) to 5 (poor growth). All models are assessed independently for consistency. This index is used nationally in the UK so that cleft units can get feedback about their outcomes and can gauge their outcomes against national averages.

Group	General features	Predicted Long-term outcome
1	• Positive Overjet with average inclined or retroclined incisors • No crossbites/open bites • Good maxillary shape and palatal vault anatomy	excellent
2	• Positive overjet with average inclined or proclined incisors • Unilateral crossbite or crossbite tendency • +/- open bite tendency around cleft site	Good
3	• Edge to edge bite with average inclined or proclined incisors, or Reverse overjet with retroclined incisors • Unilateral crossbite • +/- open bite tendency around the cleft site	Fair
4	• Reverse overjet with average inclined or proclined incisors • Unilateral crossbite +/- bilateral crossbite tendency • +/- open bite tendency around the cleft site	Poor
5	• Reverse overjet with proclined incisors • Bilateral crossbites • Poor maxillary arch form and palatal vault anatomy	Very poor

Figure 27 - Grades for dental arch relationship according to '5 year old index'

ii. GOSLON Yardstick

The Great Ormond Street, London and Oslo, Norway (GOSLON) Yardstick was developed for categorising the degree of malocclusion, relating to maxillary growth with unilateral cleft lip and palate (UCLP) (Mars et al., 1987). The GOSLON Yardstick varies from other systems, as it is treatment-linked and is therefore more useful than a specific anomaly-score alone. Both the effect and skeletal pattern are examined in this scoring system (Haque et al., 2015). So it is valuable at predicting the need for orthodontic or surgical treatment. This system is used for assessing the degree of malocclusion in 10-year-old children with UCLP. It categorises malocclusions in patients with UCLP by looking at all 3 planes of space: antero-posterior , vertical labial segment and transverse relationships. It can only be used for UCLP and as it is an ordinal scale it is less powerful than an objective constant numerical scale.

Group	Description	Long term Outcome
1	Positive Overjet with average inclined or retroclined incisors with no crossbite or open bite	Excellent
2	Positive Overjet with average inclined or proclined incisors with unilateral crossbite or crossbite tendency with or without open bite tendency around the cleft site	Good
3	Edge to edge with average inclined or proclined incisors or reverse overjet with retroclined incisors. Unilateral crossbite with or without open bite tendency around the cleft site	Fair
4	Reverse overjet with average inclined or proclined incisors. Unilateral crossbite or crossbite tendency with or without open bite tendency around the cleft site	Poor
5	Reverse overjet with proclined incisors. Bilateral crossbites and poor maxillary arch form and palatal vault anatomy	Very poor

Figure 28 - Grades for dental arch relationship according to GOSLON Yardstick

iii. EUROCRAN Yardstick index

The EUROCRAN Yardstick is a modification of GOSLON Yardstick and 5-year-old index and is designed to assess surgical outcomes in patients with UCLP. This index enables assessment of 2 planes of space (AP and vertical) as well as the palatal form using study models. It was developed by using findings following an assessment of 118 cases using the GOSLON Yardstick and the 5-year-old index. The scores showed that only one case was graded 5, and two cases graded as 1, making the extremes of the scale redundant. Therefore the scale was reduced to

4 for the anteroposterior, vertical and transverse dimensions and a 3-grade scale was allocated for rating the palatal form. However there are many details to consider with too many modifications and scoring the palate is both challenging and subjective.

Grade	Dental arch relation	Treatment need	Prognosis
1	Skeletal Class I or Class II	No orthodontic treatment need	Best
2	Skeletal Class I Teeth on cleft side are malposed and rotated	Orthodontic treatment on cleft side	Good
3	Apical base edge to edge or mild skeletal Class III or skeletal Class I with moderate open bite	Complex orthodontic treatment	Fair
4	Skeletal Class III with marked openbite	Orthodontic treatment + Orthognathic surgery	Worst

Figure 29 - Grades for dental arch relationship according to EUROCRAN index

iv. Modified Huddart-Bodenham (MHB) Index

Modified Huddart and Bodenham (mHB) can be used for UCLP and BCLP and applied to primary and permanent teeth at any age above 3 years. It has 5 categories for scoring incisors, canines and molars, making it much easier to use. It is more reliable, objective and sensitive than the GOSLON and 5-year-old Yardstick indices (Agrawal et al., 2019). Measurements can be used to assess digital images as well as study models. However, it does not score for anteroposterior skeletal and vertical discrepancies, and does not take into account of incisor inclinations.

As the MHB Index be used to assess the malocclusions of all clefts of the lip and/or palate and all ages, it can be used as a standardized measurement of outcomes in cleft lip and palate patients' malocclusions to optimize cleft treatment protocols (Altalibi et al., 2013).

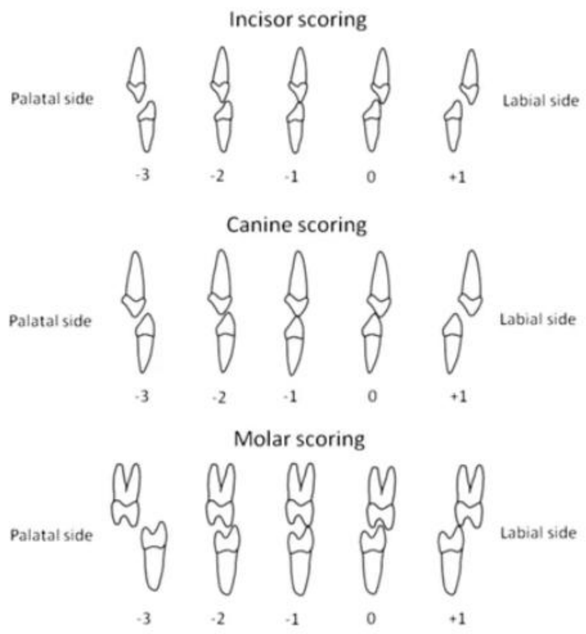

Figure 30 - Huddart-Bodenham scoring of buccolingual dental relationship(with kind permission [Creative Commons CC BY](Noverraz et al., 2015))

Score	Overjet	Incisor scoring	Canine scoring	Deciduous molar/ Premolar scoring	Molar scoring
0	Normal				
+1	Increased				
-1	Edge-to-edge				
-2	Reverse				
-3	Increased reversed				

Figure 31 - Scoring chart for Modified Huddart and Bodenham Index

IV. Speech

Cleft palate surgery aims to restore the possibility of normal speech, help with feeding and help with drainage of the middle ear. Further surgery may be required if a fistula forms or there is wound breakdown from the original surgery or if the palate is too short or has poor muscle function. The more severe the original cleft is, the higher the chance of needing further surgery in later years to attain the best speech outcomes. The national standard is that there will be no evidence of a structural problem and no further surgery required for at least 70 percent of children to help improve speech.

For speech rated through consensus judgement with ‘Cleft Audit Protocol for Speech –(CAPS-A)’ scores, the national standard is for 50% or more children to have normal speech. This outcome is achieved when children have normal scores across all 16 CAPS-A speech parameters. Articulation is also assessed looking at clarity and intelligibility and the national standard is more than 50 percent of children should have no cleft-type articulation difficulties at age five, that require either therapy or surgery.

Because languages differ in the phonetic characteristics of consonants, the potential impact a cleft palate may have on speech varies between languages (Hutters and Henningsson, 2004). To obtain the patient reported perspective regarding speech, the CLEFT-Q Speech subscale or Speaking subscale is used. The speech subscale focuses on the patient perception related to the mechanics of speaking, and the speaking subscale focuses more on psychosocial effects of the speaking process.

V. Psychology

Sociologic concerns begin in the neonatal period, with parent-child bonding and the doctor-family relationship (Stock and Rumsey, 2015). Although these relationships are important, no appropriate measure has been identified to assess this in younger years. In later life, psychological and sociological issues can be assessed with a CLEFT-Q Social Life subscale at age 8 and 12, and paired with the CLEFT-Q Feelings subscale. Quality of life surveys can allow for qualitative measures of life, psychosocial well being and patient satisfaction using validated instruments such as the CLEFT Q or the Child Oral Health Quality of Life questionnaire.

VI. Audiology

To assess audiologic function, you can examine patient use of hearing aids, frequency and chronicity of otitis media, use of tympanostomy tubes and development of complications such as; cholesteatoma and mastoiditis (Gani et al., 2012). Audiological tests such as pure tone audiometry, speech audiometry and tympanometry can provide quantitative data on hearing thresholds, speech discrimination abilities and middle ear function.

VII. Breathing

Cleft lip nasal deformity and palatal deformity can lead to airway obstruction. Nasal breathing can be appraised by the Nasal Obstruction Symptom Evaluation (NOSE) scale (Stewart et al., 2004). This scale is a preoperative screen for nasal obstruction and a postoperative measure of degree of symptom improvement. It has not been specifically validated for the cleft population but has been used by cleft teams to assess the effectiveness of cleft rhinoplasty.

VIII. Appearance

Aesthetic outcomes of cleft surgery is subjective. Some successful grading methods look at average ratings from a review panel (Asher-McDade et al., 1991), (Tobiasen et al., 1991), others use computing analysis to examine symmetry and form (Bearn, 2002, Bearn et al., 2002, Fisher et al., 2008, Pigott and Pigott, 2010) and qualitative patient reported outcomes in relation to aesthetics using different CLEFT-Q scales to assess cleft lip scar, face, jaws, lips, nose, nostrils and teeth.

i. Asher McDade Scale

Asher McDade scale allows subjective/qualitative assessments using standardized photographs analysed by a panel of judges to enable valid, reliable, and reproducible ratings of cleft outcomes. This scale looks at 4 nasolabial components; nasal form, nose symmetry, nasal profile and the vermilion border and grades each component by a 5-point scale.

However it is not without its weaknesses, the scale is designed to evaluate patients in late childhood after years of multidisciplinary treatment. Instead of focusing on aesthetic results of a single surgical intervention, such as primary cleft lip repair. The scale looks at 4 nasal components but only one in relation to the lip and does not specifically look at critical elements of the lip repair such as the philtrum, white roll, lateral lip and the balance of cupid’s bow. To improve the accuracy and reliability of nasolabial aesthetic outcomes a more standardized and objective measurement needs to be developed (Mercado et al., 2011).

ii. Unilateral Cleft Lip Surgical Outcomes Evaluation (UCL SOE)

The Unilateral Cleft Lip Surgical Outcomes Evaluation scale measures symmetry of 4 individual anthropomorphic components of the cleft repair (nose, cupid's bow, lateral lip and free vermillion) and sums these for a total score. Each element is scored on a 3 point scale: 2 (excellent), 1 (mild asymmetry), 0 (unsatisfactory). The scores of the 4 individual scores are then summed for a total score of 0 (lowest) to 8 (highest).

Figure 32 - The UCL SOE scores symmetry of 4 individual anthropomorphic components of the cleft repair (Cupid's bow, lateral lip, nose, and free vermillion (with kind permission Plast Reconstr Surg Glob Open. 2017 (Campbell et al., 2017))

IX. Other outcomes -

iii. Peer Assessment Rating (PAR)

The PAR index is a reliable measure of orthodontic treatment outcomes. Assessment requires examination of pre and post-treatment orthodontic study models. A score is given to each feature that does not meet an ideal occlusion (contact point displacement, differences between upper and lower teeth and how well the teeth interdigitate). Scores are added together to give a score that represents the severity of the malocclusion. Percentage reduction in PAR scores between pre and post treatment models is calculated and this can be categorised into 4 groups: Great improvement: 70%-100%, Improvement: 50%-69%, Little improvement: 30%-49% or No improvement: <30%.

iv. The Index of Orthodontic Treatment Need (IOTN)

IOTN is a tool used by orthodontists to assess the severity of malocclusion and the need for orthodontic treatment, helping prioritize treatment based on dental health impairment and aesthetic concerns. The Dental health component examines the severity of; crowding, spacing, overjet, overbite, crossbites and is graded 1-5. With 5 being the greatest need for orthodontic treatment. The aesthetic component uses standardized photographs to compare the patient's dental appearance with defined standards of attractiveness. Both scores are combined to determine an overall treatment need.

v. Alveolar Bone grafting (ABG)

Alveolar bone grafting outcomes are assessed clinically and radiographically (Guo et al., 2011). One method looks at the height of the interdental septum adjacent to the erupted canine and is based on radiographs taken 12 months after grafting (Bergland et al., 1986). Three dimensional radiographic assessment shows that bone grafts are almost completely lost in short-medium term, unless a tooth erupts through the area or is moved orthodontically into the graft to close the space anteriorly (Gillgrass, 2023a). An alternate approach, used prior to the eruption of the permanent maxillary canine, compares pre and postoperative anterior occlusal radiographs and grading of the degree of 'bone fill' in the alveolar cleft.

13. Asymmetry

Perfect facial symmetry is rare and mild asymmetry occurs during the normal development of the human face (Ferrario et al., 2001b). Deviation from perfect symmetry of the face, in healthy individuals is considered a normal part of human variation and is not usually noticeable when carrying out facial expressions. Symmetrical faces are seen as more attractive (Perrett et al., 1998) and even babies have been noted to stare longer at an attractive face (Quinn et al., 2008). Historically symmetry was seen as a sign of reproductive advantage, health and fertility and absence of disease (Livshits and Kobyliansky, 1989). One third of patients presenting with a dentofacial deformity had a clinically notable asymmetry (Severt and Proffit, 1997). Asymmetry may be due to an underlying skeletal asymmetry or it may be caused by a soft tissue asymmetry, and therefore facial asymmetry needs to be assessed during analysis of the face.

One side of the face may show slightly more movement or may be a different shape when compared to the contralateral side during expressions. One previous study stated that the difference between the most symmetric and most asymmetric groups was <2.5mm (Ferrario et al., 2001a). Soft tissue asymmetry is predominately present in the lower-third of the face (Fan et al., 2022), and so if we look at a subject's whole face, it may dilute any existing regional asymmetry.

I. Asymmetry in cleft population

Asymmetry in patients with cleft lip has been looked at by a number of studies, using facial measurements, static 2D and 3D photography. A video-based tracking system has previously been used to look at maximum smile, cheek puff, lip purse, mouth opening and natural smile for cleft lip and palate patients. It found 28% less upper lip movement than non-cleft individuals. They were also notably asymmetric and most restricted when smiling (Trotman et al., 2007).

Patients with UCLP also showed a greater asymmetry in vertical planes when compared to non-cleft subjects (Ras et al., 1994). Patients with a CLP had obvious distortions in both the static and dynamic form of the nasolabial region. Impairments such as; movement restriction, asymmetry, or compensatory movements elsewhere in the face were noted. Sadly, in society today, noticeable minor asymmetries on the face can elicit unwarranted staring or isolation among peers (Bradbury, 2012). This can create a sense of shame, anxiety, depression and a lack of ego development for affected children (Bradbury and Hewison, 1994). Patients with clefts have also experienced stigma and social exclusion alongside negative responses from others. There have even been reports that people looked at individuals with cleft lip and palate as less popular and facially unattractive. This is a huge social stigma and there is a tendency to socially exclude (Sousa et al., 2009).

A study (Gattani et al., 2020), compared maximal smile asymmetry in patients with unilateral cleft lip and palate and control patients and used 4D imaging for analysis. This study showed statistically significant differences between the UCLP group and the non-cleft controls. The average magnitude of nasolabial asymmetry for unilateral cleft lip and palate patients was more than 3 times (1.8mm) that of the control group (0.5mm). It would be beneficial to establish where and how these impairments manifest. However another study (Trotman et al., 2005), suggested that directly comparing patients with cleft lip and palate and non-cleft subjects could be misleading due to large variations in the mean, recommending instead to look at the normal scale of movement and assess if any differences arise.

The path of motion was looked at using 4D imaging to look at facial expressions during smiling and pouting (Hallac et al., 2017). This confirmed asymmetry in the magnitude of motion and with the path of the motion which could be a consequence of scar tissue following lip repair or due to abnormal anatomy in a patient with cleft lip or a combination of both.

Extreme movements appear to be most affected and disfigurement can remain even after surgery (Ritter et al., 2002). Asymmetry of the upper lip significantly increases during maximum smile and residual asymmetries at the nares and the philtrum can be accentuated, due to the abnormal functioning of orbicularis oris muscle. This is likely due to two factors, mechanical limitations in maximum movements secondary to lip scarring and the impairment of the maximum force capacity of the lip muscles in cleft cases (Al-Rudainy et al., 2019). The upward forces of the perioral lifting muscles affect the lip directly. The nose is less affected due its complex structure, which offers more resistance to muscular force imbalances during maximum smile.

In daily function and interaction, the nasolabial area is rarely static, so for an accurate assessment of asymmetry, dynamic facial measurements need to be examined to establish the presence of any impairment. Circumoral displacement of the lips could confound subjective evaluation of movement or function.

II. Does growth affect symmetry

Four years after surgical repair cleft lip and palate patients had a more pronounced degree of asymmetry (Al-Rudainy et al., 2019). This suggests that, in a group of patients with a cleft lip, asymmetry will become more evident as they age creating a greater dissimilarity between these two groups.

There is limited information in the literature regarding the impact of facial growth on residual facial asymmetry following cleft repair. Having more evidence for growth related changes could help to indicate the timing of lip revision surgery, which could help to minimise any residual scarring contributing to facial asymmetry.

We know that inadequate approximation of the orbicularis oris muscle fibres during primary surgery can cause tension on the skin and scar tissue formed during healing can pull the lip towards the cleft side. By studying a population that is still growing or near the end of their growth period, it may help highlight the extent of impairment resulting from scarring. Ferrario (2001) studied asymmetry from adolescence to mid-adulthood in healthy individuals and found no significant gender or age-related differences for individual asymmetry (Ferrario et al., 2001a). Another two studies also found no change in asymmetry during growth for healthy individuals. When tracking children (Primozic et al., 2012) from age 5 to 10, it was found that facial asymmetry was already present at an early developmental stage and did not show any tendency to increase or decrease with growth in the pre-pubertal period. Djordjevic et al (2013) carried out a longitudinal 3D assessment of facial symmetry in healthy adolescents aged 10-13 and found that gender and age did not significantly influence the prevalence and extent of the asymmetries (Djordjevic et al., 2013). On the other hand Sforza (2010) reported a reduction in facial asymmetry in healthy individuals as they grew. This study looked at 3D Facial Asymmetry from Childhood to Young Adulthood and found a general trend of reduced asymmetry with growth and development, for both sexes (C. Sforza, 2010).

III. How does growth affect treatment outcomes for patients with Cleft lip and palate

In contrast, a study (Al-Rudainy et al., 2019) examining cleft lip and palate patients and found a more pronounced degree of asymmetry four years after surgical repair. Suggesting that, in a group of patients with a cleft lip, asymmetry will become more evident as they age creating a greater dissimilarity between them and unaffected individuals.

Another study (Al-Rudainy et al., 2018) established that vertical asymmetry of the upper lip was restored after primary lip surgery but residual asymmetry at the corner of the mouth was noted four-years following surgery. To overcome this deficiency adequate rotation of the orbicularis oris muscle during the primary surgery and an incision anterior to the inferior turbinate that extends superiorly along the pyriform rim is necessary (Al-Rudainy et al., 2018).

Patients with repaired orofacial clefts can also have significantly altered growth with a delay in skeletal and dental maturation. This can present as an underdeveloped maxilla (Batwa et al., 2018) or as narrowing of the anterior maxilla (Mladina et al., 2015). Often these patients have a hypoplastic mid face which may be secondary to surgical scarring (Figueroa and Polley, 2007, Shi and Losee, 2015). The cleft lip repair in UCLP, may be linked to mandibular hypoplasia and a concave midface. Skeletal growth changes may arise from the tissue deficiency within the cleft defect itself (Venkatesh, 2009), or growth deficiency could be linked to functional limitations such as constriction of the nasal alae, deviation of the nose or nasal mucosal hypertrophy (Mladina et al., 2015, Bishara et al., 1976). Maxillary protrusion was observed in unilateral cleft lip patients. An important modifiable factor to consider, is the timing of surgery, as poor timing may cause growth deficiencies.

Due to these factors patients and their parents should be notified of the potential deterioration of facial asymmetry mainly at the nasolabial region in the anteroposterior direction with age. It is not unreasonable to predict further deterioration due to facial growth as the children get older and the facial asymmetry may become more pronounced. It is, therefore, logical to suggest delaying any other surgical intervention to improve on facial appearance, until the cessation of growth.

IV. Revision

Following cleft lip and palate surgery there is muscle scarring and thinner tissues around the surgical site. As a consequence patients may experience poor mobility of facial muscles and increased facial asymmetry during movement. Many patients with a repaired CLP require lip revision surgery for optimum aesthetics. Some may need multiple revision procedures and they are generally performed between 5 and 8 years of age, or later during adolescence (Trotman et al., 2010).

The aim of the initial cleft repair and any subsequent cleft revision surgeries, is to minimise post-surgical scarring, achieve optimal facial aesthetics and restore function to the orbicularis oris muscle. The decision for lip revision surgery is based on a subjective evaluation by a surgeon of lip limitations. It has been hypothesised that lip revision surgery would cause more scarring, making any impairments worse. However, there has been some reported improvement in movement after lip revision (Trotman et al., 2010). An objective evaluation would be beneficial to enable the assessment of the initial cleft repair and establish if there is a need for future corrective surgery.

V. Adverse Consequences of Unilateral Cleft Lip Surgery

- Dehiscence - not very commonly observed during or after the repair. Possibly due to improper orbicularis oris muscle approximation using sutures or due to excessive tension at the repair site (Narayanan and Adenwalla, 2013).
- Scarring - a transverse scar along the columella-labial junction can lead to hindered movement of facial muscle in that area. Immediately following surgery, scarring is observed in the cupid's bow and vermillion notching is seen on the cleft side but this usually settles in most cases. However, scarring may persist if the initial rotation was not adequate or if the lateral lip element was too short. Scarring could be controlled by the following factors:
    - I. Intrinsic factors - type of sutures and their tightness and tension created
    - II. Extrinsic factors - tension at the repair site due to tissue approximation
    - III. Patient factors - their response to a surgical trauma

  The intrinsic and extrinsic factors are controllable by the surgeons. However, patient factors are not easily controlled.

- Notching of the Vermillion border - seen as a delayed response to surgical repair. In UCLP cases, notching is seen laterally due to:
    - I. Inadequate rotations
    - II. Inversion of suture edges - Undermining the mucosa helps prevent inversion
    - III. A deficient Orbicularis Oris muscle
    - IV. Straight line scar contracture which can be avoided by Z-plasty technique

- Deformities in the nasal region - alar depression on the cleft side, inward rotation of the cleft side ala, increased nostril width, shortened columellar length and deviation of septum anteriorly towards the non-cleft side (Huffman and Lierle, 1949).

VI. Surgical timing

Surgical timing is an important consideration during management as there can be advantages and disadvantages for different timings of certain procedures involved in the treatment of cleft lip and palate. There has been (Wolford and Stevao, 2002) reported maxillary growth defects arising as result of poor timing of lip repair. Ideally lip repair should be done no sooner than 3 months old, as some reports also suggest that early lip repair (<2 months) could affect the overall growth of the child (Hammoudeh et al., 2017). It is recommended that alveolar repairs are done at 9 years or older because (Ross, 1987) found that cleft alveolar repair can result in a reduction in maxillary height. Procedures carried out during periods of rapid growth can disrupt normal growth patterns. Millard used specific surgical timing; lip adhesion performed at 3 months, lip revision or rotation-advancement performed at 6-8 months, cleft closure at 18-24 months and an alveolar bone graft at 8-10 years of age, to try and minimise any negative impacts to growth (Millard, 1964b). The optimal time for cleft closure 18-24 months or later. (Berkowitz et al., 2005).

14. How to evaluate impairment

Clefting may cause the surrounding tissues and structures, such as muscles, blood vessels and nerves to be indirectly affected or displaced. This can potentially lead to changes in sensation or function. If there is circumoral displacement of the lips, this can confound subjective evaluation of movement or function. There was more impairment during maximum smile than natural smile and impairments can remain even after surgery is carried out (Ritter et al., 2002).

Features that could be looked at when analysing lips during a smile are:

- **Smile Duration -** how long a smile lasts and how it changes over time, analysing the onset, peak and offset of the smile.
- **Smile Intensity -** by analysing the degree of facial muscle movement and deformation.
- **Lip Movement -** tracking the movement of the lips during a smile, including the curvature of the lip contours and any asymmetries.
- **Teeth Visibility -** how much tooth is exposed during a smile by tracking the movement of the lips and the opening of the mouth.
- **Smile Symmetry -** assess symmetry of the smile by comparing different movements and changes on both sides of the face.
- **Temporal Dynamics -** how a smile changes over time i.e. timing of lip movement and other facial muscle actions.
- **Gender Differences -** are there gender-specific variations in the features of a smile.

i. Smile Duration

One study of 87 healthy adult women found that the maximum speed at the cheilions for onset was 0.03 frames per second and offset 0.024 frames per second. Other literature suggests the average onset duration of a smile ranges from 0.5-0.57 seconds and offset duration 0.64-0.68 seconds (Guo et al., 2018, Schmidt et al., 2006).

Posed/deliberate smiles showed larger and more asymmetric movement than spontaneous smiles, so if comparing different individuals, it is necessary to ensure they carry out the same type of smile in a standardized way.

When looking at 400 subjects under 18 years, the total duration of genuine smile can range from 0.5-4 seconds, but posed smiles can vary (Ekman and Friesen, 1982). Deliberate expressions are more likely to have a very brief (<0.5 s) or very long (>5 s) durations than spontaneous expressions (Ekman, 2009). A paper by Schmidt (Schmidt et al., 2003) which found that the length of a smile in a healthy individual lasts on average 3-4 seconds, and another paper by Guo found that posed/deliberate smiles of healthy individuals lasted for approximately 3 seconds (Guo et al., 2018), and the duration for cleft individuals appears to be 4 seconds which was based on the paper by Seaward (Seaward et al., 2022).

ii. Speed of expressions

Analysing the speed of the lips could highlight differences in movement asymmetry during facial animation that cannot be assessed when analysing magnitude displacement alone or establish if certain facial muscles are affected during the movement. Looking at the dynamics of the expression including the timing, magnitude and directionality of the lip movement could be examined by looking at the movement vector or speed can be examined by looking at the displacement and time. Movement of the face is directly related to muscle contraction involved during each facial expression. This is influenced by the orientation of the muscle fibres and their anatomical position. If a patient has a cleft lip, scar tissue could affect the movement of the upper lip or the mechanics of the repair itself.

Even healthy individuals demonstrate asymmetry during normal motion, with statistically significant differences in vector direction in the oral commissures, the subnasal area and upper lip, during both closed lip and open lip smiles and the lower lip during open lip smile (Seaward et al., 2022). However they actually didn’t find statistically significant differences in vector deviation within the cleft group, except at the oral commissure in the closed lip smile. These results, however, were for a small sample of 13 in each group and wide age range (4-15 years), where results may be confounded by various growth phases.

The cleft group did have reduced magnitude of movement, on the cleft side at the oral commissure, upper lip and lower lip during the open lip smile, as may be expected with a scar. When comparing the two groups, cleft and control, they did however find statistically significant vector direction differences for the oral commissures, upper lip and lower lip regions during posed smile (Seaward et al., 2022).

I. How to analyse facial expression

We can evaluate impairment subjectively or objectively and using 2D, 3D or 4D imaging. Most early studies looking at facial movement were subjective, using grading scales to analyse movements on photographs of specific facial areas, directly or indirectly. Direct anthropometry is a standard technique for quantifying facial dysmorphology by carrying out measurements directly on the face using measurement devices such as a ruler or callipers. This technique is also used during treatment planning, surgical procedures and to assess treatment outcomes (Wong et al., 2008). Indirect anthropometry uses digital measurements or can be carried out using photographs. However using 2D techniques doesn't accurately quantify the complexity of facial expressions.

Subjective evaluation of surgical outcomes and assessing if further surgery is required can be unreliable and inaccurate (Trotman et al., 2007). Agreement among clinicians varies regarding the severity of the deformity or success of surgical outcomes (Asher-McDade et al., 1991). Subjective scales previously used to evaluate facial expression in patients with facial nerve paralysis are 'The House-Brackmann (HB)' or 'Sunnybrook Facial Grading System (SFGS)'. A limitation of these scales are that both rely on precise landmark position to be placed repeatedly on the 3D image over several occasions, leaving the potential for operator error.

Objective assessments allows quantifying the facial movements of facial images, videos and 3D facial expressions. These imaging devices are more accessible than physical interventions devices such as electroneurography, electromyography, or motion tracking of facial markers. Landmark based facial asymmetry measurements rely on landmark accuracy and tracking. Objective evaluation of facial movements in surgically managed cleft lip and palate patients has been studied with 2D images and also using 3D images of static faces with images at rest and at maximum facial expressions.

Static images aren't a true reflection of normal day to day function which involves dynamic expression. To assess the dynamics of facial movements, facial expression needs to be recorded in real time (4D). We can then assess different characteristics of the expression at various time intervals. Assessing facial muscle movements in a dynamic state allows analysis of the speed, magnitude, pattern and symmetry of facial muscle movement which static capture cannot. Objective quantification of facial asymmetry following primary cleft lip repair is an important outcome measure for successful surgery (Bell et al., 2014).

i. Clinical Examination

Clinical examination involves observing the face at rest to look for asymmetry, scarring, drooping or muscle atrophy. During spontaneous expression the face is inspected for lack of movement or involuntary movements. Further assessment is carried out by gently palpating the major facial muscles, orbicularis oculi and zygomaticus major, which assesses muscle tone and detects any atrophy or hypertrophy. It also identifies any tenderness or masses which may affect facial movement.

To assess functional movement the patient is instructed to perform specific movements and evaluation of functions, such as raising the eyebrows to assess frontalis muscle function and closing the eyes tightly to assess the orbicularis oculi muscle. Looking at the smile observes the zygomaticus major and minor muscles, checking for symmetry, the extent of mouth elevation and whether it is equal on both sides. Examining the duration that a patient maintains the smile and if there are any compensatory movements from other facial muscles is also assessed. By asking the patient to frown, symmetry and depth of the frown can be assessed. To assess the symmetry of the orbicularis oris muscle, ask the patient to pucker the lips. Two gestures evaluate buccinator function: 1. asking a patient to show their teeth assesses muscle coordination and 2. a cheek puff can assess the strength of buccinator muscles.

ii. Electromyography (EMG)

EMG measures the electrical activity of facial muscles at rest and during movement. Electrodes are placed on the skin overlying the facial muscles and the patient performs the different facial expressions. The electrical activity is recorded and analysed and can assess the amplitude and pattern of muscle activity. This can indicate muscle strength and coordination.

iii. Rulers and Calipers

Rulers/calipers are a low cost, practical and reliable method to obtain objective measurements of facial expressions. They can be used to measure distances between facial landmarks and to track changes over time. They are useful in a clinical setting as they are readily available, don't require specialised software, minimal training is required and the techniques are not time consuming. They provide objective measurements which can be documented and tracked over time. There are limitations with precision, reduced reproducibility from human measurement error and it is not as efficient as digital measurements. The patient needs to be still and reproduce the same expression at each visit for measurement comparison. They provide a linear measurement and do not give any information on muscle activity. They are therefore not suited to assess dynamic movement, and they cannot provide any information on speed, timing, or coordination of facial movements.

iv. 2D

A two-dimensional image does not record depth and can only be viewed properly from straight on. They do not reflect real life viewing in the third dimension and can be inaccurate as they are dependent on correct positioning. There can be magnification error as well as limited visual perspective. Objective assessment of 2D photographs of UCLP cases has satisfactory reproducibility (Asher-McDade et al., 1991) but cannot be used to assess dynamic expression. De Kerf (2021) compared 2D and 3D methods of facial movement and showed that 2D measurements underestimated measurements by 43% when compared with 3D (De Kerf et al., 2021).

v. 3D

Three dimensional imaging is when a series of 2D photographs of a patient's face is turned into an image which allows in-depth visualization and manipulation. These images are viewable at any angle and can provide better quality, resolution and depth perception than 2D imaging. Three dimensional imaging provides a comprehensive recording of the facial morphology which allows both objective and subjective assessment (Thierens et al., 2018). If the primary goal is to capture and analyse static expressions, 3D photogrammetry may be sufficient as you do not need to observe changes or dynamics over time.

vi. Cone beam Computerized Tomography (CBCT)

A systematic review looked at other 3D imaging techniques for quantitative assessment of facial soft tissues in cleft lip and palate patients (Kuijpers et al., 2014). Cone Beam Computerized Tomography (CBCT) allows the face in its entirety to be viewed and assessed in a time period. CBCT's acquire 3D images of the skull and teeth as well as soft tissues, but soft tissue images are not of ideal quality. They are expensive to run , have a limited field of view and a major drawback is that patients are exposed to radiation which is higher than conventional X ray's. Other 3D techniques that can be used are MRI, IOS, stereophotogrammetry and laser scanning.

vii. Laser Scanning

Laser Scanning places a known pattern of laser light onto an object, making sure to protect the patient's eyes, and then using geometric principles it can obtain a 3D model of the object (Z. Majid et al., 2005). It is a non-invasive, reliable, reproducible imaging system (Hajeer et al., 2004) and can produce facial surfaces with accuracy (Hennessy and Salanitri, 2005). However, it takes about 30 seconds to capture the image which requires a great deal of patient compliance. Another limitation is that the laser scanners cannot capture surface texture and so identifying landmarks is challenging.

viii. Intraoral optical Scan

Intraoral optical scan (IOS) is a nonionizing 3D imaging method which provides acquisition of 3D images and facilitates subjective evaluation and quantification of any cleft deformity. IOS is easily portable, simple to use, readily available in dental hospitals and it doesn't require a trained photographer or a dedicated imaging room. It is accurate for extraoral application (Liu et al., 2019) so is suitable to image the nasolabial region.

ix. Stereophotogrammetry

Stereophotogrammetry estimates the 3D coordinates of points on an object using measurements from 2 or more images taken from different positions to capture simultaneous images of the object (Kau et al., 2005). This allows interpretation of depth, length and width of an image. Calibration ascertains the distance between the cameras, the focal lengths and the exact position of the camera with respect to the object (Z. Majid et al., 2005). The cameras are apart from each other and the face to be imaged is placed in the same area where the calibration target was imaged. A 3D face can then be reconstructed using the 3D coordinates.

Stereophotogrammetry is an excellent choice for facial imaging of cleft patients, especially children, as no direct patient contact is required, it's safe and has a fast capture time (Ayoub et al., 2003). Patients are not subject to radiation, so it can be used for imaging multiple times. It has been used to assess cleft related asymmetry since 1994 (Ras et al., 1994). The main downsides of stereophotogrammetry are the space required for the multi-pod camera system, the need for calibration before image capture, a trained photographer is needed for image acquisition and it is more expensive than IOS.

x. 4D

Assessing facial expression with static 3D imaging is superior to 2D photographs, however, it doesn't capture facial muscle movements. The development of four-dimensional imaging allows us to go a step further and create a time sequence for facial animations that can be used for quantification of facial dynamics. It allows us to monitor changes, analyse movement, track growth and capture time-based variation alongside the static features. A 4D capture system can be used as an objective tool to assess the impact of surgical interventions on facial soft tissue movements (Shujaat et al., 2014). Four dimensional analysis uses two detection systems; marker-based motion detection and a marker less detection system. Marker based systems consist of camera pairs tracking motion from active markers or passive reflective markers e.g. C3D or Microsoft Kinect. The markerless systems detect motion using video recordings e.g. the Di4D and the 3DMD systems.

15. How to analyse facial dysmorphology

Previously the most commonly used way to analyse facial morphology, was to divide the face into halves and use a set of linear and angular measurements (Ferrario et al., 2001b). However this approach may not be possible if you are unable to identify the mid sagittal plane and it does not describe the spatial characteristics of facial morphology. When you are unable to divide the face in two, you can use a mirror image technique, which superimposes the original 3D facial image and its mirror copy. This method allows quantification of asymmetry by reflecting any differences between right and left sides of the face. However, this method may underestimate facial asymmetry and it may recognise large differences but underestimate subtle asymmetries (Verhoeven et al., 2016).

I. Landmark placement

Three dimensional marker-based photogrammetry (Trotman et al., 2013) can give a more accurate insight to facial expressions. To record dynamic facial expressions, the movements of the muscles are tracked by applying markers on the patient's face, this can be done directly prior to image capture or digitally retrospectively. This creates a sequence of 3D images representing the movements of the facial muscles. If markers are placed in relation to corresponding muscle groups, you can quantify changes depending on the displacement of these markers. One limitation when using markers can be marker error, if placement varies between sessions or among operators. It can be time consuming, if using direct placement on the patients face, limiting practicality for regular clinical use and suitability for use in children. However the introduction of digital landmark placement retrospectively has increased the potential clinical use and use in subjects of all ages, as patient co-operation is not required.

II. Generic face mesh

Stereophotogrammetry has facilitated the development of marker-less recording of facial expressions. Using an applied generic mesh to assess facial expressions has reduced the time constraint and reduced the risk of landmark error (Al-Hiyali et al., 2015). It also overcomes landmark limitations by using dense correspondence analysis (Alagha et al., 2018). The conformed mesh is like a fingerprint that captures facial patterns and morphologic characteristics of each patient's face. Landmarks are digitized on the first 3D frame of the set of images, as a guide only, to allow the conformed mesh to be placed. The mesh allows the automatic tracking of up to 3,000 anatomic corresponding "vertices" which allows analysis of motion patterns and evaluation of the magnitude and direction of facial movements. It also allows superimposition of the anatomical corresponding points (Al-Rudainy et al., 2019) of the two images, allowing in depth facial analysis to be carried out, by corresponding the vertices of a group of images (Mao, 2006).

III. Research Rationale and Justification

The justification of this study is to provide insight into the assessment of facial expression in unilateral cleft lip and palate subjects and understand the differences between individuals with a cleft and unaffected individuals. It aims to improve the quality of care and outcomes for patients born with a cleft by helping to inform surgical decisions on whether surgical revision may be required.

Chapter 2. Methodology

1. Aim

The aim of this study is to improve the quality of care and the treatment delivered to patients with UCLP. By utilizing 4D imaging as an objective assessment tool, it can allow comprehensive assessment of dynamic dysmorphology of the full face at rest and during a maximum smile (Shujaat et al., 2014, Al-Hiyali et al., 2015). Quantifying the asymmetry, speed and motion path of facial expressions allows correlation between non-cleft individuals and individuals with a repaired unilateral cleft lip, which can identify the contribution of each group of facial muscles to the asymmetry in speed and motion path of the maximum smile. This knowledge would assist the decision making process, regarding the diagnosis and management of residual dysmorphology and dysfunction following the surgical repair of UCLP, helping to guide the most appropriate time for lip revision surgery to reduce residual scarring and any associated abnormal facial muscle movements. If this study achieves its goal, it could act as a reliable guide for clinicians regarding the management of distorted muscle movements during facial expression. This could be used to assess the cleft repair and establish if there is a need for future corrective surgery.

I. Primary objective

Quantification of any abnormalities or asymmetry relating to speed during maximum smile in surgically managed cleft cases.

II. Secondary objective

Comparison of the dynamics of facial soft tissue movements during smiling in cleft cases with those of non-cleft controls.

III. Null hypothesis

This study will test the null hypothesis that there are no statistically significant differences in the dynamic speed of maximum smile within the surgically managed cleft cases and control group.

2. Study design

This study is partially retrospective, using existing data for the subject group and some of the control group, but the additional collection of 4D facial images will be carried out prospectively to augment the control group.

The study sample will comprise a maximum of 31 complete data sets of GG&C health board UCLP patients, who have previously had 4D facial imaging recorded as part of routine NHS post-operative follow-up and a matched control group of 31 subjects, 21 of which have control data sets already available from a previous PhD study. Prospective data will be collected by recruiting new volunteers, in the same age range within Glasgow Dental Hospital and School, to augment the existing control group to match the subject number.

I. Ethical considerations

As the subject group and control group contain children. Parental consent was obtained for both the images and for their use in research and assent was also obtained from those children with capacity to understand. Due to data protection all images were securely stored on encrypted and password protected computers or hard drives and to increase privacy, each patient was given a participant number and the patient identifier was not used.

The subject data was retrospective but the control group was a mix of previously recruited control participants and the prospective recruitment of control cases. Participation was voluntary and participants were not advised or pressured into taking part. Recruitment flyers were posted and patient information sheets and consent forms were provided in age appropriate form. The previously collected facial images of the non-cleft cases and the planned augmentation cases were utilised exclusively for the research purposes of this study. Therefore, Caldicott approval was required to allow the analysis of these images.

Ethical approval was obtained from the research ethics committee (REC) of southeast Scotland (REC Reference 24/PR/0139) prior to study commencement. As the 4D facial images are identifiable, Caldicott approval was also obtained, and the university was notified about the recruitment of healthy volunteers for a control group (UGN23SG500). The UCLP subjects had also been used in a previous master's project which examined different parameters of the maximum smile (IRAS ref: 314363; REC Ref: 22/SS/0090).

The comparative control group for was comprised of 24 non-cleft subjects in the same age range and geographic location, that were collected during a previous PhD project (REC ref: 17/SW/0233). The additional non cleft subjects were recruited during the period of this project. To ensure consistency and reduce the risk of selection bias, they were provided with the same documentation and recruitment process as the other non-cleft subjects.

i. Subject group inclusion Criteria

- 4D images of adequate quality
- Patient has non syndromic unilateral cleft lip and palate
- Surgical primary repair completed
- Patients 13-17 years old

ii. Subject group exclusion criteria

- No 4D images collected or images were damaged/corrupted and not able to be utilised
- Syndromic unilateral cleft lip and palate
- Any other cleft diagnosis
- Unrepaired cleft
- Patients outside the age range
- Doesn't meet inclusion criteria

iii. Control group inclusion criteria

- Non-cleft individuals between the ages of 13 and 17 years (Mix of retrospective-existing data from previous PhD study and prospective data new controls recruited)
- 4D Images of adequate quality

iv. Control group exclusion criteria

- Poor quality images
- Outside the required age range
- Excessive movement during capture

- Incorrectly calibrated

Some participants in both groups had fixed appliances on. These participants were not excluded because it has been found that metal orthodontic appliances do not have a negative effect on the aesthetic perception of a smiling face by either lay people or orthodontists (Berto et al., 2009).

3. Sample size considerations

There were 31 UCLP individuals recruited for a previous study which was selected as our subject group. Practical considerations such as availability of control participants and logistical constraints such as imaging room availability, time constraints for image capture and analysis were considered when deciding on the number of control participants. To achieve adequate statistical power the size of the control group needs to be at least equal to the study group (Hulley et al., 2013). Although for statistical reasons, there is little gained by including more than two controls per case (Lewallen and Courtright, 1998).

No previous studies have compared the speed and motion path of a smile for these groups. Other facial expression studies comparing cleft and control individuals have used a range of sample sizes, from a matched number of controls up to 3 times the number of controls (Seaward et al., 2022, Hennessy et al., 1999, Gattani et al., 2020, Othman and Aidil Koay, 2016, Golshah et al., 2022, Trotman et al., 2013). When looking at the velocity of a smile for UCLP and controls of a younger age group a meaningful result was found using a matched control sample (Seaward et al., 2022). As this study is looking at similar features with an older age group, it was felt that obtaining a matched sample would be adequate as there was no risk of loss or attrition of the groups as the study was retrospective and the images were recorded at a single time point.

i. For a two independent sample study

$$k = \frac{n_2}{n_1} = 1$$

$$n_1 = \frac{(\sigma_1^2 + \sigma_2^2/K)(z_{1-\alpha/2} + z_{1-\beta})^2}{\Delta^2}$$

$$n_1 = \frac{(1.3^2 + 1.3^2/1)(1.96 + 0.84)^2}{1^2}$$

$$n_1 = 27$$

$$n_2 = K * n_1 = 27$$

Where:

Δ = | ц2 - ц1| (absolute difference between two means)

σ1, σ2 = variance of the mean for group 1 and 2

n1 = sample size for group 1

n2 = sample size for group 2

α = probability of type I error (0.05)

ß = probability of type II error (0.2)

Z = critical Z value for a given α or ß

k = ratio of sample size for group 2 and group 1

Our anticipated mean for the control group is 3, with a standard deviation of 1.3. This is based on a paper by Schmidt (2003), which found that the length of a smile in a healthy individual lasts on average 3-4 seconds (Schmidt et al., 2003). The anticipated mean for the cleft group was 4 seconds which was based on the paper by Seaward (Seaward et al., 2022). The level of significance or probability of making a type I error(α) was set at 0.05 indicating we have a 5% chance of getting a false positive or rejecting the null hypothesis when it is actually true. The probability of making a type II error (ß) was set at 0.20, which indicates a 20% chance of getting a false negative or failing to reject the null hypothesis when it is actually false. Giving the study a power of 0.80, meaning there is an 80% chance of correctly rejecting the null hypothesis when the alternative hypothesis is actually true. This calculation showed that the minimum number of subjects that need to be enrolled in this study for a matched control sample, to have sufficient statistical power to detect a small effect difference, we would need a total of 54 subjects (27 in each group). We have exceeded the minimum sample size required to detect a small difference with 31 UCLP subjects and 34 control subjects.

4. Participant baseline characteristics

I. Unilateral Cleft lip Subject group

The 4D photogrammetric images of the UCLP subjects had been recorded by the NHS Medical Illustration Department at Glasgow Dental Hospital, as part of the routine post-surgical follow-up for these patients. These subjects only had a primary repair of the cleft completed and images were not collected specifically for research purposes. The subjects were identified as part of a previous study by another MSc student (IRAS ref:314363, REC ref: 22/SS/0090), and all of the subjects in the cleft group met the inclusion criteria requirements for this study, none had to be excluded.

This was a retrospective cross sectional study involving all 31 subjects, aged between 13-17 years old and had a unilateral cleft lip and palate. The mean age for the select group of patients was 14.61 and there was a standard deviation of +/- 1.45.

When looking at the demographics of the subject cohort, there was n=20 male participants (64%) and n=11 female patients (35.5%) and a unilateral left sided cleft was more common, n=19 (61.3%), than a right sided cleft, n=12 (38.7%). In the UCLP group n=8 (25.8%) had fixed appliances on and n=23 (74.2%) did not. However, orthodontic appliances do not have a negative effect on a smiling face (Berto et al., 2009). All patients had the same surgical protocol, a modified Millard repair when they were infants.

5. Recruitment

Following the sample size calculation there needed to be at least a matched control group for comparison with the subject group. The control group was comprised of twenty four 13-17 year old subjects that were recruited for a previous PhD study in 2018/2019 but this needed to be supplemented to achieve the appropriate sample size. This study had the same inclusion criteria as the initial recruitment; subjects had to be in the same age group (13-17 years old), from the same geographical location and be healthy individuals not affected with a cleft.

Recruitment took place over a 6 month period at Glasgow Dental Hospital, between April 2024 and September 2024. Participants were voluntarily recruited by placement of recruitment notices throughout the Glasgow Dental Hospital, inviting potential participants and parents/carers to take part in the study. The notice explained what the study was for and that participation was entirely voluntary, the patient had to contact myself to opt in to the project (appendix).

The potential participants were allowed 48 hours to consider their decision and then if happy to proceed the participants were invited to attend, at a time that was convenient for them, to have the images taken. The contribution from the participants only entails one visit, for the images to be taken and no further commitment. If they decided to proceed with the study they were given an information sheet highlighting what the images will be used for and then asked to sign a consent form before agreeing to participate. For the individuals under 16 the consent of the parent was required and for those over 16 they were allowed to consent for themselves. There were separate age appropriate consent forms and information sheets for both groups. They were offered a voucher for taking part, to contribute toward the cost of their travelling expenses to attend the image capture session, which was sent via email after the images were captured.

II. Control group baseline characteristics

The control group comprised of 24 sets of images that were previously captured as part of a PhD study (REC ref: 17/SW/0233). However 3 of these images were excluded due to poor quality or excessive movement during capture. The control subject group was augmented through recruitment at Glasgow Dental Hospital to achieve the desired sample size.

There needed to be at least a matched control group for comparison with our subject group and the final control group was comprised of participants recruited over two time periods. The twenty one 13-17 year old subjects that had been recruited for the previous PhD study and the newly recruited individuals during this study to obtain the correct sample size. Seventeen extra control participants in the same age group were recruited during the duration of this project. However 4 of the newly recruited control participants also had to be excluded due to poor image quality or excessive head movement. Resulting in a control group number of 34 individuals.

The previously collected facial images of the control group and the newly recruited participants were exclusively utilised for research purposes, so personal characteristics or identifiers were not recorded. Meaning I was unable to establish the average age, however before image capture it was confirmed that all participants were within the correct age bracket.

When looking at the demographics of the control cohort, there was n=21 female participants (61.8%) and n=13 male participants (38.2%). This was a similar breakdown to the cleft subject group but in reverse order, with more females than males. The control group has similar quantities of participants with and without fixed appliances on, n=10 (29.4%) had fixed appliances in place and n=24 (70.6%) has no appliances.

6. Assessment of Facial Expression Dynamics in Cleft Lip Reconstruction

Surgical repair of a unilateral cleft lip results in a residual deformity of the circumoral musculature, which can cause asymmetry during smiling. There is a need to objectively assess the difference between subjects with a cleft and non-cleft controls. Although there are many advanced techniques for imaging faces, there is still limited information regarding the dynamics of facial muscle movements (Samsudin WS, 2014). Subjective assessment of facial expressions can be susceptible to human error (Niziol et al., 2015). Being able to objectively quantify the extent of facial distortion, would allow comparison of different treatments and their success and monitor for any sign of worsening or relapse (Fattah et al., 2015). Objective methods such as the use of rulers or callipers don't examine the dynamics of facial expression. However, video stereophotogrammetry of the repaired cleft lip have demonstrated asymmetry in both the magnitude of motion as well as asymmetry of the path of the motion (Hallac et al., 2017). This is more asymmetric during dynamic expression for individuals with a cleft than in individuals without a cleft of the lip even after muscle reconstruction during lip repair.

III. Facial Expression Analysis: Maximum Smile

The facial expression we have chosen is the maximum smile, as a smile plays a vital role during daily communications and the lips are often a focus of attention in social situations. The presence of residual facial asymmetry after surgical repair can affect the patients self-esteem and negatively impact on their social interaction (Eckstein et al., 2011). The maximum smile was chosen, as it is reproducible and it allows comparison across the cohort. When evaluating lip movement, the lower lip has been suggested to be the most accurate and sensitive (Alagha et al., 2022), so landmarks on the lower lip were included in the analysis.

7. Equipment

I. 4D Imaging system

To investigate the dynamics of facial movements, we need to use images recorded using 3D real time capture also known as 4D imaging. This will enable us to quantify the various factors contributing to the asymmetry of facial expression, such as; the magnitude, pattern and the speed of facial muscle movements on the cleft and the non-cleft sides.

The 4D imaging system used in this study is the 3D motion capture system, Di4D manufactured by Dimensional imaging, Glasgow, Dynamic Stereo photogrammetry systems capture (fig 24). The system consisted of 2 grey-scale cameras (Model aVA 1600- 65km/kc; resolution 1600x1200 pixels; sensor model KAI-02050; Kodak, Basler, Germany) and 1 colour camera. The grey-scale cameras capture the video sequence of the area examined and the colour camera captures the surface texture and an external illuminating light source is used (Model DIV-401-DIVA LITE; Kino Flo Corp., USA). This system captures 4 megapixel 3D dynamic facial images at a rate of 60 frames/second, thus generating 180 frames as each expression usually takes about 3 seconds to record.

Examining these features with 4D stereophotogrammetry, gives us a comprehensive understanding of the dynamics of a smile and how emotion is conveyed. This analysis could have applications in psychology, human-computer interaction, communication studies, and more. The imaging system is based on passive stereo-photogrammetry which produced full textured 4D sequences and 3D images from ear to ear. The Di4D system used in this study used image capturing software (Di4D Capture) and post-capture processing and viewing software (Di4D View), both running on a high-performance PC. The attached computer had the following feature specifications: • Windows 10 • Intel core • LCD Monitor (i7 CPU 3.07 GHz).

The Di4D software allows automatic tracking of facial landmarks throughout the sequence of facial expression frames. The clinical validity of the automatic tracking of facial landmarks has been studied and applied clinically (Al-Anezi et al., 2013), (Shujaat et al., 2014, Al-Hiyali et al., 2015). Landmarks are manually located and placed on the first frame and then automatically tracked across subsequent frames.

Figure 33 - The Di4D facial performance imaging system

II. Computer Software

The captured images were processed, built, examined and analysed on a 6-core Intel CPU (Intel i7-4930K at 3.40GHz) with 32 GB RAM using a 64-bit version of Windows 10 Interprise, with a standard keyboard, mouse and LCD monitor.

8. Storage

The 4D images of the surgically managed cleft cases, and the existing images of the control group, are stored on a password-protected NHS computer, which is located in a room dedicated to 3D and 4D imaging, with a coded door lock. The images are periodically transferred, by the Medical Illustration staff, to secure encoded hard drives, which are then stored in a safe within the Medical Illustration Department. Only the Medical Illustration staff and approved researchers have access to the 3D imaging room, its PC, and the coded drives. The new 4D images for the augmented control group were captured using the same facilities, following the same standard protocol and securely stored.

For this project the required 4D images were stored, built and processed on a secure encrypted desktop hard drive (diskAshur DT2 1TB). This drive requires a pin to authenticate and when the drive is disconnected all data is encrypted using AES-XTS 256-bit hardware encryption. It has been certified to the highest government accreditations (FIPS 140-2 Level 3, NCSC CPA, NLNCSA BSPA and NATO) and in compliance with data regulations from GDPR, SOX, CCPA and HIPAA. It has a EAL5+ secure microprocessor. There was a large volume of data produced by the 4D capture process as each expression was recorded three times and multiple expressions were recorded, for both subject and control patients, and so a large hard drive was required.

Each patient's data was assigned a special coding number to ensure confidentiality. The codes linking identifiable patient information to research data, was held separately from the data, on university computers.

9. Capture

I. Consent

For the images captured as part of previous studies, the consent included an explicit statement permitting further use of the images in subsequent studies. For the newly recruited subjects there was informed written consent obtained prior to 4d images being captured and analysed. There were two different consent forms that were age appropriate so that both participants and parents could understand the research aims and how the stored images may be used. Prior to the image acquisition process it was highlighted to the patients that by signing the consent form they permitted the use of their images for the purpose of research in this project but also possibly for subsequent studies.

The assent/consent forms are stored in a protected physical folder, in a cupboard in the locked imaging capture laboratory.

II. Calibration

The Di4D system was calibrated before each capture session to synchronize the intrinsic camera parameters, image centres and focal length location and to orient the cameras. This automated process was carried out with a calibration target, that consisted of a black board with 100 white circles of specific known sizes separated by a known distance from each other. The calibration software extracted the co-ordinate distances between the circles on the target and could correspondingly measure the intrinsic parameters of all three cameras automatically. For this calibration process, the calibration target was captured eight times at varying angles and following this, the calibration of the system was carried out automatically.

By capturing the subject at multiple different angles, it achieves a 3D image. The benefit of this process is that the only time the operator needs to intervene is during positioning of the calibration target and changing the angulation in front of the camera.

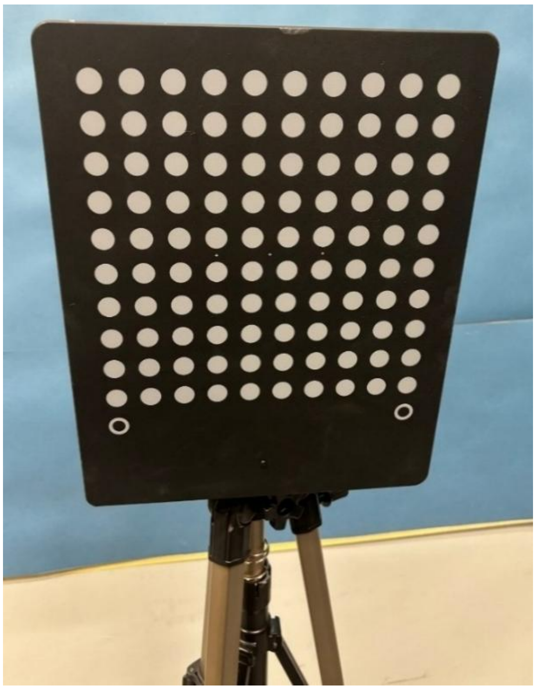

Figure 34 - Calibration board used

III. Image Capture

All images were captured with the same Di4D imaging system (Dimensional imaging, Ltd. Hillington Park, Glasgow, Scotland) and controlled by the Di4D capture software and calibrated in the same way. All images were captured with the lighting system illuminated at maximum intensity.

The participants were seated upright in a comfortable position in front of the imaging system, parallel to the cameras, at the set distance of 95cm. The head was not stabilized with a head support, as this could have restricted the facial expression recorded. To enable the camera to focus solely on the participants, they were asked to remove any glasses, jewellery or piercings and there was a neutral blue background. To keep capture standardised the participants were also provided with a hairnet, to prevent any hair from obstructing the facial field of view and affecting the captured facial morphology.

During capture each participant performed a series of 4 facial expressions; maximum smile, cheek puff, lip purse and grimace. Before capture, each patient was trained by myself, on how to achieve the maximum expression. Participants were advised to keep their head still and keep their back teeth together during the expression. Prior to the final capture they were given an opportunity to practice, to achieve a rhythm and fluidity.

To try and achieve the best quality images, the participants were asked to repeat each expression 3 times. The best facial expression was then selected by a single independent reviewer, who critiqued the expression in relation to, the duration, the image quality, if there was any head movement or interferences. In order to increase reliability and strengthen the study, a second independent reviewer also reviewed the images and selected the best one. If the two results varied then there was a joint discussion and re-evaluation of these images before choosing the final image to be examined.

There were 2 different capturers for the participants, one who captured all the UCLP subject group and 21 of the control group and a second capturer for the additional 13 control participants.

i. Maximum Smile

As maximum smile is the most reproducible facial expression, it was a good choice to compare the subject group to the control group (Johnston et al., 2003). The total duration of a genuine smile can range from 0.5-4 seconds, while posed smiles can be either longer or shorter. Ekman and Friesen (1982), looked at the average time taken for a smile in healthy individuals and found that posed smiles lasted approximately 3 seconds (Ekman and Friesen, 1982).

For the maximum smile expression, the subjects were asked to bite their posterior teeth together and smile as wide as possible, exposing their teeth and ensuring maximum stretching of the commissures and the smile was recorded from the rest position and ending at maximal animation. All the expressions started from rest to maximal facial expression before returning to the rest position. The expression was captured at a rate of 30-fps and lasted approximately 3-5 seconds, creating a minimum of 180 frames for each expression. The participant was directed when to start the maximum smile expression, advised to hold for approximately 1 second at the maximum smile and then told when to relax. This was to allow an adequate period at maximum smile, to ensure an appropriate image for examining.

Each expression was repeated three times so that the best image could be selected. To increase reliability a second independent reviewer also reviewed the images and agreement was on which image was the best expression to be analysed. If the opinions differed, then discussion/re-evaluation of images took place until agreement was achieved.

ii. Data Building

As the captured 4D images are saved as compressed raw data, the images first were reviewed and assessed for quality, to ensure no artefacts or interferences before the image was built into the 4D imaging sequence. This process was carried out using the Di4D capture software and could take up to 60minutes per facial expression for each participant. This meant that there were large quantities of data and it was important to have an appropriate storage drive.

At this stage when critiquing the quality of the images, 3 of the previously recorded control subjects had to be excluded and of the seventeen new participants recruited 4 had to be excluded.

10. Landmark identification

Each patient's 3D capture sequence was imported into Di4DView and a total nine landmarks were identified on the image; six landmarks were used to analyse lip motion and three additional facial landmarks were selected to track the effect of head motion and to align the frames. Landmarks are manually located and placed on the first frame and then automatically tracked across subsequent frames. The automated facial analysis processing method creates a common frame of reference stabilizing the head and separates facial movement from expressions and facial movement due to rigid head movements, which allows assessment of lip motion irrespective of head motion (Cohn et al., 2003).

The modified Procrustes fit method matches the most stable landmarks of each frame during function, to frames at rest to eliminate head motion. Previous studies have used from 10-30 landmarks (Trotman et al., 2000). However, Bookstein suggested using 3 stable markers.(Bookstein et al., 1991)

Minimizing the head motion during the capture of facial animations in this study was carried out by identifying 3 reference landmarks; including the right endocanthion (Landmark 7), left endocanthion (Landmark 8), and pronasale (Landmark 9). These landmarks are far from the lips being studied, would not have been affected by lip repair surgery and move minimally during smiling. All landmarks in the subsequent image frames were aligned based on these stable landmarks from the starting frame.

There needs to be equal landmarks on each side, for comparison within the same individual, to compare the affected side with the contralateral side, and this also allows comparison with an unaffected individual (Ju et al., 2016). For each subject, nine landmarks were manually digitized on the first frame of the smile expression. Identifying the landmarks and on-screen digitization took approximately 2–3 min per subject. The landmarks were tracked automatically across the animation at approximately 60 3D facial images per second over the duration of the animation. The accuracy of the automatic tracking using this Di4D software has previously been validated and the absolute mean error was within 0.55 mm (Al-Anezi et al., 2013).

I. Landmark table of points

Tracked facial markers:

Landmark No.	**Abbreviation**	**Definition of landmark**
1	chR	Cheilion right: the most lateral point located at the right corner of the mouth on the labial commissure
2	cphR	Crista Philtri right: the point on the right elevated margins of the philtrum above the vermillion line
3	cphL	Crista Philtri left: the point on the left elevated margins of the philtrum above the vermillion line
4	chL	Cheilion left: the most lateral point located at the left corner of the mouth on the labial commissure
5	llL	Lower lip left: the point below the vermillion line,opposite the cphL
6	llR	Lower lip right: the point below the vermillion line, opposite the cphR

7	ecR	Right endocanthion: the point at which the inner ends of the upper and lower eyelid meet (Stabilising landmark to account for head motion)
8	ecL	Left endocanthion: the point where the inner ends of the upper and lower eyelid meet (Stabilising landmark to account for head motion)
9	Pn	Pronasale: most anterior midpoint of the nasal tip (Stabilising landmark to account for head motion)

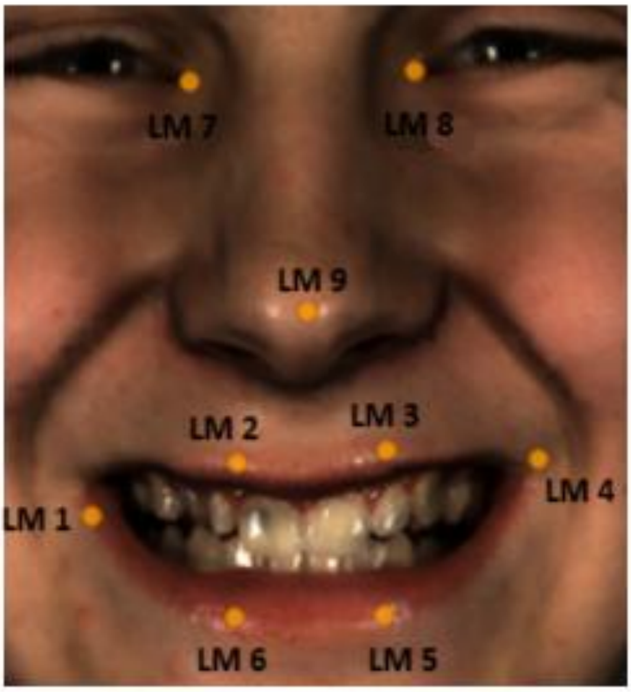

Figure 35 - Landmarks placed on control participant on 4d imaging system

On the initial frame, after location of the crista philtri landmarks, a ruler was used to position landmark LM6 parallel to LM2 and LM5 parallel to LM3. The centre point on the upper and lower lip will not be included in the set points used for analyses, as they can't be used to calculate intra-subject asymmetry.

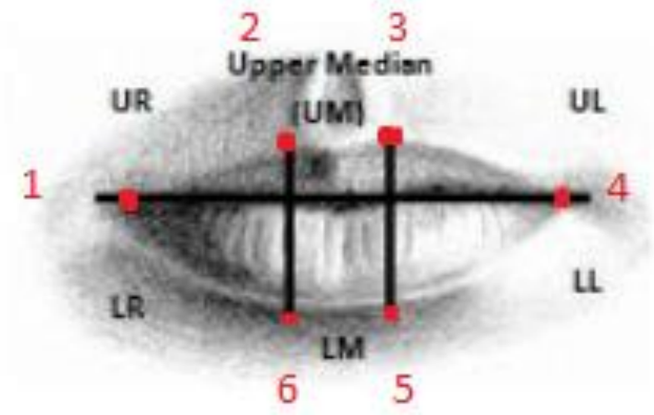

Figure 36 - Diagram showing the landmarks located on the lips

11. Data Analysis

To study the dynamics of the maximum smile, an initial rest frame was selected for each individual, the maximum smile frame selected was the median frame of the maximum smile and a final rest frame was identified. The median frame was selected as it is objective and can be used consistently throughout the groups. It is also less influenced by extreme values, which may have been caused by sudden movements/artefacts, compared to the mean and more accurately reflects the subjects typical behaviour. The maximum smile may have faster transitions at the beginning or the end of the movement but the median frame will most likely fall within the most stable phase of movement (the midpoint) without being swayed by transient variation in muscle activation creating a clear frame for analysis.

The x, y, and z co-ordinates of the landmarks were used for the analysis. The data were exported in PC2 file format, and using a software package developed in Glasgow, the data were imported into Excel. The magnitude of each facial animation was calculated by measuring the landmark displacement (the Euclidean distances) from the starting frame (rest expression) to the median frame of maximal smile. The duration was calculated as the time to reach the median frame of the maximum from the initial rest position.

I. Intra-rater Reliability (Repeatability)

To reduce repeatability error, the system was calibrated for every imaging session and the landmarks were placed in the same environment with the same equipment. The landmarks were placed by the same single rater in order to assess the reliability of the landmark placement. There was a standardized procedure for landmark placement and set sequence for the landmarks.

A random sample of 10 subjects was selected. These participants were selected using a web-based randomization tool to minimize selection bias. The same landmarks were then re-recorded after initial placement, by the same rater, one month after the initial landmark placement. This allowed assessment of landmark placement consistency, over a period of time.

i. Findings:

There was very little error between the repeated landmarks. The average difference between repeated landmarks in the x axis was 0.17mm, Y axis 0.14mm and the Z axis had the lowest reproducibility with a 0.36mm difference. This shows accuracy with repetition and consistent measurement of the landmark points over the 2 different assessment periods. This was also confirmed statistically with the intraclass correlation of these values 0.99. Indicating that the landmark placement was very consistent and reproducible.

Table 1 - Intraclass correlation between landmark placement over two time periods

	Intraclass Correlation	**P value**
Single Measures	0.998	<0.001
Average Measures	0.999	<0.001

As $p < 0.001$, this suggests strong inter-measure agreement and that almost all of the variance in the data can be attributed to differences between the groups rather than within the groups.

II. Speed of maximum smile

To study the speed of the maximum smile, an initial rest frame was selected for each individual and a frame representing the maximum smile. The frame selected for the maximum smile was the median frame, the central frame, as it could be objectively chosen for all individuals. The median frame is less influenced by faster or slower transitions at the beginning or end of the maximum smile movement. The median frame usually falls during the most stable phase of movement (the midpoint) without being swayed by transient variation in muscle activation creating a clear frame for analysis.

Spontaneous smiles have been found to have a longer duration during the onset, apex, and offset phases than posed smiles (Guo et al., 2018). This was why it was important to capture all the participant smiles in a standardised and reproducible manner.

The speed of the maximum smile was assessed by looking at the time taken for the lip landmarks to reach this maximum smile for both groups and the magnitude of displacement for each landmark, the x, y, and z co-ordinates of the landmarks were used for the analysis. The magnitude of each facial expression was calculated by measuring the landmark displacement (the Euclidean distances) from the starting frame (rest) to the median frame of maximal smile. The duration was calculated as the time to reach the median frame of the maximum from the initial rest position.

The speed (S) of each landmark from starting frame to maximum smile, was calculated by dividing the maximum landmark distance (d) by time ‘t’. [speed=d/t]

The affected side (cleft) of the UCLP group, was standardized so that the cleft side was always on the left side and was compared to the corresponding left side of the controls. This was done by mirroring the cleft side onto the left for the subjects that had the cleft on the right side. So for comparison all the clefts are on the left and will be compared against the left side of the control group. The unaffected side which will be the right for the UCLP group will be compared against the right side of the control group.

ii. Time periods of the maximum smile that were examined:

- Onset time - the length of time from start of facial expression to the moment the movement reaches maximum smile/plateaus. Also known as the contraction phase
- Apex time - the duration of the maximum smile/ plateau
- Offset time - length of time from the end of apex back to the final rest position (Guo et al., 2018). Also known as the relaxation phase.
- Total smile expression duration - From rest back to rest

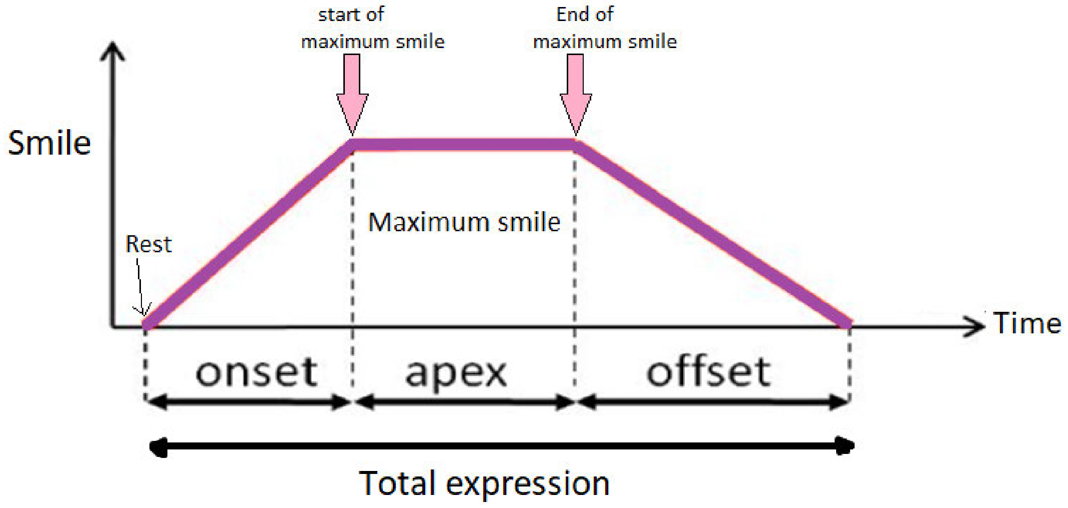

Figure 37 - Diagram showing the different periods of the smile expression

12. Statistical Analysis

I. Assessment of normality

Kolmogorov-Smirnov and Shapiro-Wilk tests were used to study the normality of data. However the Shapiro Wilk test was the one our subsequent statistical tests were based on as our samples consisted of a small to medium-sized dataset. The test statistic compares the observed distribution of data to a theoretical normal distribution. A high value indicates the data is normally distributed $p>0.05$, while a low value suggests the data significantly deviates from normality $p<0.05$. For both statistical tests used the null hypothesis was that the data was normally distributed, and the alternative hypothesis was that the data was not normally distributed. If the data was normally distributed then a parametric test can be used but if it is not normally distributed then non parametric tests will be used.

II. Comparative analysis

Statistically significant differences of the characteristics of facial expressions within the two groups, the surgically managed cleft cases and the control group, will be investigated using a paired t-test for parametric data and Wilcoxon signed rank test for non-parametric variables.

For assessment of the facial movement differences between the two groups (speed and magnitude), Mann Whitney U test will be applied for non parametric data and an independent t test was used for the parametric data. Box plots will be used to illustrate the differences in magnitude and speed of facial expressions in each study group.

Chapter 3. Results

1. Time periods for the smile of the Control group smile

The smile expression was divided up into different phases: onset, apex and offset (Guo et al., 2018). The total smile expression duration was from the initial rest frame back to the final rest frame. Looking at the control group (34 participants), initially each phase of the smile was assessed to establish baseline values for unaffected individuals.

I. Control group Onset period

The mean was 0.19 seconds, with a 95% confidence interval ranging from 0.16-0.22s, indicating a precise estimate of the mean. As the median was lower than the mean (0.17seconds), it shows a right-skewed distribution with most values clustered at the lower range. There was low data variability with a standard deviation of 0.09 seconds but the range was 0.33 seconds, suggesting the data is spread due to the presence of some outliers.

Figure 38 - Initial rest frame at the start of the onset phase in one of the control participants

Shapiro Wilk test was used to detect deviations from normality as it was a small-to-moderate sample size (<50). The normality tests for the control group onset showed significant deviation from normal $p < 0.001$. As the data was not normally distributed, non parametric tests were used for further analysis (Mann-Whitney U).

II. Control group Apex period

The mean for the apex period in the control group was 0.96 seconds, with a 95% confidence interval 0.8-1.12 seconds, suggesting the true mean lies within this range. Median value was slightly lower than the mean, 0.91 seconds, with a right-skewed distribution, so the median represents the central tendency better than the mean. The Standard deviation was 0.46 seconds, suggesting a moderate spread of data and a large range of 2.17 seconds, suggesting substantial variation in individual data points. Shapiro Wilk test had a p value of 0.02, indicating that the data significantly deviates from a normal distribution and a Mann Whitney U test was used for analysis.

Figure 39 - Frames showing the start and end of maximum smile, start and end of apex phase in control participant

III. Control group Offset period

The majority of offset values lay within a small spread, mean and median were both 0.18 seconds, with a 95% confidence interval ranging from 0.15-0.21 seconds. The dataset has low variability, standard deviation 0.08 but a moderate spread, range 0.35 seconds. Normality testing showed significant deviation from normal (Shapiro-Wilk $P < 0.001$) and non-parametric methods used for analysis.

Figure 40 - Frame back to rest after maximum smile, end of offset phase in control participant

IV. Control group Total smile duration values

The mean for the total smile duration was 1.33 seconds, the median was 1.26 seconds and the majority of the data was tightly clustered with a low variability. There was no deviation from normal (Shapiro-Wilk p=0.31) so parametric methods were used for analysis.

2. Time periods for the smile of the Unilateral Cleft lip and Palate group

The Unilateral cleft lip and palate subject group had 31 participants and the phases of the smile were assessed for each individual; onset, apex, offset and the total smile duration.

I. UCLP group Onset period

Onset in the UCLP group showed a stable central tendency, mean 0.45 seconds and a median of 0.43 seconds. The standard deviation was 0.11 with most values close to the mean but the range was 0.48 seconds suggesting some spread to the data. Normality had a p value of 0.12 (Shapiro Wilk), indicating no significant deviation from normal.

Figure 41 - Initial rest frame at the start of the onset phase in one of the UCLP participants

II. UCLP group Apex period

The apex period in the UCLP group had a mean of 1.14 seconds (95% CI: 0.95-1.32) and a median 1.17 seconds. There was moderate data spread with standard deviation 0.51 and a large range of 2.48 seconds, indicating outliers, but the interquartile range was narrower 0.43. The data did not follow normal distribution (Shapiro-Wilk $p<0.001$) and non-parametric statistical tests were used (Mann-Whitney U test).

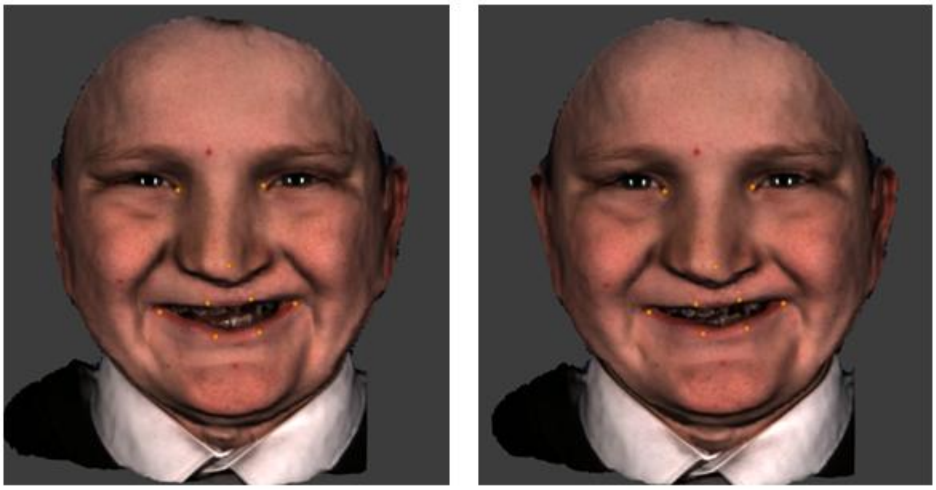

Figure 42 - Frame showing the start and the end of the maximum smile, start and end of apex phase in UCLP participant

III. UCLP group Offset period

Offset data had a mean of 0.43 seconds (95% CI: 0.36 to 0.51) and a slightly lower median of 0.38 seconds. There was low variability (SD 0.21), the minimum value was 0.1 and maximum was 1.17 giving a large range (1.07). There was a small interquartile range 0.1, indicating most values were concentrated near the centre and only a few extreme values. The data did not follow a normal distribution (Shapiro Wilk test $p<0.001$) and non parametric statistical methods were used.

Figure 43 - Frame back to rest after maximum smile, end of offset phase in UCLP participant

IV. UCLP group total smile duration values

Total smile duration in the UCLP group had a mean of 2.02 seconds (95% CI: 1.80 to 2.23) and the median was slightly lower 1.97 seconds. The standard deviation was 0.59 seconds, there was a large range (3.23) but a small interquartile range of 0.43. The data did not follow a normal distribution (Shapiro Wilk $p<0.001$) and non parametric statistical methods were used for analysis.

3. Comparing time periods for the UCLP participants and the Control participants

Comparing these 2 groups can help improve understanding of craniofacial development and the impact of cleft-related anomalies on normal dynamic expression such as aesthetic and functional capability. By comparing the phases of the smile for the UCLP group and the unaffected control group, it can allow assessment of the surgical outcomes for the UCLP group and whether they differ from their peers. The control group provides a baseline for the smile phases in an unaffected individual to establish if the presence of a cleft lip and palate affects how the facial muscles function; symmetry and the coordination of movements.

Table 2 - Comparing the time periods for the control and UCLP participants

Time period	**Median Time Control participants (seconds)**	**Median time UCLP participants (seconds)**
Onset (rest-maximum smile)	0.17	0.43
Apex (duration at maximum smile)	0.91	1.17
Offset (maximum smile to rest)	0.18	0.38
Total expression length	1.26	1.97

i. Results interpretation

During the Onset phase, the UCLP participants take significantly longer than control participants to transition from rest to maximum smile (control 0.17secs, UCLP 0.43secs). UCLP participants maintain the maximum smile for slightly longer on average than the control participants during the apex (Control: 0.91 secs, UCLP 1.17 secs). However, the time at maximum smile doesn't accurately represent the apex period for these groups, as the subjects were directed when to stop the maximum smile during the capture process and it was subject to operator variability. During offset the UCLP participants take approximately twice as long to transition back to rest than the control group (Control 0.18 secs, UCLP: 0.38

secs). The total smile duration is significantly longer for UCLP participants (1.97secs) than the controls (1.23 secs).

UCLP participants exhibit slower transitions during onset and offset of a smile compared to unaffected individuals which contributes to longer overall smile expression times. These differences highlight motor and structural challenges for UCLP participants during smiling. Standard deviation for the UCLP participants was higher which also suggests greater variability than the control group.

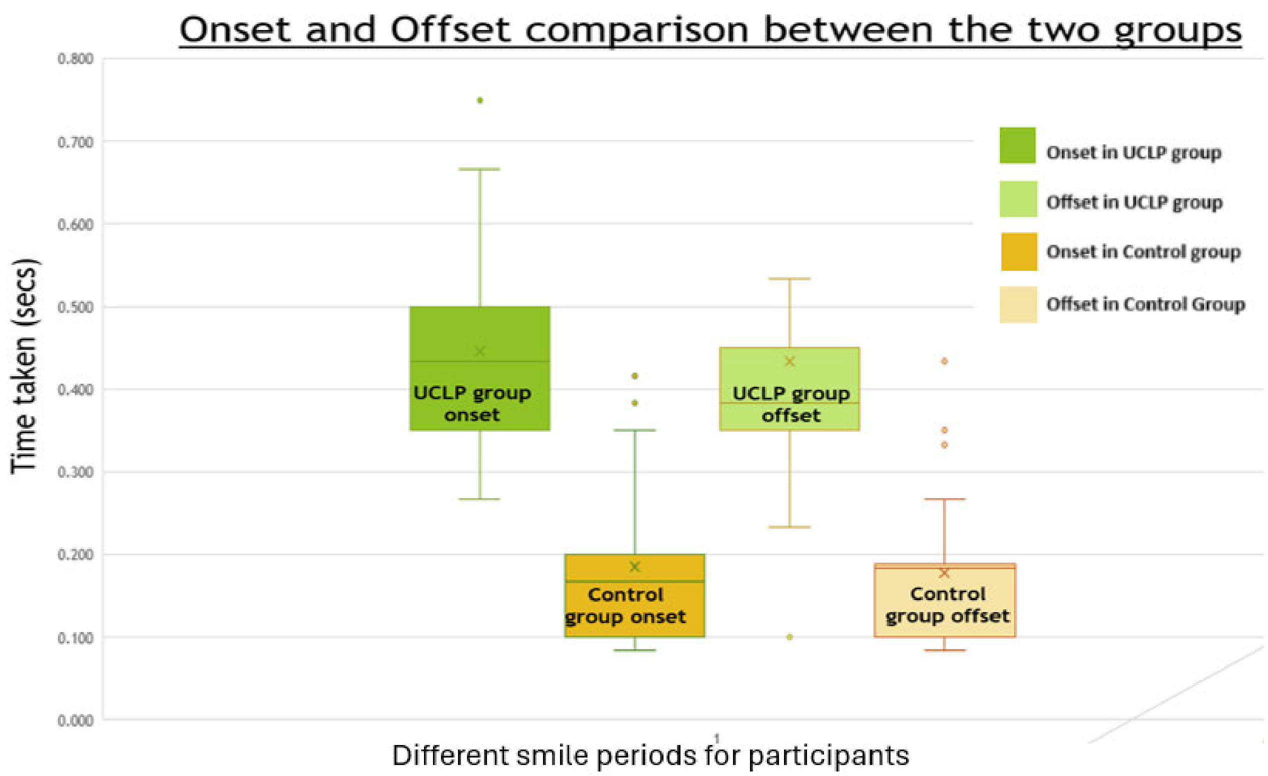

Figure 44 - Boxplot showing the time differences for the onset and offset phases for the UCLP and control groups

V. Statistical comparison of phases of smile between groups

To assess if the differences between the time periods for the two groups were statistically significant, a Mann Whitney U test was carried out.

Table 3 - Mann Whitney U Test comparing the UCLP and control group for the phases of the smile

	Onset/ Start of smile	**Apex/ plateau**	**Offset/ Back to rest**	**Total smile expression**
P value	<0.001	0.16	<0.001	<0.001

ii. Results Interpretation

The Mann-Whitney U test produced a P value of < 0.001 for comparison of the offset, indicating a statistically significant difference between the groups, with the control group having a shorter onset than the UCLP group.

The Apex time for the 2 groups had a p value of 0.16, as the p-value is > 0.05, there is no statistically significant difference between the UCLP and control groups for the apex period. This was expected because of how the maximum smile was captured. The participant was directed when to start the maximum smile expression, advised to hold for approximately 1 second at the maximum smile and then told when to relax. This was to allow an adequate period at maximum smile, to achieve an appropriate image for examining. There were 2 different capturers for the participants, one who captured all the UCLP subject group and 21 of the control group and a second capturer for the additional 13 control participants. As there was no statistically significant difference between the two groups this shows good reliability between the different capturers.

There was a statistically significant difference for the Offset time between the control group and the UCLP group, p< 0.001. The UCLP group takes longer to complete the relaxation phase of the smile than the control group. This was also replicated for the total duration of the smile expression, p value of <0.001, indicating a statistically significant difference between the groups, with the control group producing shorter smiles.

I. How do relaxation and contraction phases compare between the groups

To assess if the individuals within the group are more likely to have a certain phase of the smile that is longer, a chi square test was carried out. This can establish if the contraction (onset) or relaxation (offset) phase dominates for the individual and if this is replicated through the whole group. Assessment of the intrasubject variation between onset and offset phases, showed that the control group had an equal number of participants where the relaxation phase was longer than the contraction phase and vice versa (41% for each). In 18% of participants the relaxation and contraction phases took the same amount of time. The distribution was similar in the UCLP group, 39% had longer contraction phase, 45% had a longer relaxation phase and 16% of participants took the same amount of time for relaxation and contraction phases.

There was no statistically significant difference between the groups, Chi Square test p- =0.95. Distribution across the three phases was similar for both groups as well as the smile pattern. Some had a longer onset phase, some had a longer offset phase and for some both phases were equal, meaning the dominant phase (either contraction or relaxation) varied by subject, and was not dependent on the presence of a cleft.

4. Magnitude

Assessing the magnitude of the maximum smile provides an objective measure to evaluate dynamic differences between the groups, giving insight into the individual's facial aesthetics and if surgical repair has restored muscle coordination and symmetry. Comparing individuals with a UCLP to the control group can show how the smile magnitude in the UCLP group aligns with unaffected individuals, evaluating if functional impairments have been minimized following the surgical repair or if a deficits persists on the cleft side or the contralateral side.

Figure 45 - Median frame of maximum smile used to assess the magnitude of landmarks in one of the control participants

5. Control Participants

Table 4 - Descriptive characteristics for the magnitude of the control landmarks to reach maximum smile

Landmark	**Mean (mm)**	**Std Dev (mm)**	**Median (mm)**
Left cheilion control group	37.22	17.46	32.65
Right cheilion control group	40.03	21.53	34.26
Left philtrum control group (crista philtri)	14.44	9.94	11.29
Right philtrum control group (crista philtri)	13.39	8.8	10.17
Left lower lip control group	26.88	19.35	21.92
Right lower lip control group	25.25	17.34	18.39

i. Findings

In the control group, the left cheilion had a mean of 37.22 mm with a Std Dev 17.46 mm. The median was lower (32.65) indicating a slight positive skew. The range for these values was 65.31 mm (Min = 15.44 mm, Max = 80.75 mm). The right cheilion had a larger mean, 40.03 mm, with a Std Dev = 21.53 mm and a lower median 34.26 mm. There was a greater range, 92.71 mm (Min = 8.32 mm, Max = 101.03 mm).

Comparing philtrum landmarks within the control group, the left side had a mean of 14.44 mm, SD 9.94 mm and median 11.29 mm. There was a range of 42.98 mm (Min = 4.31 mm, Max = 47.29 mm) with a strong positive skew. The right philtrum had a slightly smaller mean, 13.39 mm with a Std Dev of 8.8 mm and a median 10.17 mm. The data was positively skewed and the range was 43.38 mm (Min = 3.53 mm, Max = 46.91 mm).

The left lower lip landmarks had a mean of 26.88 mm, SD 19.35 mm and median 21.92mm. There was a large range 76.64 mm (Min = 7.92 mm, Max = 84.56 mm) with a strong positive skew. The lower lip landmark on the right had lower values, mean 25.25 mm, Std Dev = 17.34 mm and a median of 18.39 mm. The data was also positively skewed and had a lower range 62.57 mm (Min = 10.85 mm, Max = 73.42 mm).

Shapiro Wilk test for both cheilion landmarks indicate deviation from normality, the left cheilion p value= 0.002, and right cheilion p value= 0.025. Both philtrum and lower lip landmarks showed significant deviation for normality p value's <0.001.

I. Statistical analysis for control intrasubject magnitude comparison

As all landmarks deviated from normality, a Wilcoxon signed rank test was used to check for statistical significance.

Table 5 - Wilcoxon Signed Rank test for the control landmarks

Control Intrasubject paired landmark	**P value**
Magnitude of paired right and left cheilion landmarks	0.533
Magnitude of paired right and left philtrum landmarks	0.156
Magnitude of paired right and left lower lip landmarks	0.505

ii. Wilcoxon Signed Rank test Results interpretation

Comparison of paired right and left landmarks within the individuals of the control group showed no significant difference between the sides for any landmarks; cheilion, philtrum and lower lip, suggesting that in a individual not affected by a cleft, there should be no significant difference in magnitude between opposing sides.

6. Unilateral Cleft Lip and Palate Participants

Figure 46 - Median frame of maximum smile used to assess the magnitude of landmarks in one of the UCLP participants

Table 6 - Descriptive characteristics for the magnitude of the UCLP landmarks to reach maximum smile

Landmark	**Mean (mm)**	**Std Dev (mm)**	**Median (mm)**
Cleft Side Cheilion	27.24	11.79	27.48
Non Cleft Side Cheilion	29.49	10.62	30.18
Cleft Side Philtrum (crista philtri)	6.84	4.05	5.96
Non Cleft Side Philtrum (crista philtri)	7.59	3.68	6.7
Cleft Lower Lip	19.85	11.34	16.6
Non Cleft Lower Lip	18.04	10.24	15.1

i. Findings

Magnitude of cheilion landmarks on the cleft side of the UCLP group had a median of 27.48mm, with a standard deviation 11.79mm and a range of 42.51mm (Min: 6.97mm, Max: 49.48mm). The non cleft side had a median of 30.18mm, standard deviation 10.62mm and range 44.74mm (Min: 6.99mm, Max: 51.73mm). The non-cleft side had slightly larger measurements than the cleft side, but the difference was minimal.

Magnitude of philtrum landmarks on the cleft side had a median of 5.96mm, a standard deviation of 4.05mm and a range of 17.75mm (Min: 1.59mm, Max: 19.34mm). The median on the non cleft side was 6.7mm, a standard deviation of 3.68mm and a range of 15.22mm (Min: 1.48mm, Max: 16.7mm). The magnitude of the philtrum on the non-cleft side was slightly larger and less variable, with a more symmetrical distribution compared to the cleft side.

For lower lip landmarks on the cleft side the median magnitude was 16.6mm, with a standard deviation of 11.34mm and a range of 48.17mm (Min: 3.19mm, Max: 51.35mm). The non cleft side had a median of 15.1mm, with standard deviation 10.24mm and a range 40.35mm (Min: 4.72mm, Max: 45.07mm). The lower lip magnitude on the cleft side was slightly larger and showed a greater variability than the non-cleft side.

There was a normal distribution for cheilion landmarks on both sides (Shapiro Wilk test cleft side p=0.45, non cleft side p=0.94). The philtrum landmarks on the cleft side showed significant deviation from normality (p=0.005) but the data on the non cleft side followed a normal distribution (p=0.16). The lower lip landmarks were significantly deviated from normal (cleft side p=0.01, non cleft side p=0.007).

I. Statistical analysis for UCLP intrasubject magnitude comparison

Cheilion values for the UCLP participants were normally distributed and a paired t test was used to assess for statistical significance between magnitude on cleft and non cleft sides.

Table 7 - Paired T test results

	Group	**Mean (mm)**	**Std deviation (mm)**	**P value**
Cheilion	Cleft side UCLP group	27.24	11.79	0.09
	Non cleft side UCLP group	29.49	10.62	

i. T test Results interpretation

There was a strong positive correlation between cleft and non-cleft sides. However the T Test value was p = 0.09, showing no statistically significant difference. The mean difference on the cleft side was smaller than the non-cleft side by approximately 2.25 mm.

Data for the philtrum and lower lip landmarks were not normally distributed so a Wilcoxon signed rank test was used for statistical analysis.

Table 8 - Wilcoxon Signed Rank test for the philtrum and lower lip landmarks

Intrasubject paired landmark	**P value**
Magnitude of paired cleft and non cleft philtrum	0.007
Magnitude of paired cleft and non cleft lower lip	0.03

ii. Wilcoxon signed rank test Results interpretation

Intrasubject comparison for the magnitude of philtrum and lower lip paired landmarks in the UCLP participants indicated statistically significant differences in magnitude between cleft and non-cleft sides (philtrum landmarks p=0.007 and lower lip p=0.03), showing an asymmetry between opposing sides for both the lower lip and philtrum.

iii. Summary

Statistically significant differences were found for magnitude of philtrum landmarks between the cleft side and non affected side, in an individual with a unilateral cleft lip and palate. The cleft side had smaller magnitudes than the unaffected side. Although the cheilion on the cleft side exhibited lower magnitudes, there was no statistically significant difference between the sides. There was a statistically significant difference between the two sides on the lower lip but it was the cleft side that had a greater magnitude than the non affected side.

7. Comparing magnitude of the affected cleft side in UCLP group and the left side in the control group

To establish if individuals with a cleft experience magnitude limitation during smiling , non parametric testing was used to compare the cleft side in the UCLP group and the left side of the control group. The unaffected side in the UCLP group was also compared with the right side in the control group, to assess if the contralateral side of the smile was also restricted by the presence of a cleft.

Table 9 - Mann Whitney U test comparing magnitude between the two groups

Landmarks	**Side/group**	**P Value**
Cheilion	Cleft side/ UCLP	0.03
	Left side/ control	
	Non cleft side/UCLP	0.95
	Right side/ control	
Philtrum	Cleft side/ UCLP	<0.001
	Left side/ control	
	Non cleft side/UCLP	0.001
	Right side/ control	
Lower lip	Cleft side/ UCLP	0.189
	Left side/ control	
	Non cleft side/UCLP	0.049
	Right side/ control	

I. Cheilion landmarks

There was a statistically difference (p=0.03) between the magnitude for cheilions on the cleft side of the UCLP group and the left side of the control group. Lower mean ranks were seen in the UCLP group (27.68mm) than the control (37.85mm).

However there was no significant difference for magnitude reached between the unaffected side in UCLP group and the right side of the control group, p= 0.95. Although the mean rank in the UCLP group was lower, 28.9mm, than the control group, 36.74mm.

II. Philtrum landmarks

There was a highly significant difference for the philtrum magnitude on the cleft side of the UCLP group and the left side of the control group (p <0.001), and a large difference between mean ranks, 22.77mm on the cleft side and 42.32mm for the control group.

There was also a significant difference between the philtrum magnitude on the non affected side of the UCLP group and right side of the control group (p =0.001) and the UCLP group had a lower mean rank, 24.95mm, and control group, 40.34mm.

III. Lower Lip landmarks

There was no significant difference (p= 0.19) when comparing the lower lip on the cleft side of the UCLP group and the left side of the control group. Although, there was a difference in the mean ranks (cleft side 29.77mm, control group 35.94mm).

However there was a significant difference between the lower lip on the unaffected side of the UCLP group and right side of the control group, p = 0.049 (just under the threshold for significance). The mean ranks were 29.16mm for the UCLP group and 37.41mm for the control group.

i. Summary

Significantly smaller magnitudes were seen for the philtrum on both sides of the mouth in an individual with a UCLP when compared to a healthy individual. The reduced magnitude seen on the non cleft side indicates a restriction in muscular activity regardless of which side has the cleft. The cheilion on the side affected by the cleft also showed significantly smaller magnitudes than the control group. However for the lower lip, it was the non cleft side that was more restricted than the cleft side, when compared to the control group.

8. Speed of the maximum smile

The speed (S) of each landmark from starting frame to the maximum smile, was calculated by dividing the maximum landmark distance (d) by time (t), [speed=d/t].

The affected side (cleft) of the UCLP group, was standardized so that the cleft was always on the left side and could be compared to the left side of the controls. The cleft side was mirrored onto the left for the subjects that had a right sided cleft. For comparison all the clefts were on the left and were compared against the left side of the control group. The unaffected side, which was the right side for the UCLP group, was compared against the right side of the control group.

9. Unilateral cleft lip and palate group

Table 10 - Descriptive characteristics for the speed of lip landmarks to reach maximum smile

Landmark	**Mean (mm/s)**	**Std Dev (mm/s)**	**Median (mm/s)**
Cleft Side Cheilion	28.69	14.14	28.6
Non Cleft Side Cheilion	32.05	16.25	31.11
Cleft Side Philtrum	7.24	4.52	5.98
Non Cleft Side Philtrum	8.22	4.79	7.65
Cleft Lower Lip	20.98	11.72	20.66
Non Cleft Lower Lip	19.22	10.95	20.2

i. Summary:

Comparing cleft and non-cleft sides revealed several differences, cheilion speeds were greater on the non-cleft side (mean = 32.05mm, SD = 16.25) compared to the cleft side (mean = 28.69mm, SD = 14.14), with greater range on the non-cleft side. Similarly, the philtrum had greater speeds on the non-cleft side (mean = 8.22mm, SD = 4.79) than the cleft side (mean = 7.24mm, SD = 4.52). For the lower lip, the cleft side exhibited greater speeds (20.98 mm, SD = 11.72) than the non-cleft side (19.22mm, SD = 10.95). Overall, non-cleft sides generally had larger speeds and greater variability, particularly for cheilion and philtrum measurements.

ii. Normality tests for the UCLP group intrasubject comparison of speed

The Cheilion on both sides (cleft p= 0.56, non-cleft p= 0.09) showed a normal distribution. The Lower Lip also had a normal distribution for cleft and non-cleft sides (p = 0.14 and p = 0.11, respectively), so a paired t test could be used. However the data was not normally distributed for the Philtrum landmarks, cleft side p = 0.013 and non cleft side p = 0.032. As the data did not meet the normality assumption, non-parametric tests were used (Wilcoxon Signed-Rank).

Intrasubject Speed comparison

I. Comparing the speed of cheilion landmarks on the cleft side and the non affected side

For the cheilion, the non-cleft side had a higher median (31.11mm/s) than the cleft side (28.6mm/s). The non-cleft side showed greater variability (SD = 16.25) and a wider range

(75.02) than the cleft side (SD = 14.14, range = 56.45). The non-cleft side distribution was more skewed (0.98) than the cleft side (0.29).

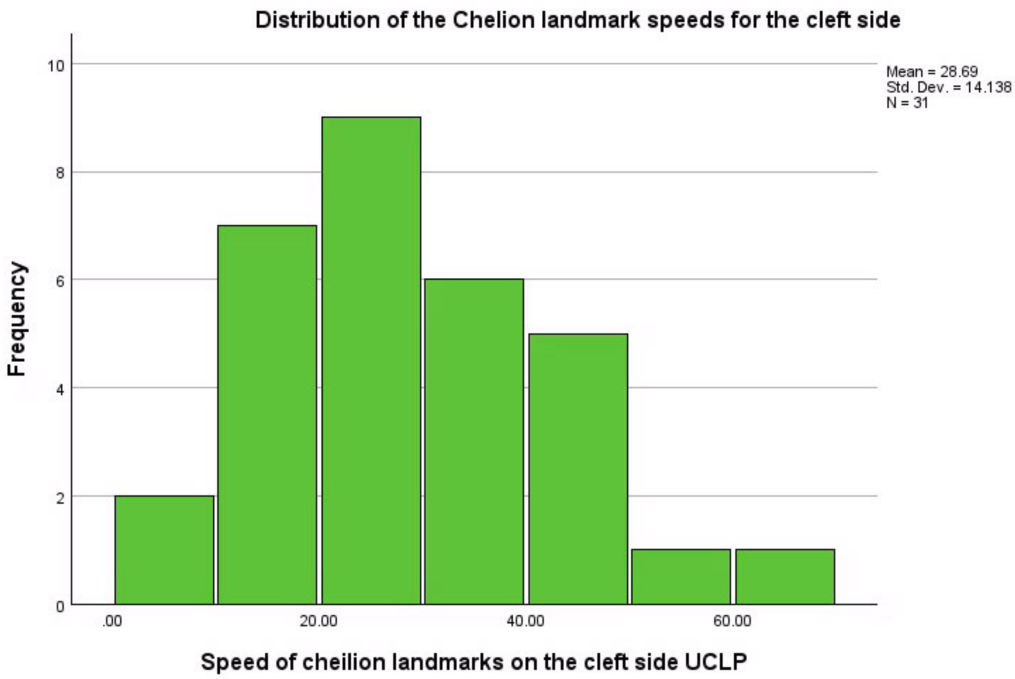

Figure 47 - Distribution of speed values for the Cheilion landmark on the cleft side

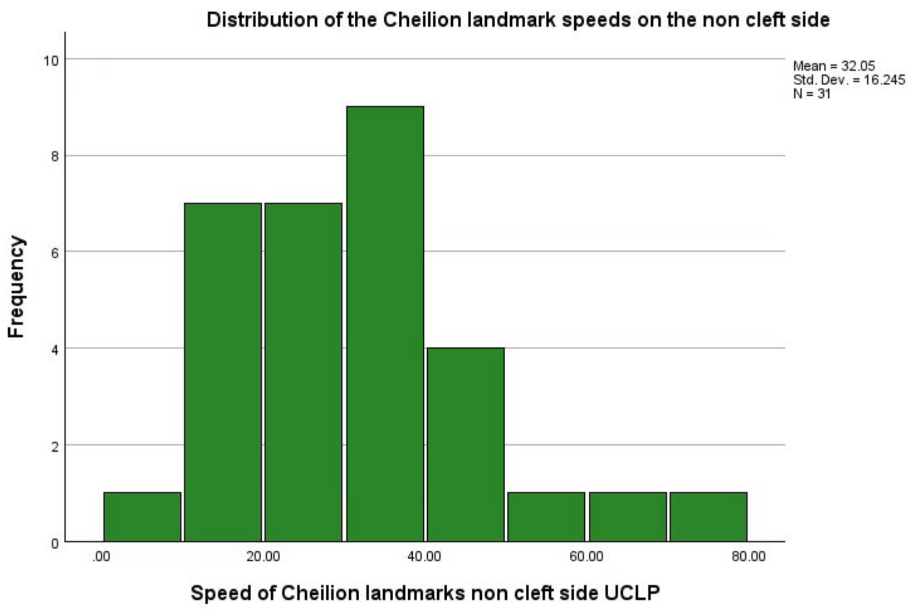

Figure 48 - Distribution of cheilion landmark speeds non cleft side of UCLP group

II. Comparing the Speed of philtrum landmarks on the cleft side and the non affected side

The philtrum on the non-cleft side had a higher median (7.65mm/s), than the cleft side (5.98mm/s), a wider range (21.27 vs. 19.11) and slightly higher variability (SD = 4.79 vs. 4.52). Both sides had right sided skewness (1.04 non-cleft, 1.17 for cleft).

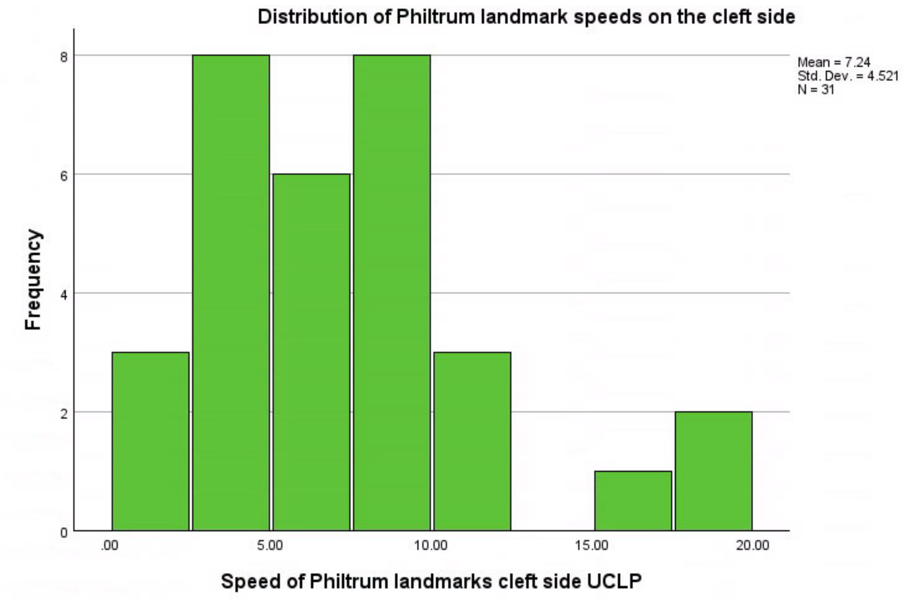

Figure 49 - Distribution of Philtrum landmark speeds on the cleft side of UCLP

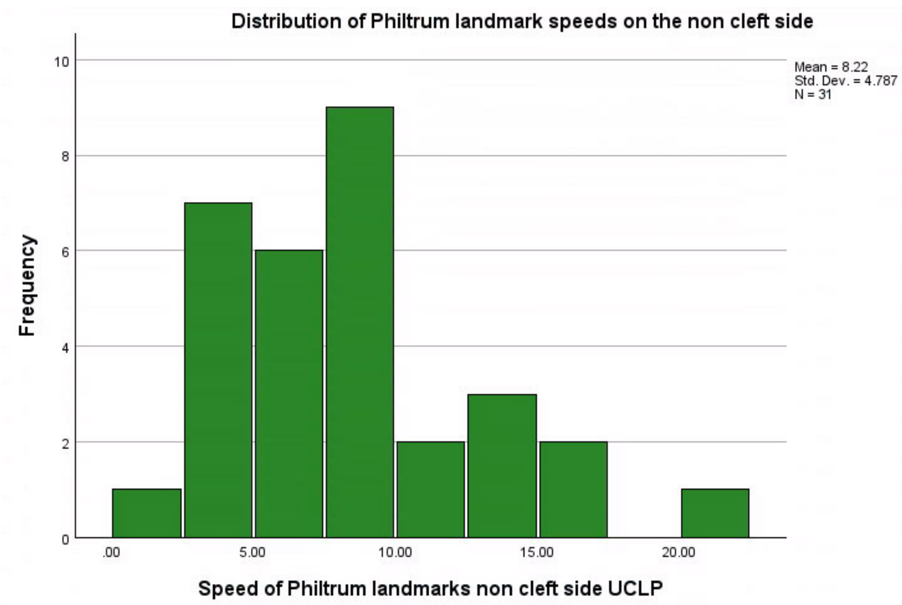

Figure 50 - Distribution of Philtrum landmark speeds on the non cleft side of UCLP group

III. Comparing the Speed of lower lip landmarks on the cleft side and the non affected side

The cleft side had a slightly higher median (20.66mm/s) than the non-cleft side (20.2mm/s) for the lower lip. Variability was similar between the sides, with standard deviations of 11.72 (cleft) and 10.95 (non-cleft).

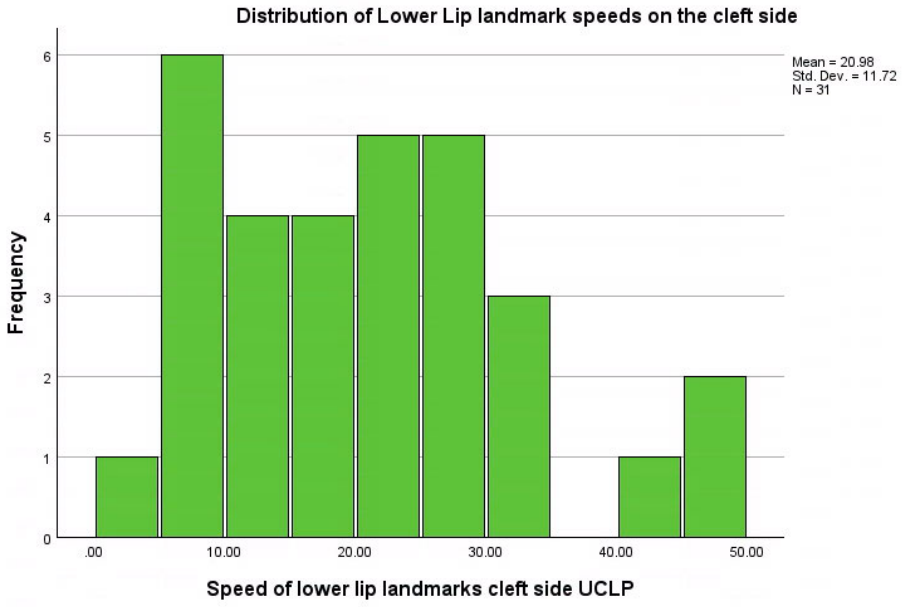

Figure 51 - Distribution of Lower lip landmark speeds on the cleft side of UCLP group

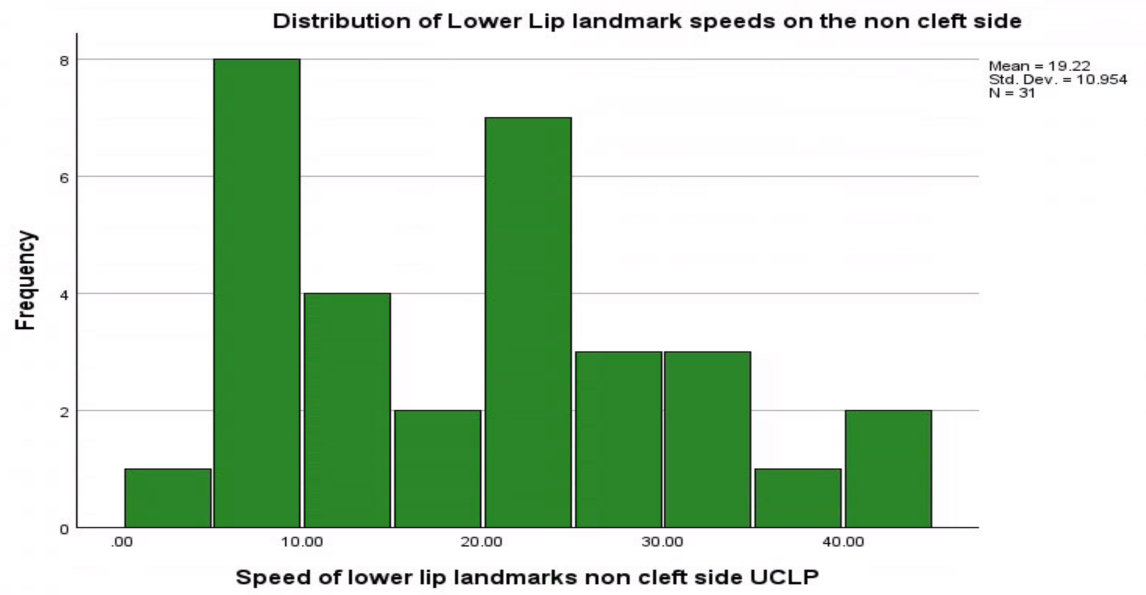

Figure 52 - Distribution of Lower lip landmark speeds on the non cleft side of UCLP group

i. Summary of Findings:

In summary, the non-cleft sides generally exhibited higher speeds, greater variability, and wider ranges compared to the cleft sides.

10. Statistical analysis for UCLP intrasubject speed comparison

To establish if differences between contralateral sides within the UCLP individual were statistically significant, a Wilcoxon signed rank test was used for philtrum landmarks and a paired t test for the cheilion and lower lip landmarks.

Table 11 - T test group statistics to compare the intrasubject cheilion and lower lip landmarks

	Group	**Mean (mm/s)**	**Std deviation (mm/s)**	**P value**
Cheilion	Cleft side UCLP group	28.69	14.14	0.072
	Non cleft side UCLP group	32.05	16.25	
Lower Lip	Cleft side UCLP group	20.98	11.72	0.036
	Non Cleft side UCLP group	19.22	10.95	

I. T test Results interpretation

There was no statistically significant difference (p=0.07) for the speed of cheilion landmarks. The average speed of the cheilion on the cleft side (28.69mm/s) was slightly lower than the non-cleft side (32.05mm/s). However the one-sided p-value 0.04 was statistically significant, meaning there was a difference in one direction, the speed on the non-cleft side tended to be greater. These results suggest a trend towards significance in favour of greater speeds on the non-cleft side.

Speed of the lower lip on the cleft side (20.98mm/s) was significantly greater than the non-cleft side (19.22mm/s) and p-value = 0.04. The one-sided p-value (0.02) was also significant, reinforcing this finding.

Table 12- Wilcoxon Signed-Rank Test for the Philtrum landmarks

Intrasubject paired landmark	**P value**
Cleft Side Philtrum vs Non Cleft Side Philtrum	0.007

i. Wilcoxon Signed Rank test Results Interpretation:

Comparing philtrum measurements on the cleft and non-cleft sides within subjects showed a statistically significant difference (P= 0.007) and strong evidence that the cleft and non-cleft sides differed. Observed differences are unlikely due to chance, highlighting a measurable asymmetry in philtrum dimensions between the two sides.

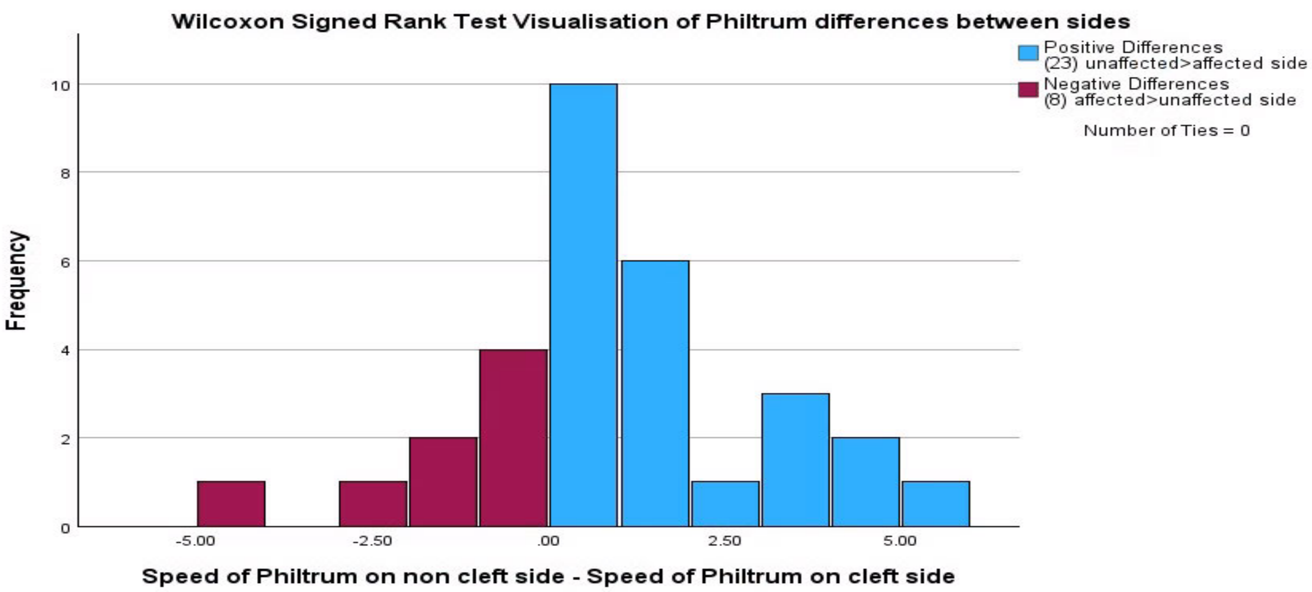

Figure 53 - Graph showing the Wilcoxon signed rank differences between the sides of the UCLP participants

Positive differences occurred when the speed of the unaffected side had a greater speed than the cleft side (23 times). The negative differences occurred when the speed of cleft side was greater than the non cleft side (8 times). The asymmetry showed that more participants had greater speed on the unaffected side.

11. Control group Participants

Table 13 - Descriptive characteristics for the speed of landmarks to reach maximum smile

Landmark	**Mean (mm/s)**	**Std Dev (mm/s)**	**Median (mm/s)**
Left Side Cheilion	63.58	38.72	53.91
Right Side Cheilion	69.76	49.6	58.36
Left Side Philtrum	22.7	10.02	19.32
Right Side Philtrum	20.43	9.13	20.24
Left Lower Lip	39.08	22.31	28.46
Right Lower Lip	40.36	21.56	29.54

i. Summary

The right side had higher mean values and greater variability for cheilion and lower lip measurements, while the philtrum measurements were similar between sides, with the left side being larger on average. The distributions were generally right-skewed.

ii. Normality tests for the control group intrasubject comparison

Cheilion and lower lip landmarks on both sides showed significant deviations from normality ($p < 0.002$) and a Wilcoxon signed rank test was used for comparison. The philtrum landmarks followed a normal distribution ($p = 0.15$ left and $p = 0.29$ right), so a paired t test was used for analysis.

Intrasubject Speed comparison

I. Comparing the Speed of Cheilion landmarks on the left and right sides in an unaffected individual

The right cheilion had a higher median speed (58.36mm/s) than the left side (53.91mm/s), with a greater variability (Std Dev: 49.6 vs. 38.72) and a wider range. Both sides were skewed to the right (1.67 and 1.66).

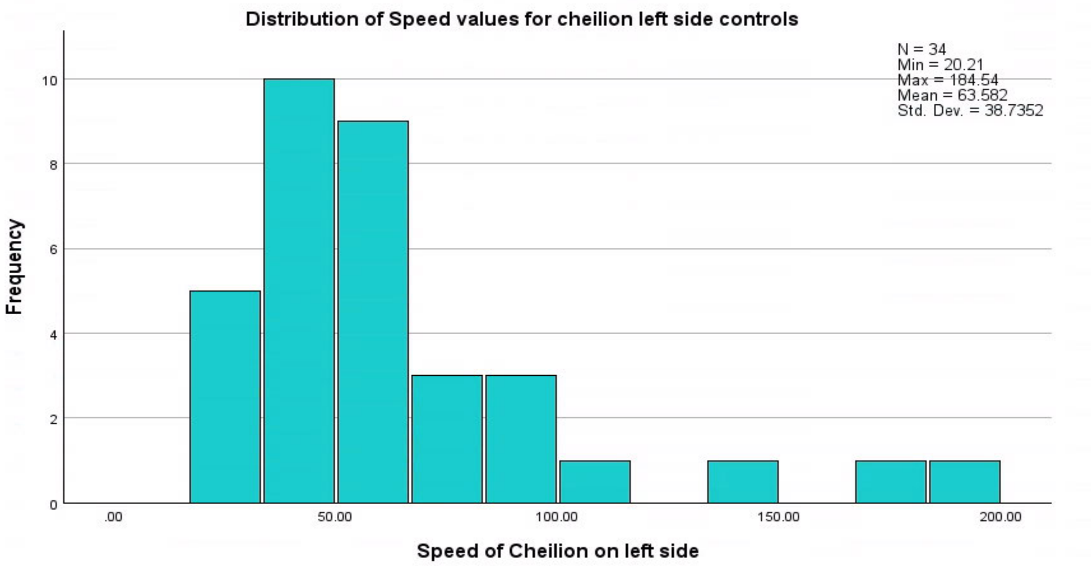

Figure 54 - Distribution of the cheilion landmark speeds for the left side of the control group

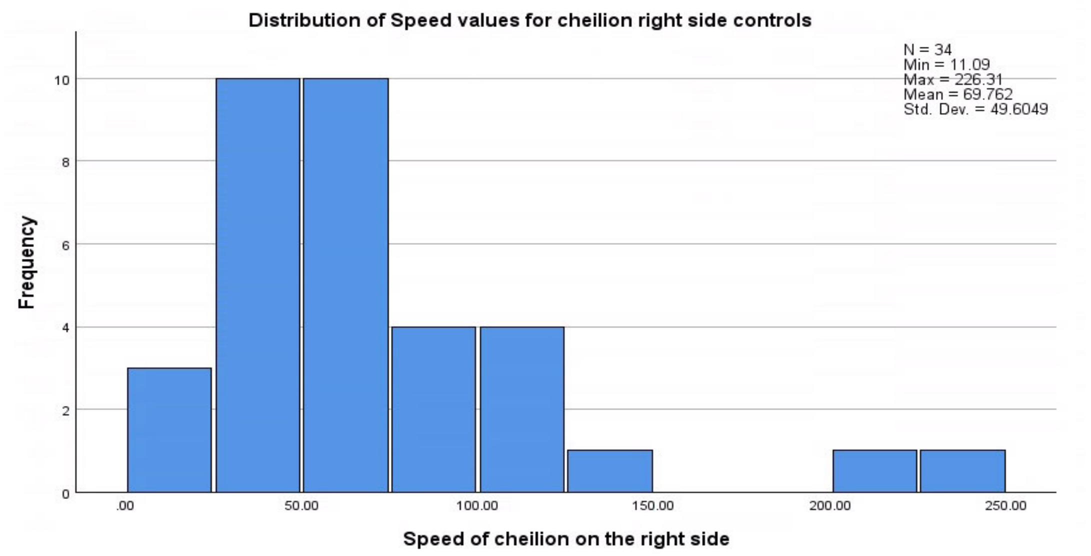

Figure 55 - Distribution of the cheilion landmark speeds for the right side of the control group

II. Comparing the Speed of philtrum landmarks on the left and right sides in an unaffected individual

The speed for the left philtrum had a smaller median (19.32mm/s) than the right side (20.43mm/s), with a similar variability (Std Dev: 10.02 vs. 9.13). Both sides had a relatively symmetric distribution.

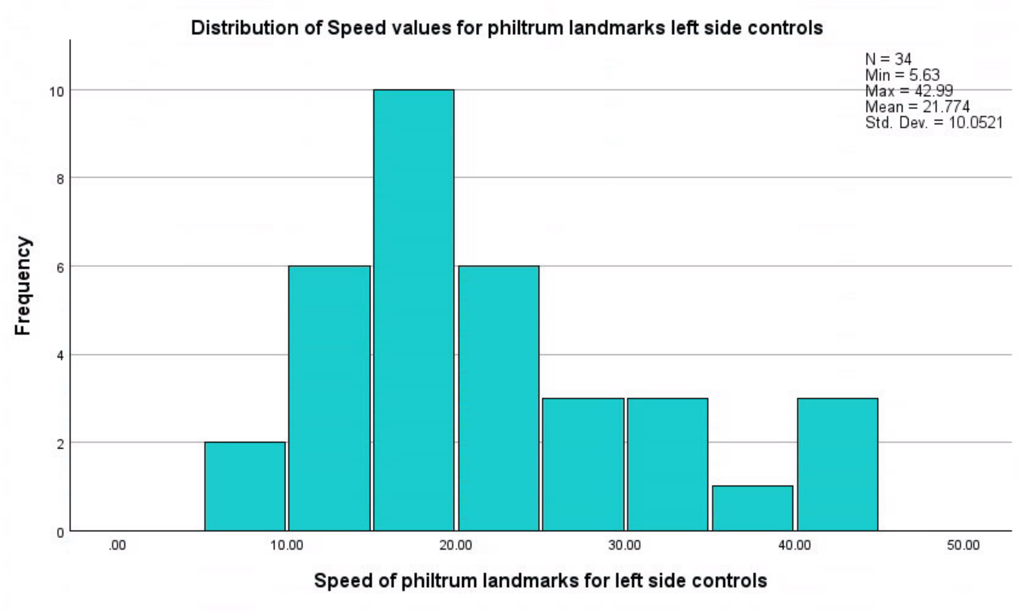

Figure 56 - Distribution of the Philtrum landmark speeds for the left side of the control group

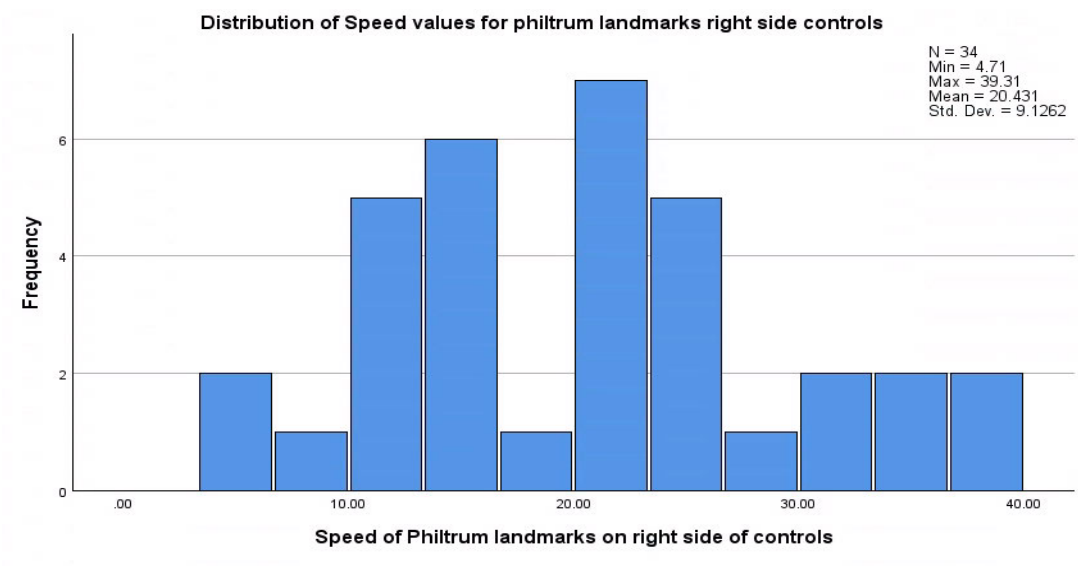

Figure 57 - Distribution of the Philtrum landmark speeds for the right side of the control group

III. Comparing the Speed of lower lip landmarks on the left and right sides in an unaffected individual

Mean speeds (right 40.36mm/s, left 39.08mm/s) were markedly higher than the median speeds (right 29.54mm/s, left 28.46mm/s) for lower lip landmarks. The median values were a better representation of the data spread due to right skewed distribution (skewness: 0.94 and 1.47). The speeds were similar on the right and left sides and both sides had similar variability (Std Dev: 21.56 vs. 22.31) but there was a wider range on the left side (right 78.6 vs. left 92.8).

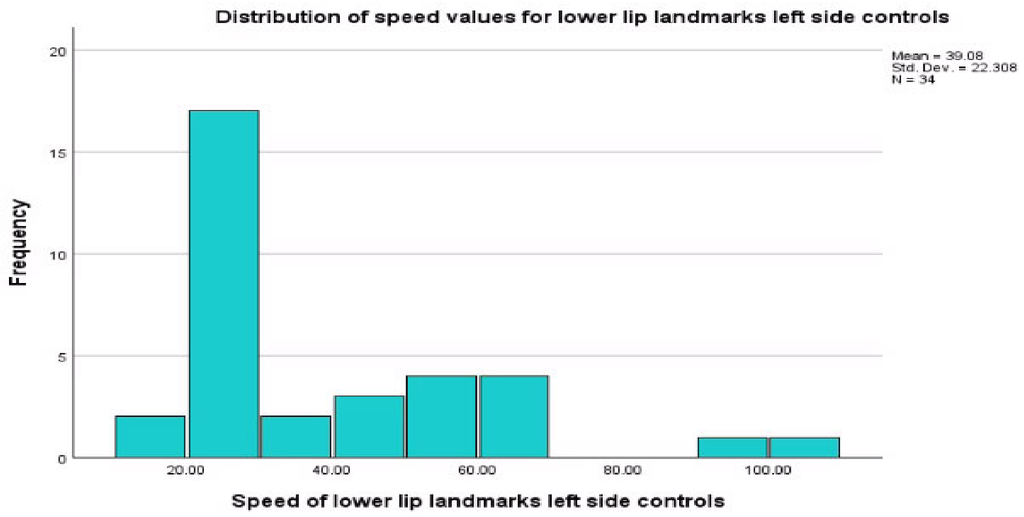

Figure 58 - Distribution of the lower lip landmark speeds for the left side of the control group

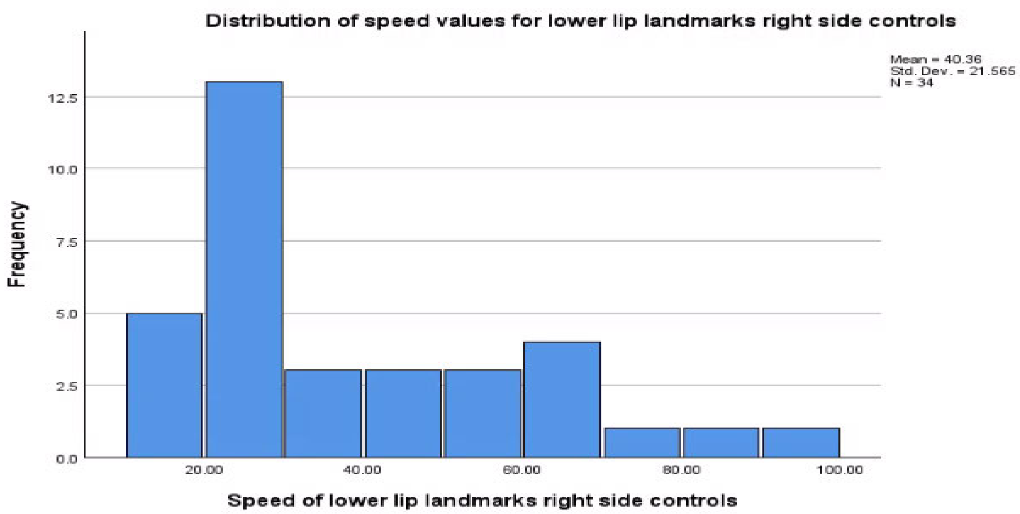

Figure 59 - Distribution of the lower lip landmark speeds for the right side of the control group

12. Statistical analysis for Control intrasubject Speed comparison

A paired t test was carried out to establish if there was a statistically significant difference between left and right philtrum landmarks in the control group and a Wilcoxon signed rank test was used to compare the paired landmarks for cheilion and lower lip landmarks, as they were comprised of non parametric values.

Table 14 - T test group statistics to compare the intrasubject philtrum landmarks

	Group	**Mean (mm/s)**	**Std deviation (mm/s)**	**P value**
Philtrum	Left side Control group	21.77	10.05	0.29
	Right side Control group	20.43	9.13	

i. T test Results interpretation

Both right and left philtrum landmarks had similar means (left 21.77mm/s, right 20.43mm/s) but the left side had higher variability (SD 10.05) than the right (9.13). There was a strong correlation ($p<0.001$) between left and right philtrum speeds but there was no statistically significant difference between the philtrum speeds ($p=0.29$).

Table 15 - Wilcoxon Signed Ranks Test for Cheilion and lower lip landmarks

Intrasubject paired landmark	**P value**
Cheilion left v right control group	0.34
Lower lip left v lower lip right control group	0.87

ii. Wilcoxon Signed Rank test Results interpretation

When comparing the cheilion speeds, the left (63.58mm/s) and right (69.76mm/s), there was no statistical significance (P= 0.34). The lower lip speed was similar on both sides, left 39.08mm/s and right 40.36mm/s, with no significant difference (p=0.87).

Based on these findings, for a healthy non affected individual, there should be no discernible difference between the speed of the lower lip, cheilion and philtrum on opposing sides of the mouth within an individual.

13. Comparing the Speed to reach maximum smile for UCLP and control subjects

During analysis the landmarks (cheilion, philtrum and lower lip landmarks) on the cleft affected side (left side of the UCLP group) were compared with the left side landmarks of the control group.

Table 16 - Comparing speed for UCLP cleft side and control left side landmarks

Landmark	**Mean (mm/s)**	**Std Dev (mm/s)**	**Median (mm/s)**	**Min (mm/s)**	**Max (mm/s)**
Cleft Side Cheilion	28.69	14.14	28.6	5.55	62
Left Cheilion control	63.58	38.72	53.91	20.21	184.54
Cleft Side Philtrum	7.24	4.52	5.98	0.83	19.94
Left Philtrum control	22.7	10.02	19.32	5.63	42.99
Cleft Lower Lip	20.98	11.72	20.66	1.66	47.55
Left Lower Lip control	39.08	22.31	28.46	13.09	105.89

i. Summary

There were large differences in speed for the cleft side of the UCLP group and the left side of the control group. Cheilion and philtrum landmarks on the cleft side showed smaller speeds than the control group, with narrower ranges and less variability. Speeds were slower for the lower lip on the cleft side (20.98mm/s) than the control group (39.08mm/s), with a smaller range and less variability. There were distinct differences in lip speed between individuals with UCLP and unaffected individuals.

ii. Tests of Normality for the cleft side UCLP vs left side control group

The cheilion landmarks on the cleft side of the UCLP group followed a normal distribution (Shapiro-Wilk $p = 0.56$). However the cheilions on the left side of the control group did not follow a normal distribution ($p < 0.001$). Philtrum landmarks on the cleft side of the UCLP group significantly deviated from normal ($p=0.013$) but the control values on left side followed a normal distribution ($p=0.29$). The lower lip landmarks on the cleft side followed a normal distribution ($p=0.14$) but the left side of the control group did not follow normal distribution ($p<0.001$). For each pairing, one set of values was not normally distributed so a Mann Whitney U test was used for analysis, to establish if there was a difference between the groups.

I. Comparing the Speed of Cheilion landmarks on the UCLP cleft side vs control left sides

The cheilion landmark on the cleft side had a much lower mean speed (28.69mm/s) than the control group left side (63.58mm/s). The UCLP group had a smaller standard deviation (14.14 vs. 38.72), indicating less variability, and the control group had a much broader range (164.33 vs. 56.45). The control group was more asymmetrical than the cleft group.

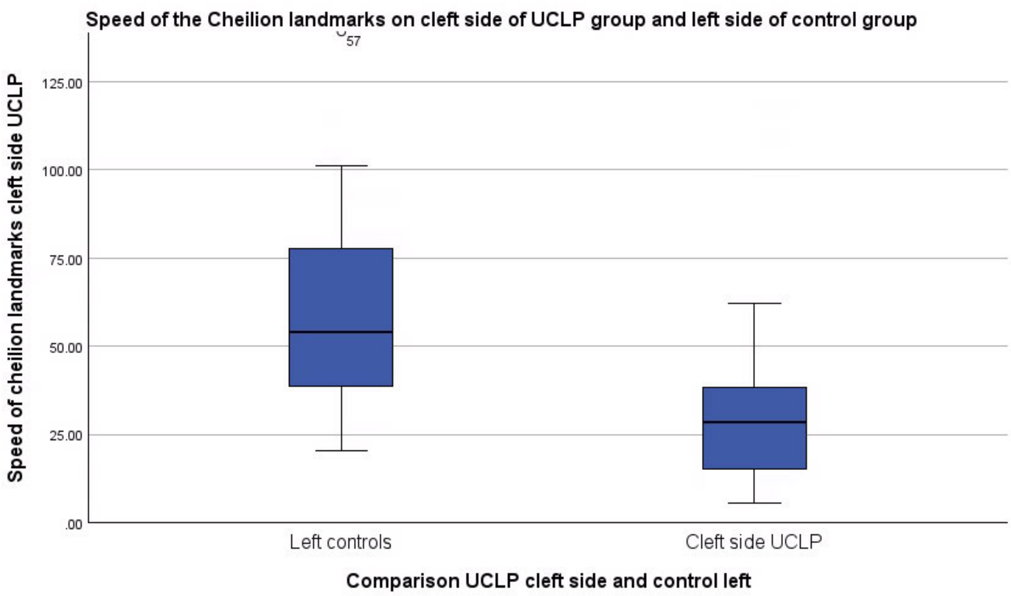

Figure 60 - Box plot graph comparing the speed of cheilion landmarks Cleft side (left) in UCLP group and unaffected control group left side

II. Comparing the Speed of Philtrum landmarks on the UCLP cleft side vs control left sides

Speed of the philtrum on the cleft side had a lower mean (7.24mm/s) than the left side of the control group (mean 22.7mm/s). The cleft group also had a narrower range (19.11 vs. 37.36) and a lower median (5.98 vs. 19.32) than the control group. The cleft group had positively skewed values which clustered at the lower end.

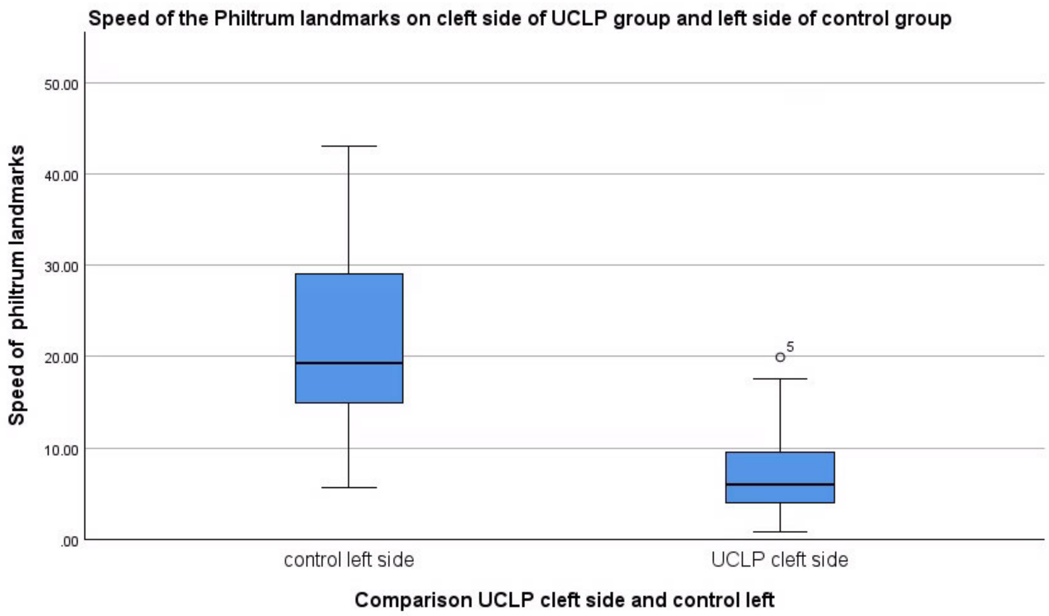

Figure 61 - Box plot graph comparing the speed of philtrum landmarks Cleft side (left) in UCLP group and unaffected control group left side

III. Comparing the Speed of Lower lip landmarks on the UCLP cleft side vs control left sides

Speed of the lower lip landmarks on the cleft side was lower (mean 20.98mm/s) than the control group left side (39.08mm/s). There was a narrower range in the cleft group (45.89 vs. 92.8), suggesting less variability.

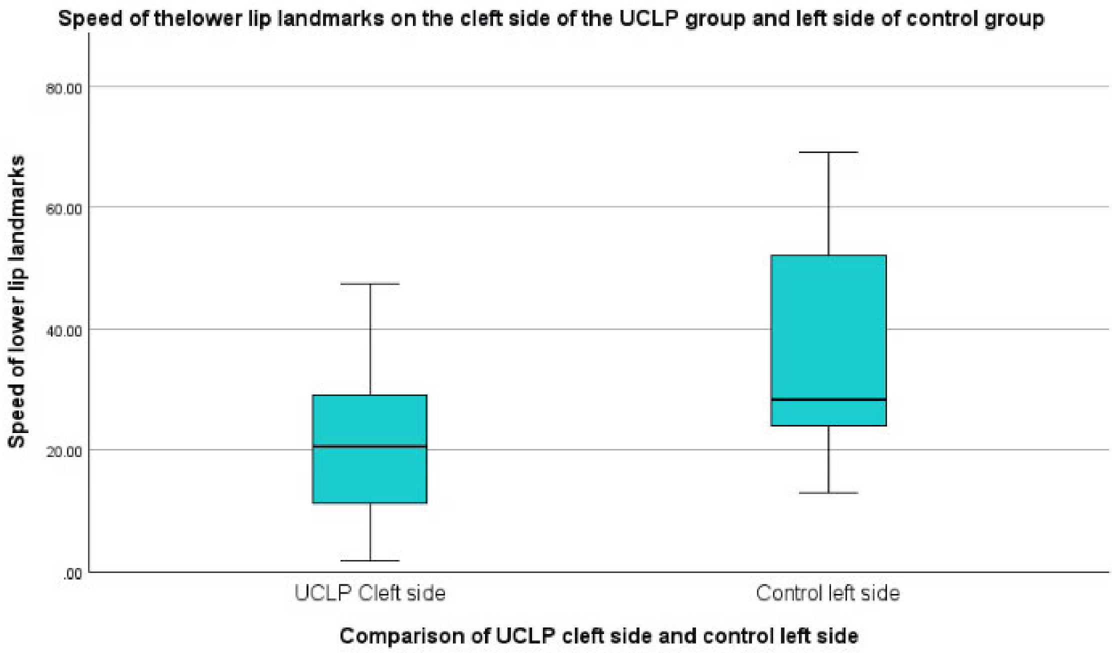

Figure 62 - Box plot graph comparing the speed of lower lip landmarks Cleft side (left) in UCLP group and unaffected control group left side

14. Statistical analysis comparing speed on the Cleft side with control group left side

Each pairing had one data set not normally distributed, non parametric testing (Mann Whitney U) was used for statistical analysis.

Table 17 - Mann Whitney U test comparing the speed of paired landmarks between the two groups

Landmarks	**Side/group**	**P value**
Cheilion	Cleft side/ UCLP	<0.001
	Left side/ control	
Philtrum	Cleft side/ UCLP	<0.001
	Left side/ control	
Lower lip	Cleft side/ UCLP	<0.001
	Left side/ control	

i. Mann Whitney U Results interpretation:

The Cheilion landmark on the cleft side of the UCLP group had a significantly lower mean rank (21.42mm/s) than the Control group (43.56mm/s), which was statistically significant ($p < 0.001$). A similar pattern was seen for philtrum landmarks, which had statistically significant differences ($p < 0.001$) and a lower mean rank (18.45mm/s) in the UCLP group, than the control group (46.26mm/s). There was also statistically significant differences ($p<0.001$) for the lower lip, where the cleft side had a lower mean rank (23.68mm/s) than the control group (41.5mm/s).

15. Comparison of the speed of the landmarks on the unaffected side of the UCLP group and the paired landmarks on the right side of the control group

To establish if the presence of a cleft only provides a limitation to the affected side or if the difference is also reflected to the contralateral side, the unaffected side of the UCLP group (due to mirroring, the right side), was also compared to the right side of an unaffected individual.

Table 18- Comparing speed for the unaffected side in UCLP group and control right side landmarks

Landmark	**Mean (mm/s)**	**Std Dev (mm/s)**	**Median (mm/s)**	**Min (mm/s)**	**Max (mm/s)**
Non Cleft Side Cheilion	32.05	16.25	31.11	3.64	78.66
Right Side Cheilion	69.76	49.6	58.36	11.09	226.31
Non Cleft Side Philtrum	8.22	4.79	7.65	0.77	22.04
Right Side Philtrum	20.43	9.13	20.24	4.71	39.21
Non Cleft Lower Lip	19.22	10.95	20.2	2.46	42.6
Right Lower Lip	40.36	21.56	29.54	16.45	95.08

i. Summary

For all landmarks, there were noticeable differences between the non-cleft side and the right side. The cheilion, philtrum and lower lip landmarks in the control group had greater speeds and more variability. These differences highlight asymmetry in facial measurements between the two sides.

ii. Tests of Normality for the unaffected cleft side UCLP vs right side control group

The speed of cheilion landmarks on the non cleft side of the UCLP group were normally distributed (p=0.09) but the speeds for the right side of the control group deviated from normality ($p < 0.001$). Philtrum landmarks on the non cleft side of the UCLP group deviated from normality (p=0.03) but philtrum landmarks in the control group did not deviate from normal (p=0.29). The lower lip landmarks on the non cleft side, did not deviate from normal (p = 0.11) but the right side of the control group deviated significantly from normal (p = 0.002).

As each pairing had one value that deviates from normality, a Mann Whitney U test was used for statistical analysis.

I. Comparing the Speed of Cheilion landmarks on the UCLP non cleft side vs control right side

The speed of the cheilion on the non-Cleft Side has a mean of 32.05mm/s with a standard deviation of 16.25 and a range 75.02mm/s. The cheilion on the right side had a mean speed of 69.76mm/s with a standard deviation of 49.6 and a range 215.22mm/s.

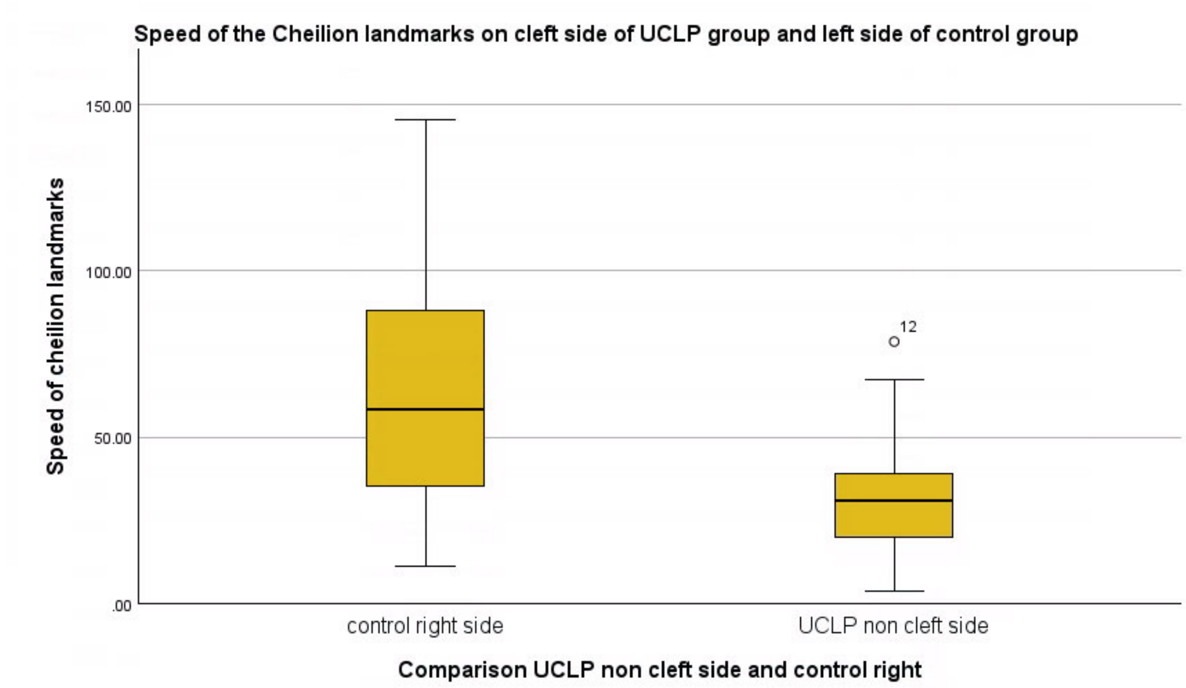

Figure 63 - Boxplot showing the difference in speed of the cheilion landmarks on the right side of the control participants and the non cleft side of the UCLP participants

II. Comparing the Speed of philtrum landmarks on the UCLP non cleft side vs control right side

The speed of the philtrum landmarks on the non-Cleft Side had a mean of 8.22mm/s with a standard deviation of 4.79 and a range of 21.27mm/s. The speed of the philtrum landmarks in the control group had a mean of 20.43mm/s with a standard deviation of 9.13 and a range of 34.6 mm/s.

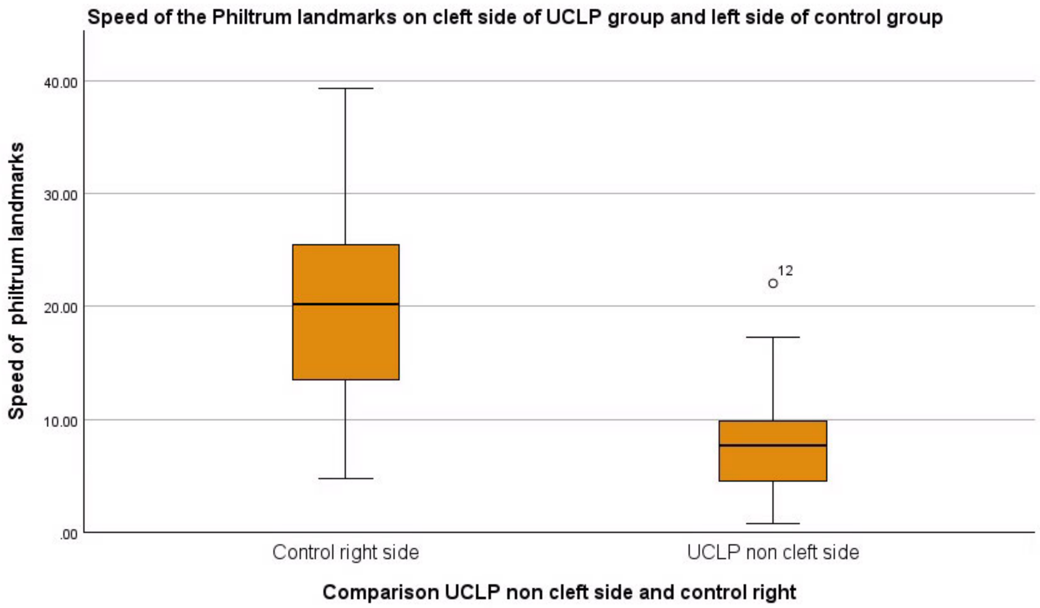

Figure 64 - Boxplot showing the difference in speed of the philtrum landmarks on the right side of the control participants and the non cleft side of the UCLP participants

III. Comparing the Speed of lower lip landmarks on the UCLP non cleft side vs control right side

The speed of the lower lip for the non-cleft side had a mean, 19.22mm/s with a standard deviation of 10.95 and ranges from 2.46-42.6. The mean for the control group was 6.69mm/s with a standard deviation of 5.41 and the range 0.95-22.14.

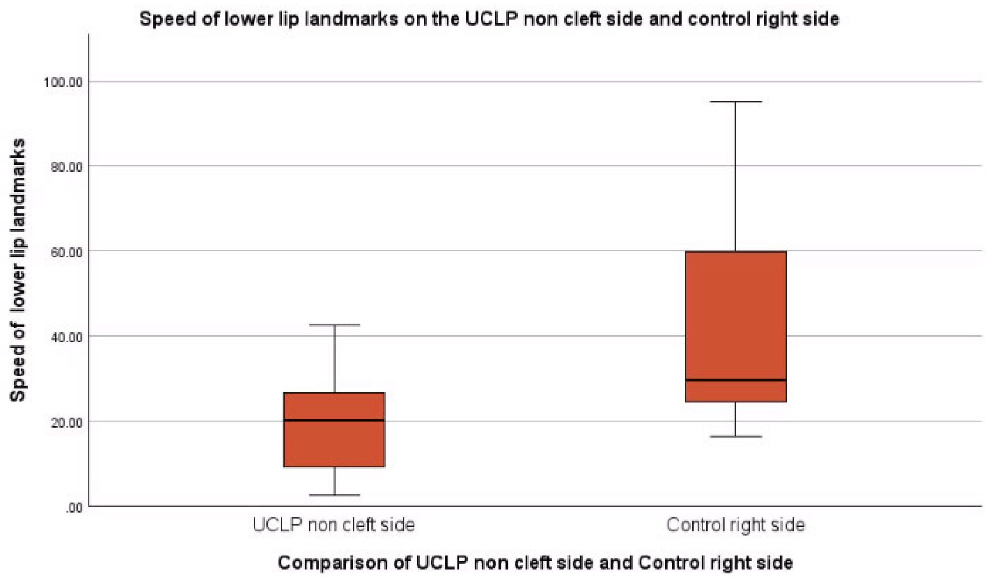

Figure 65 - Boxplot showing the difference in speed of the lower lip landmarks on the right side of the control participants and the non cleft side of the UCLP participants

16. Statistical analysis for comparison of speed on the non cleft side with right side in the control group

Table 19 - Mann Whitney U test for statistical comparison of the two groups

Landmarks	Side/group	P Value
Cheilion	Non cleft side/ UCLP	<0.001
	Right side/ control	
Philtrum	Non cleft side/ UCLP	<0.001
	Right side/ control	
Lower lip	Non cleft side/ UCLP	<0.001
	Right side/ control	

i. Mann Whitney U test Result Interpretation:

Comparing paired landmarks on the unaffected side of the UCLP participants and the right side of the control participants showed statistically significant speed differences for cheilion, philtrum and lower lip landmarks ($p<0.001$). Across all landmarks, the control group had consistently greater speeds than the UCLP group even though it was examining the unaffected side. In an individual with a cleft, even the unaffected side will have restriction or limitation in movement, affecting the facial dynamics.

17. Risk analysis

In order to establish if the presence of a cleft increases the chance of a subject having slower speeds during smiling, an odds risk ratio was carried out. Assessing if the left side was generally slower than the right side, and how often the presence of a cleft predisposed the subject to having a slower smile.

i. Findings

In the UCLP group the affected side (left) is more commonly slower at the cheilion (68% of cases) compared to only 52% of the control group. The control group shows a more balanced distribution for which side is slower (left 52% and right 48%). Looking at the philtrum landmarks, the cleft (left) side is regularly slower (81%) than the unaffected side. Compared to the control group, where the slower side is more evenly distributed (55% slower left vs. 45% slower right). However, for the lower lip, the cleft group is more likely to be slower on the non-cleft/right side (61%) than the affected side, the opposite finding than that for cheilion and philtrum landmarks. Again the control group has a balanced distribution for which will be slower (52% left side and 48% right side).

These results suggest the cleft group exhibit patterns of asymmetry, with the cleft side slower for cheilion and Philtrum landmarks, but the non affected side is slower for the Lower Lip.

Table 20 - Odds Risk Ratio

Landmark	**Odds Ratio (OR)**	**Risk Ratio (RR)**	**Interpretation**
Cheilion	1.87	1.28	Cleft affected side being slower is 28% more likely in the UCLP group
Philtrum	3.29	1.44	Cleft affected side being slower is 44% more likely in the UCLP group
Lower lip	0.56	0.73	Side affected by the cleft is less likely to be slower in UCLP group

ii. Risk Estimate:

For the Cheilion landmarks the odds ratio is 1.87, meaning the odds of the side affected by the cleft being slower are 87% higher in the UCLP group than the control group. The risk ratio (RR) of 1.28 shows the cleft affected side is 28% more likely to be slower in the UCLP group.

For the Philtrum landmarks the odds ratio is 3.29, where the odds of the side affected by the cleft being slower are more than three times higher in the UCLP group than the control group. There is a significantly increased chance that the cleft side will be slower than subjects in the control group, indicating a substantial asymmetry for the Philtrum. The risk ratio is 1.44, showing the side affected by the cleft is 44% more likely to be slower in the UCLP group.

Unlike the other landmarks, the lower lip on the cleft side is likely to be faster than the lower lip speed in an unaffected individual, the opposite trend. The odds ratio is 0.56, meaning the odds of the cleft side being slower are 44% lower than the left side of an unaffected individual. There is a 27% chance that the side affected by the cleft is faster in the UCLP group (risk ratio 0.73).

18. Summary of results

I. Expression duration

The UCLP group took longer (0.43secs) than the control group (0.17secs) to reach maximum smile and the relaxation phase also took longer in the UCLP group (0.38secs, control 0.18secs). The duration of the smile expression was longer in individuals with a cleft (2.02 secs) than the group of unaffected individuals (1.33 secs).

II. Intrasubject comparison of magnitude and speed for UCLP group

The cleft group had a statistically significant difference in comparison with the control group, regarding the magnitude and speed reached by the philtrum landmarks. The cleft side had a smaller magnitude (6.84mm) than the unaffected side (7.59mm). Although the same pattern was seen for cheilion landmarks of the cleft group, this did not reach statistical significance (cleft side 27.24mm and non cleft side 29.49mm). In contrast the magnitude of movement of the lower lip landmarks was greater on the side affected by the cleft (19.85mm) than the non affected side (18.04mmm) and this reached statistical significance. The asymmetry in movement noticed in the lower lip in the UCLP group is due to the distorted muscle dynamics which are secondary to the asymmetry of the upper lip muscles during the phases of the maximum smile. This could be due to less muscular development on the cleft side, causing weakness, less control, and tension, from scar tissue limiting upper lip movement causing the lower lip to compensate for the deficit.

The speed of the cheilion on the cleft side (28.69 mm/s) is lower than the non-cleft side (32.05 mm/s). This was not statistically significant but there was trend towards significance. For the lower lip landmarks the side of the cleft exhibited significantly greater speeds, the cleft side 20.98 mm/s and the non-cleft side 19.22 mm/s. There was a statistically significant difference between cleft and non-cleft sides for the philtrum landmarks, 7.24mm/s cleft side and 8.22mm/s on the non affected side. This measurable asymmetry in philtrum speeds between the two sides showed that the cleft side is significantly slower.

III. Intrasubject comparison of magnitude and speed for the control group

When comparing the magnitude of paired right and left landmarks within the individuals of the control group, there was no significant differences noted between the sides for any of the landmarks. Suggesting that in an individual not affected by a cleft, there should be no significant difference in magnitude between opposing sides.

Looking at the speed of the maximum smile in the control group, philtrum landmarks had similar speeds on left (21.77mm/s) and right sides (20.43mm/s), as did cheilion landmarks left (63.58mm/s) and right (69.76 mm/s) and lower lip (left 39.08mm/s) and right (40.36mm/s). Showing no statistically significant differences between the opposing sides for all landmarks. In a healthy non affected individual there should be no discernible difference for the speeds or magnitude of the lower lip, cheilion and philtrum landmarks within an individual.

IV. Comparison of magnitude and speed for UCLP group against a control group

When comparing the side affected by the cleft with a matched side of an unaffected individual, there are significant differences observed for the magnitude of the cheilion and philtrum landmarks. The cleft side had smaller magnitudes than the control group. There were also significant differences for the unaffected side in a UCLP subject and the matched side of an unaffected individual, which may indicate restriction in muscular activity on both sides regardless of which side has the cleft. For the lower lip landmarks the difference was smaller but the control group still showed a greater magnitude than the UCLP group.

When looking at the differences in speed between the two groups, there are statistically significant differences between the cleft side of the UCLP group and the left side of the control group for all landmarks; cheilion landmarks (cleft 28.69 mm/s and left 63.58mm/s), philtrum landmarks (cleft 7.24mm/s and left 21.77mm/s) and lower lip (cleft 20.98mm/s and left 39.08mm/s). Speed on the cleft side was significantly reduced when compared to the control group.

The speed of landmarks for the unaffected side of the UCLP cases was significantly lower than for the control cases. The control group had consistently faster lower lip movement (cheilion 69.76mm/s, philtrum 20.43mm/s and lower lip 40.36mm/s) than the UCLP group, even when looking at the unaffected side (cheilion 32.05 mm/s, philtrum 8.22mm/s and lower lip 19.22 mm/s). This shows that even the unaffected side of UCLP cases has some restriction / limitation in movement, which can affect the facial dynamics.

V. Odds risk ratio

In our study, the odds of the cleft side exhibiting reduced speeds for the movement of cheilion are 87% higher than the movement of the same point on the same side in the control group. There are three times increased odds that the philtrum on the cleft side would be slower in the UCLP group than the same side being slower in the control group, indicating a substantial asymmetry. Unlike the other landmarks, the lower lip is less likely to be slower on the side affected by the cleft than the control group. Having a cleft increases the likelihood of the subject experiencing a slower speed on the affected side for philtrum and cheilion landmark.

Chapter 4. Discussion and Conclusions

1. Discussion

The research questions to be answered, focused on quantifying any abnormalities or asymmetry relating to speed during maximum smile in surgically managed cleft cases and comparing the dynamics of facial movement during smiling in cleft cases with non-cleft controls. Looking at the dynamics of the expression including the timing, magnitude and directionality of the lip movement can allow assessment of the movement speed. Analysing the speed of the lips enables assessment of movement symmetry during facial animation that cannot be examined when analysing magnitude displacement alone.

This research found significant restriction in upper lip movement on the cleft side and reduced speed and magnitude of movement at the corner of the mouth on the cleft side. Interestingly the lower lip had greater magnitude and speed on the cleft side suggesting compensatory movement on this side. UCLP cases had more restriction in their upper lip magnitude and speed than unaffected individuals.

Movement of the face is due to the muscles contracting during each facial expression and so will be influenced by the orientation of the muscle fibres and their anatomical position. Scar tissue from the cleft of a lip, can affect movement of the upper lip or the mechanics of the repair may incorrectly approximate muscle fibre. Improving the standard of care for patients and ensuring adequate surgical outcomes for those entering the cleft pathway could improve patient function.

A small study of children under 15 years, looked at vector deviation during closed lip smiles in individuals with a cleft and healthy individuals, and found that even the healthy individuals demonstrate asymmetry during motion at oral commissures and the subnasal area. The cleft group had statistically significant differences for the oral commissures, upper lip, and lower lip regions during posed smile (Seaward et al., 2022). However this study was carried out in younger individuals and they had yet to mature fully. Four dimensional imaging can be used as an objective tool to assess facial soft tissue movements, monitor changes, track growth and capture time-based variation alongside the static features (Shujaat et al., 2014).

A difference in speed of landmarks within the individuals with a cleft and no difference in speed for individuals without a cleft shows a disparity exclusive to the affected group which may be recognised by the public. A significant difference in speed between the UCLP group and the unaffected group could be perceived by peers or the general public in social interactions. They may not consciously notice a slight delay but they may subconsciously note that something is different, or 'off' about a slower smile, even if they cannot pinpoint what the difference is. Being able to determine what stage during the smile expression is most affected by speed changes (the start of the expression, during maximum smile or during the relaxation phase) can help show the importance of 4D imaging as an assessment tool and also help determine the aetiology of the smile disparity.

2. Study design and subject selection

This study was a mainly retrospective case control study utilising quantitative methodology. A study from Mishima concluded that there was moderate intraindividual variability during smiling so a reproducible method would be useful (Mishima et al., 2009). They recommended a future study to compare lip motions in cleft lip and palate patients and normal individuals to assess dynamic differences between the two groups. The incidence of non syndromic cleft lip and palate subjects is low, with 1 in every 700 live births in the UK being diagnosed with a cleft and only 22% of these having a UCLP (CRANE, 2021). To ensure an adequately sized cohort of subjects for this study retrospective analysis was chosen. The control group was comprised of both subjects previously recruited and supplemental subjects which were prospectively recruited. The control group individuals that had been captured previously, were aged matched for this particular UCLP group and captured by the same operator as the UCLP group. Unfortunately there was not enough of these participants for at least a matched sample and to ensure we had the adequate sample size to ascertain if there is statistical significance between the groups. If an entirely new control group was recruited prospectively it may have reduced the potential for measurement bias within the control group, by ensuring one operator for the whole group. However, recruitment was slow and would have substantially increased the time and resource burden. Also by having one operator that captured images for both groups improved consistency, reduced variability and minimized observer bias between the two different groups.

When deciding which cleft diagnosis to choose as the subject group, syndromic cleft subjects were excluded as facial features linked to the syndrome could confound the results. Other features causing underlying asymmetry and muscles affected due to the syndrome may compromise the results making it harder to establish differences due to the cleft alone. A unilateral cleft lip and palate was chosen, as bilateral clefting is a symmetrical defect and would make quantification of disparity within the individual difficult, as there is no unaffected side for comparison. Having an unaffected side within the cleft subject meant it was possible to assess if the presence of a cleft caused any restriction on the unaffected side. The cleft side was mirrored in the UCLP group, so that it was present on the same side of the whole group, to enable comparison of the cleft subjects with the unaffected individuals. The 13-17 year old age group was chosen as it included patients pre, during and post pubertal growth spurt and so it includes changes seen due to growth and what patients may experience into adulthood. Surgical revision if required would be carried out between the ages of 16 and 20, and so by looking at this cohort, it can be used as an outcome measure to help establish if there is a need for lip revision.

I. Maximum smile

For this study the maximum smile was analysed, as it is reproducible, reliable and patients are generally capable of performing the action easily (Gattani et al., 2020) making it a good choice for comparing two groups. Spontaneous smile was not chosen to be assessed as it can vary greatly within the individual and between individuals making it less useful for comparisons, and so a posed maximum smile was chosen. Spontaneous smiles have also been found to have a longer duration during the onset, apex, and offset phases than posed smiles (Guo et al., 2018). So it was important to capture all the participant smiles in a standardised and reproducible manner. Previous studies have found greater asymmetry during maximum smile than a subject at rest (Al-Rudainy et al., 2019). Although only the maximum smile was assessed in this study, the subjects were directed to carry out four facial expressions during capture; cheek puff, maximum smile, lip purse, and grimace. These expressions could be looked at in a future study as there is now a matched case control group.

The frame selected for the maximum smile was the median frame as it could be objectively chosen for all individuals. The median frame is less influenced by faster or slower transitions at the beginning or end of the maximum smile movement. The median frame usually falls during the most stable phase of movement (the midpoint) without being swayed by transient variation in muscle activation creating a clear frame for analysis.

II. Speed of the smile

To study the speed of the maximum smile, an initial rest frame was selected for each individual by a single independent assessor. It was chosen as the frame before the movement of the lips commenced and the smile expression started. The other frame chosen was the median of maximum smile, as previously stated. The speed of the maximum smile was then calculated by looking at the magnitude and time taken for the lip landmarks to reach this frame. The magnitude was calculated by measuring the landmark displacement from the starting rest frame to the median frame of maximal smile. The duration was calculated as the time to reach the median frame of the maximum from the initial rest position. The speed (S) of each landmark was calculated by dividing the maximum landmark distance (d) by time (t). [speed=d/t]

3. Psychosocial Challenges

Various physiological and sociocultural factors contribute to the development of psychosocial issues among individuals with any form of facial anomaly in general. Self perception plays a pivotal role in influencing an individual's self esteem and psychological adjustment affected by cleft lip and palate anomaly. The parental influence can also contribute to the individuals' psychosocial perception, through their attitudes, expectations and degree of support (Bull and Rumset, 1988). The presence of residual facial asymmetry after surgical repair can affect the patients' self-esteem and negatively impact on their social interaction (Eckstein et al., 2011). The maximum smile was analysed, as smiling plays a vital role during our daily communication. The lips are often a focus of attention in social situations. The eyes and the mouth convey different information when conversing and an individual's tendency to look at the eyes or mouth of the other person can influence what information is processed (Viktorsson et al., 2023). Looking at the mouth region is strongly associated with visual speech information and how well an individual is understood by their peers.

Many children with cleft lip and palate are perceived to have a less attractive facial appearance or more speech difficulties than their peers. This can trigger teasing about their facial appearance (Hunt et al., 2005). There is often a social stigma for individuals with a cleft they can be negatively discriminated and labelled as different from normal. The negative response from others, actual or perceived, can adversely affect self-image (Turner et al., 1997). Physical attractiveness plays an important role in the development of self belief. Physical attractiveness plays a significant role in developing relationships during various stages of life, school, romantic relationships and work. Social acceptance often depends on one's physical look. These associations between physical beauty and social acceptability indicate the difficulties for cleft lip and palate affected individuals (Turner et al., 1997).

Individuals can experience communication problems related to their cleft lip and palate from a young age. Toddlers with cleft palate exhibit 'at-risk/delayed' development in the expressive language domain at 36 months (Neiman and Savage, 1997). They may have speech and language disorders, facial disfigurement, and hearing loss compounding potential communication problems. A high percentage of cleft children are underachievers and there is evidence of behavioural inhibition, decreased expectations by teachers and parents and speech defectiveness which can affect their self-esteem (Richman and Millard, 1997).

Frustration from the limitations faced can build up over a period of time because of the societal problems faced and anxiety and depression are twice as prevalent in adults with cleft lip and palate compared with normal controls (Ramstad et al., 1995). The psychological problems were strongly associated with concerns about appearance, dentition, speech, and a desire for further treatment.

Evaluation of lip motion in individuals with cleft lip and palate shows continuous changes in lip shape which needs to be analysed along a time axis, to see the extent of the change and allow us to evaluate the naturalness and harmony of the lip motion (Mishima et al., 2009). Despite surgical correction facial asymmetry still persists from the scar tissue, muscular pull and relatively thinner tissue at the surgical site (Gattani et al., 2020). Particularly in today's society where appearance is considered as gateway to social acceptance and even minor asymmetries on the face can be associated with negative social responses such as unwarranted staring and isolation at school among peers (Bradbury, 2012). This may lead to shame anxiety depression and can lead to a lack of ego development in these children. Facial asymmetry gradually increases as patients perform maximum smile and decreases toward final resting state (Gattani et al., 2020).

Faces with excellent symmetry received significantly higher ratings of attractiveness, health, and certain personality attributes (i.e. sociable, intelligent, lively, self-confident, balanced) and faces with limited symmetry were rated as being more anxious (Fink et al., 2006). It has been found that symmetrical people of both sexes are reported to have greater emotional and psychological health, and symmetrical men were also found to have greater physiological health (Shackleford and Larsen, 1997, Perrett et al., 1998). This highlights how significant any residual deformity following cleft repair is for an individual's wellbeing. Symmetrical men and women have been rated as being more physically attractive than asymmetric individuals (Thornhill and Gangestad, 1999). This can have negative impact on relationships, being able to find a partner and self esteem for subjects who have not had a favourable surgical outcome. Any way we can limit the asymmetry in these individuals will hopefully improve their quality of life and prevent differentiation from their peers.

I. Surgical Revision

Surgical revision can be an option to manage issues related to disfigurement, as it addresses both physical and psychological issues. Surgery can result in increased self esteem, self confidence and satisfaction with appearance (Eckstein et al., 2011). Improving the aesthetic appearance in adolescents can encourage healthy psychological development. However if an individual or parent has unrealistic, high expectations post surgery this could lead to dissatisfaction and may further negatively impact an individual's self satisfaction (Sousa et al., 2009). Understanding the disparity between the individuals with a cleft lip and palate and the non affected individuals for the speed of their smile can help surgeons refine repair technique by clarifying which muscles are affected, based on the phase of the smile.

Identifying the extent of psychosocial factors related to cleft lip and palate can be very challenging. More research is required to develop a tool whereby bias in self reporting could be avoided and improved understanding of the extent of patient challenges could help minimise psychological problems. Assessing if the reduced self esteem and psychological problems are expressed clinically through changes to the facial expressions was beyond the scope of this study.

4. Muscular repair challenges

A histological sign of a cleft lip and palate is the inappropriate orientation and abnormal insertion of the muscles, particularly levator veli palatini muscle and the orbicularis oris muscle. Even patients with less severe forms of clefting, such as microform cleft lip or submucosal cleft palate still experience this muscle formation abnormality. Abnormal development of the muscles around the cleft can cause muscular imbalance, due to over stretching, weakness or improper alignment. This can then affect both contraction and relaxation phases of the smile. For functional and morphological repair of cleft lip and / or palate, there needs to be optimum reconstruction of these muscular diastases (Kim et al., 2021).

The results show that the surgically managed UCLP cases had more restricted upper and lower lip movement than the control group, which manifested as reduced magnitude and speed. They highlight the effect abnormal development during the embryological stage has. The medial nasal prominence and maxillary prominence in a cleft lip fail to fuse and when the palatal shelves don't fuse at the midline a cleft palate is formed. This causes discontinuity and mal-insertion of the peri-oral muscles, which affects the mechanics of facial movements (Hallac et al., 2017). Restriction can also be a consequence of scarring secondary to the surgical procedure. Scar tissue can contract and pull on underlying tissues distorting facial features and scarring can lead to adhesions, muscle weakness and asymmetry which affects the range of motion and magnitude of facial expressions in a unilateral cleft (McKay, 2014).

Looking within the individuals, the cleft subjects had more restricted movement at the philtrum on the cleft side than the non cleft side. However the non cleft individuals had similar speed and magnitudes for the upper lip on the right and left sides. For the lower lip it was the non cleft side that had less movement when compared to the cleft side but again there was similar movement on both sides of the lower lip in the unaffected individuals.

There are a number of muscles which insert at the oral commissure (cheilion). These muscles can be divided into the upward muscle group; levator anguli oris which pulls the cheilion straight up and the zygomaticus major which pulls the cheilion upwards, outwards and backwards and is a dominant muscle at the beginning of the smile expression. The outward muscle group comprised of the buccinator and risorius stretches the lips and pulls the commissure laterally and backwards and the downward muscle group, which mainly consists of the depressor anguli oris depressing and laterally displacing the cheilion (Sun et al., 2022). The perioral group of muscles is active during maximum smile. The superficial orbicularis oris muscle fibres can be divided into a nasal bundle (upper) and nasolabial bundle (lower).

I. Onset

Muscles which insert at the cupid's bow are the zygomaticus minor, levator labii superioris and levator labii superiors alaeque nasi. They act on the cupid's bow working to raise the upper lip by elevating each side upward and outward. The onset phase of the smile expression starts with movement of the upper lip towards the nasolabial fold by contraction of levator muscles; levator labii superioris and the levator labii superioris alaeque nasi. These muscles have complex anatomy and an intimate and intricate relationship with the facial alar crease, the nasal vestibule and the orbicularis oris. The levator labii superioris originates from below the infraorbital foramen and divides in two, attaching at the alar cartilage and into the muscles of the upper lip. There is also an extension of the muscle which originates from the malar process on the zygomatic bone and inserts near the cheilion of the mouth. The levator labii superioris alaeque nasi is lateral to the transverse nasalis muscle (Hur et al., 2010). Due to the complex interaction between these muscles and the lips, it is not surprising that poor approximation or unsatisfactory rotation of these muscles during the surgical repair could contribute to asymmetric lip movement during maximum smile and the disparity between affected and unaffected individuals.

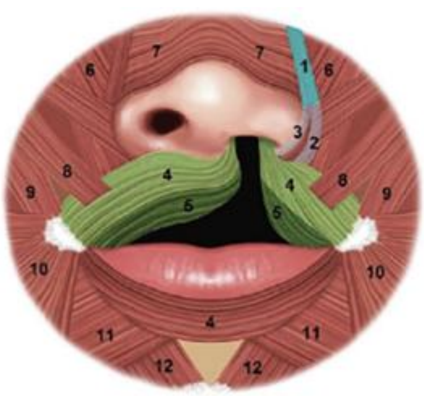

Figure 66 - Muscles affected in UCLP and requiring repair: 1,2,3. LLSAN, 4&5. orbicularis oris, 6. levator labii superioris, 7. nasalis, 8&9. zygomaticus minor & major, 10. depressor anguli oris, 11. depressor labii inferioris, 12. mentalis (With kind permissions BDJ (Houkes et al., 2023))

II. Maximum smile/ Apex

The zygomaticus major, zygomaticus minor and the risorius muscles are the main muscles contracted during the maximum smile expression. However some of these muscles aren't directly affected during cleft lip repair but they insert alongside muscles that are. Movement limitation of the zygomaticus major muscles are likely due to the scarring of the adjacent muscles. The zygomatic major muscle originates from the lateral surface of the zygomatic bone and it inserts at the corner of the mouth by blending with the levator anguli oris muscle, the orbicularis oris muscle and deeper muscular structures (Moore et al.). The Zygomaticus major pulls the cheilion up and out and the philtrum up during contraction. If someone has a dominant levator anguli oris then the cheilion moves in a more superior direction due to powerful elevation. The Zygomaticus minor muscle can be incomplete or malformed during the failed embryonic fusion of the lip. It originates from the zygomatic bone, lateral to the levator labii superioris muscle, and inserts directly into the outer part of the upper lip, blending distally with levator labii superioris muscle. If this muscle is affected, it can affect the elevation of the upper lip during the maximum smile.

The superficial orbicularis oris muscle fibres are divided into a nasal bundle (upper) and nasolabial (lower) bundle. The superficial fibres originate from other muscles of facial expression at a fibromuscular mass, the modiolus, depressor anguli oris, zygomaticus major and minor, levator labii superioris and levator labii superioris alaeque nasi (Nicolau, 1983). They insert in the skin and the decussation of fibres results in the formation of the philtral columns. A lack of insertion at the midline causes the philtral depression. The deep fibres of the orbicularis oris muscle originate from the alveolar processes of the maxilla and mandible, near the midline. These deep fibres insert into the skin and mucosa of the lips, blending with other fibres of the orbicularis oris and fibres of buccinator and levator anguli oris (Moore et al.). The deep fibres act like a sphincter around the mouth helping to close the mouth tightly and control fine movements.

The risorius is primarily responsible for pulling the corners of the mouth laterally during maximum smile. Although the risorius is not directly affected in a cleft of the lip, it originates from the zygomatic arch, fascia over the parotid gland and the masseter and inserts at the modiolus, located at the corner of the mouth. Clefting may interfere with the normal action of this muscle if the other muscles are not properly aligned, causing weakness or displacement of fibres. If the muscles isn't properly attached it can cause difficulties during smiling. So if there are asymmetry or restrictions noted during this phase of the smile, revision surgery should ensure correct approximation of the muscles fibres at the insertions (Drake et al.).

III. Offset

During the offset phase of the smile, the zygomatic major and minor, risorius, orbicularis oris and levator muscles relax to bring the upper lip back to rest. The restriction seen for the UCLP participants causing a longer time period to reach rest is due to muscles being poorly approximated and holding tension prior to reaching the rest position, which slows down the transition from the stretched muscles to the relaxed state (Gattani et al., 2020). The zygomaticus major plays the most significant role during the offset as it returns the cheilions to the neutral position. During relaxation in an individual with a cleft, the zygomaticus major and levator muscles can remain slightly elevated due to incomplete or altered muscular function which causes a delay in reaching the final rest position and can result in a residual asymmetry. The effect of the cleft on the orbicularis oris muscle can mean that the muscle doesn't relax fully leaving tension in the lips and delaying the lips from returning to the neutral/rest position.

IV. Lower lip

The usual dynamics noted for the landmarks of the lower lip in the UCLP group, are secondary to the asymmetry of the upper lip. The lower lip has to compensate for the restricted movement of the upper lip on the affected side, to overcome the limited stretch of the muscles. This was evident in these results with faster speeds and greater magnitudes noted on the cleft side than the non cleft side, whereas no difference was seen between sides in individuals without a cleft. The depressor labii inferioris muscle helps to depress and evert the lower lip exposing the lower teeth when smiling, acting as an antagonist of the orbicularis oris muscle. It originates from the mandible near the mental foramen and inserts into the skin and submucosa of the lower lip, fusing with the orbicularis oris muscle, which we know is affected during a cleft of the lip.

To reduce asymmetry during maximum smile and to restore normal speed and function of both upper and lower lips, microscopic repair of the levator muscular bundles in particular, are important to allow the upper lip to mobilise in a more balanced manner and ensuring adequate approximation of orbicularis muscle fibres can help with the lower lip movement (Gattani et al., 2020).

V. How muscular position affects the speed

Assessing the speed of the maximum smile in UCLP adolescent patients hasn't previously been assessed, and by comparing them to a group of unaffected age matched individuals, this can give a true insight into some of the subtle challenges these subjects experience day to day. This method can be used as an outcome measure, determining if there are residual discrepancies between the cleft and non cleft side of an individual related to the speed of the smile and if there is a lag for one side to reach maximum expression. It also highlights the effect that the scarring and surgical repair can have on not only the cleft side but also the contralateral side, as this side also exhibited slower speeds than unaffected individuals. By analysing the various phases of the smile expression, it became possible to determine the point at which dysmorphology was most apparent, to aid identification of the affected muscles, which can help refine and focus surgical revision procedures.

Seaward studied vector magnitude for a cohort of children and found that a control group had no statistically significant differences between the left and right during the smile expression but that these individuals with no craniofacial diagnosis did demonstrate some dynamic asymmetry during smiling. In the same study, the oral commissure on the cleft side of the UCLP group displaced less than the non cleft side. However this difference was not statistically significant during open lip smile (Seaward et al., 2022). This study also found no statistically significant difference between opposing sides for the speed of the cheilion landmarks but there was a noticeable difference for the philtrum landmarks. Disruption of the orbicularis oris muscle from the cleft may account for the fact there was no significant speed asymmetry seen within the individuals for all the landmarks. Although the scar is located on the cleft side, anomaly in the shape and direction of this muscle occurs on both sides of the cleft. So it is not accurate to say that the side not affected by the cleft is normal in orientation or function, which is why it is beneficial to compare to non affected individuals.

As the philtrum landmarks are near the midline, they should move vertically with a similar speed and magnitude, if bilateral muscle strength is equal. If there is variation in the two sides then the muscular force on the side of greater speed and magnitude is stronger. In theory the cheilion should be less affected than the philtrum as it is further from the midline and the area affected by the cleft, which was a similar pattern noted in this study. Restoration of complex muscular function during reconstruction is important so that the muscle fibres around the commissure and Cupid's bow are correctly replaced. However, when considering if revision surgery is required, this will be patient specific. As the individual grows they may experience limited movement in the muscles on the side of the cleft, or conversely they may note hyperactivity of muscles on the non affected side as a compensatory reaction. There can be different aims of revision surgery: to improve muscle fibre orientation, reduce scar tissue on the side of the cleft, or weaken/reduce activity of certain muscles on the non affected side. This can help to improve dynamic symmetry (Sun et al., 2022). Effectiveness of surgical repair may vary and muscle retraining by either speech therapy or physical therapy may also be required to restore muscular function for facial expressions.

Reduced speed or a delay in muscle activation can indicate persistent muscular impairment, which can signal the need for revision surgery. The exact threshold for surgical revision based on expression speed alone is not well established and depends on individual patient assessments (Dong et al., 2018). However this study will hopefully give some guidance on what normal speeds should be and if a patient is experiencing a worse outcome than other people with a similar diagnosis. There is some evidence suggesting that physiotherapy and targeted rehabilitation could improve muscle strength, coordination, and expression speed, in patients recovering from facial surgery or those with congenital or acquired facial dysmorphology. Physiotherapy can enhance expression speed by improving neuromuscular control and response. A study found that physiotherapy, neuromuscular retraining and electrical stimulation can enhance muscle function and improve facial symmetry and expression. This seems to have better outcomes when targeted during early growth phases (Glover, 2020). For the delayed/ limited facial expression exhibited by the individuals with a UCLP, physiotherapy based interventions could help support surgical management, by addressing surgical scarring and also any muscle weakness following the surgical repair.

VI. How scarring affects muscle function

Scar tissue is part of the healing process. It is more prevalent when the muscular tissue isn't sufficiently approximated at the cleft site and the skin is under tension. This scar tissue has no muscle fibres, which can then restrict the movement of the lips. The upper lip shifts mediolaterally towards scar tissue on the cleft side (Al-Rudainy et al., 2018) due to incomplete approximation of orbicularis oris muscle fibres, during the lip repair. Reduced magnitude of movement of the cheilion on the cleft side can be as a result of inadequate rotation of orbicularis oris muscle during the primary surgery. The orbicularis oris is comprised of superficial muscle fibres which are involved in retraction. They pass in an oblique direction before merging with the muscles of facial expression. The deep muscle fibres act as a constrictor and extend horizontally from cheilion across both sides. The superficial bundles of the orbicularis oris intersect at the midline of the lip and the insertion of these bundles at each side of the lip create the philtral ridges, no muscles insert at the philtral dimple itself. The scar tissue can also affect the flexibility and function of the zygomatic major and minor muscles, limiting their ability to produce a symmetrical smile.

When asymmetry is noticed during maximum smile it is generally due to impaired function of orbicularis oris and levator lateral alaeque nasi muscles. This can occur because of two reasons; scarring causing mechanical limitations during maximum movement and the altered anatomical position of muscles can reduce the force of the perioral muscles on the upper lip. During maximum smile, a reduction in magnitude of the upper lip is due to reduced force capacity of perioral lifting muscles which act on the lip directly. The scar tissue also causes low elasticity of the upper lip affecting the symmetry and speed of the smile. If there are problems with the normal function of the Levator Labii Superioris they will have difficulty raising the upper lip symmetrically, impacting aesthetics and their ability to smile/ form other facial expressions.

5. Limitations of the study

Some limitations of this project may be sample size. There was at least a 1:1 matched control group but there could have been more robust findings with a larger control group. The subject groups consisted of 31 and 34 participants, which are relatively small numbers but due to the prevalence of UCLP within our population, this was a significant sample and larger than many studies that use the same 4D technology.

As the expression used was a posed maximum smile this may not reflect the spontaneity of a natural smile which may be more commonly seen during day to day interaction. However, spontaneous facial expressions are known to be non-reproducible. The age group was 13-17, which does encompass growth changes as many of the cohort may be experiencing puberty during this phase. However, the mean age was 14.61 years, meaning many may not have completed their growth, so this may not reflect the final muscle movement limitations experienced once adulthood is reached. There may also be gender related differences and although we aimed for age and sex matched groups, there were more females in the control group than the cleft cohort. All participants had Milliard cleft lip repair carried out. Therefore, we are unable to compare different surgical repair techniques and if one method of repair produced better outcomes than another.

There were two different capturers for recording the control group images. Although there was a standardised protocol on how to guide subjects to carry out the smile expression, there may have been differences between the operators. However, the intra-rater reliability score showed good reproducibility of landmark placement, and the inter-rater reliability was comparable.

The directionality of lip movement in all planes of space was not considered in this study. This requires further mathematical analysis.

6. Potential ideas for future research

A multi-centre study would be highly recommended. The evaluation of various surgical techniques is desirable to establish outcome measures and prognostic indicators of surgical repair of cleft lip and palate. Assessment of an adult population, where growth is complete, may show the final restriction and limitations experienced by individuals with a cleft. Comparing dynamic expression for subjects who have had a surgical revision and those who have not had a revision procedure would also be insightful. A longitudinal evaluation of surgically-managed UCLP patients, to underpin the impact of muscle developments on the dynamics of facial expression and the nasolabial morphology would be recommended.

With the rapid progression of artificial intelligence, there may be an opportunity to examine facial expressions in even more detail due to A.I assisting with faster landmark placement and helping with the analysis of large volumes of data.

7. Conclusions

Significant restriction is noted in upper lip movement on the cleft side and reduction in the speeds and magnitude of movement at the corner of the mouth on the cleft side relative to the non-cleft side. Interestingly the lower lip shows greater magnitudes and speeds on the side affected by the cleft suggesting compensatory movement on this side. It was evident that the group of UCLP cases had more restriction in their upper lip magnitude and speed. Scarring from reconstruction of the lip can limit the lateral movements around the upper lip.

The magnitude of movement of lips was reduced on the cleft side as would be expected with a scar and consistent with previous literature (Hallac et al., 2017). Scarring within and around the perioral muscles compromises the range and speed of muscle movements and may contribute to the measured facial asymmetry of the peak expression in the UCLP group.

Microscopic repair of the nasolabial muscles during lip revision surgery may help to reduce limitations in facial expression and improve lip function. Orientation of the muscle fibres into the correct anatomical position and ensuring their correct origins and insertions, plays an important role in muscle contraction during expression. Scarring of the upper lip can cause stiffness and restriction in the muscle function which affects the dynamics of facial expression by limiting the range and speed of the maximum smile, as well as causing facial asymmetry.

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Appendices:

Date: 21st February 2024 Version 01 IRAS ID: 334720

University of Glasgow NHS Greater Glasgow and Clyde

ASSENT FORM FOR CONTROL GROUP PARTICPANTS UNDER 16

Title of Project: Assessment of dynamic facial expressions

Please circle your answer

1. Have you read the information sheet dated December 20, 2023 (Version 01) for the above project and has it been explained to you? YES / NO
2. Have you had the opportunity to ask questions, and have these been answered in a way that you understand? YES / NO
3. Do you understand what this project is about? YES / NO
4. Do you understand that your child's participation is voluntary and that they are free to withdraw at any time without giving a reason? YES / NO
5. Do you understand that the information collected about your child may be used to support other research in the future, and may be shared anonymously with other researchers? YES / NO
6. Do you understand that your child's recorded data may be used in the future for multi-centre investigations and comparison of results? YES / NO
7. Are you happy for your child to take part in this project? YES / NO

If you **are** happy for your child to take part in this project, please sign below.

Name of child: ______________________

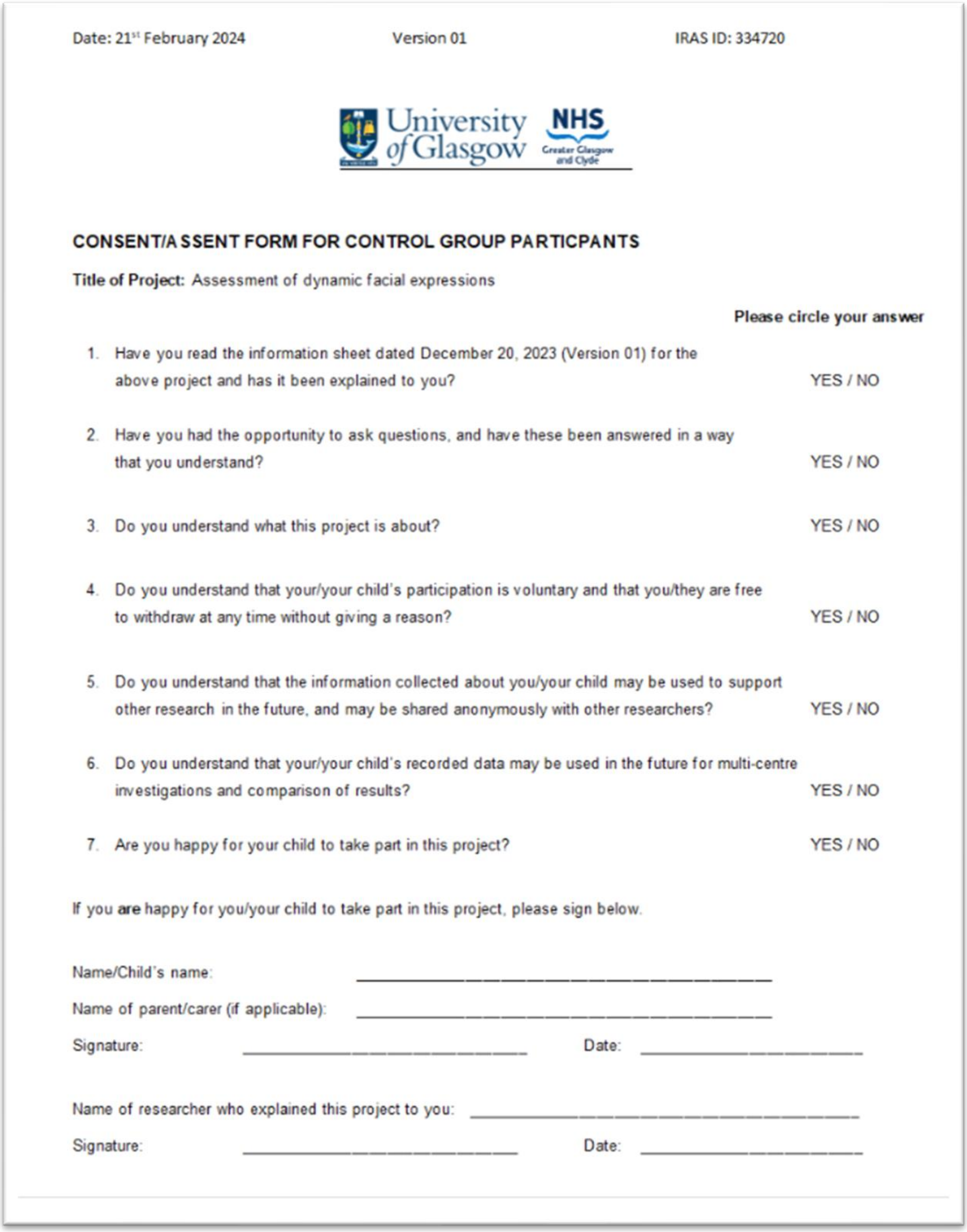
Name of parent/carer: ______________________

Signature: ______________________ Date: ______________________

Name of researcher who explained this project to you: ______________________

Signature: ______________________ Date: ______________________

Figure 67 - Consent form for research participants under 16 years old



Date: 21st February 2024 Version 01 IRAS ID: 334720

University of Glasgow NHS Greater Glasgow and Clyde

CONSENT/ASSENT FORM FOR CONTROL GROUP PARTICPANTS

Title of Project: Assessment of dynamic facial expressions

Please circle your answer

1. Have you read the information sheet dated December 20, 2023 (Version 01) for the above project and has it been explained to you? YES / NO
2. Have you had the opportunity to ask questions, and have these been answered in a way that you understand? YES / NO
3. Do you understand what this project is about? YES / NO
4. Do you understand that your/your child's participation is voluntary and that you/they are free to withdraw at any time without giving a reason? YES / NO
5. Do you understand that the information collected about you/your child may be used to support other research in the future, and may be shared anonymously with other researchers? YES / NO
6. Do you understand that your/your child's recorded data may be used in the future for multi-centre investigations and comparison of results? YES / NO
7. Are you happy for your child to take part in this project? YES / NO

If you **are** happy for you/your child to take part in this project, please sign below.

Name/Child's name: ______________________

Name of parent/carer (if applicable): ______________________

Signature: ______________________ Date: ______________________

Name of researcher who explained this project to you: ______________________

Signature: ______________________ Date: ______________________

Figure 68 - Consent form for adult research participants

Version 01, 20th December 2023 IRAS ID: 334720

Participant Information – adult control participants, and parent/carer of child control participants.

Analysis of Facial Muscles Movements – Version 01 - December 20, 2023

I am Jessica Monaghan, a Masters Research student, carrying out a research project in collaboration with a group of researchers at Glasgow University Dental Hospital and School. We are carrying out a study to mathematically analyse the way in which facial muscles move. I would like to invite you/your child to take part in this research study. Before you make your decision, I would like to explain the aim of this study and what your/your childs' participation will involve. Please take time to read the following information carefully. Feel free to ask questions if anything you read is not clear or you would like more information. Take time to decide whether or not to take part.

Background:

Surgeons are always trying to improve the quality of treatment for patients who suffer from distorted facial muscle movements (patients with cleft lip and palate). We have a special camera that allows the video recording of facial expressions in three dimensions. The recorded images can then be measured to find out which group of facial muscles is not working properly and enables new treatments to be explored. Our main objective is to compare the pattern of facial muscle movement in patients who have had surgical repair of cleft lip and healthy volunteers. You/your child are being invited to take part because having data about normal facial movements may help us to improve the quality of care we provide to cleft lip and palate patients.

What would taking part in the study involve?

If you agree/agree for your child to take part in this study you will be invited to attend an imaging session at Glasgow Dental Hospital and School. On that visit we will explain the full procedure and answer any questions you might have. You will be asked to sign a consent form allowing you/your child to take part in this study. We will then make the 3D video recording of some facial expressions (maximum smile, pursed lips, cheek puff, forceful eye closure, maximum raising of the eye-brows). This will not take more than about 10 minutes. We will offer a £10 voucher as a token of appreciation.

Who has reviewed this study?

All research studies are reviewed by an independent group of people, called a Research Ethics Committee, to protect your safety, rights, well-being and dignity.

What are the possible benefits of taking part?

There is no personal benefit for you in taking part in this study apart from helping us to assess patients with abnormal facial movements caused by cleft lip and palate.

What are the possible consequences and risks of taking part in this study?

Having a photographic image taken of your, or your child's, face is safe and does not involve any exposure to radiation. The flash lighting during the image recording may appear very bright for a few seconds.

Version 01, 20th December 2023 IRAS ID: 334720

What would happen to your image and information?

These images will be anonymised by removing details such as name, address, and date of birth. The captured images will be stored on password-protected computers, which are locked in a safe room at Glasgow Dental Hospital and School. The mathematical analysis will be mainly conducted on the geometry of the face. The measurements will be related to subjective assessment to help us validate our method. The images and information may be looked at by representatives of the study Sponsor, NHS Greater Glasgow and Clyde, to ensure that the study is being conducted correctly. The information collected may be used to support other research in the future, and may be shared anonymously with other researchers.

What would happen if you agree to take part in the study?

If you wish, or you wish your child, to participate in the study please contact the researchers (the details are provided below). A suitable date and time can then be arranged for a visit to the Dental Hospital for the images to be taken. We will, of course, be happy to answer any questions that you may have. You can always change your mind at any time, even after you have agreed to take part in the study and you don't have to give a reason.

Would I be notified with the results of this study?

Upon your request, a copy of the final report could be provided.

Thank you for reading this information. For further information, or if you wish, or wish your child, to take part in the study, please contact:

The Study Chief Investigator (The Student) is: Jessica Monaghan
Email:
Address:

The other Academic Supervisors are:

Mr Philip Benington
Telephone:
Email:
Address:

Dr Kurt Naudi
Telephone:
Email:
Address:

Prof Ashraf Ayoub
Telephone:
Email:
Address:
Dr Xiangyang Ju
Telephone:
Email:
Address:

Version 01, 20th December 2023 IRAS ID: 334720

For confidential advice, support and information on health-related matters, please contact Version 2 4 31/07/2017 Patient Advice and Support Service, NHS Greater Glasgow and Clyde, on 0141 775 3220. For complaints, please contact NHS Greater Glasgow and Clyde on 0141 201 4500 (9.00am to 5.00pm). E-mail: complaints@ggc.scot.nhs.uk.

Figure 69 - Information leaflet on Research project for adult research participants and parents of participants under 16 years

Child control group participant information sheet (13-15 years old)

Project title:

Analysis of facial muscles movements

My name is Jessica and I would like to ask for your help in a research project that I am doing. Research means finding out more about something. It is a way we try to find out the answers to questions. In this project, we would like to take a picture of your face at rest and during facial expressions, such as smiling and blowing out your cheeks.

Why is the project being done?

Some children are born with problems which prevent them from moving the muscles of their face properly. One of these problems is called a cleft lip. This study will help us to measure facial expressions so we can help those kids suffering from abnormal facial movements.

Why am I being asked?

We are asking children who have no problems with their face muscles to be part of our research study.

What do I have to do?

All you need to do is to come to the Glasgow Dental School and Hospital where we will take a photograph of your face with a special camera. You will have to make four facial expressions smiling, pouting, puffing your cheeks, and grimace. Each facial expression will take 3-6 seconds to video. Your photograph will be stored in a computer safely. The full visit would usually not take more than 10 minutes.

Will joining help me?

It will not help you personally, but what we discover might help other children who suffer from cleft lip and palate.

Do I have to take part?

No, you do not have to take part. You can say no and no one will be cross or upset. If you say yes, but later decide you do not want to take part, then that is okay as well.

Will anyone find out I am on this study?

Your name and photographs will be kept safe with the researchers and the people organising the study. The images would be viewed by a number of doctors. They will sign a confidentiality agreement to ensure that your images/video are kept private. If we feel the need to publish our discovery in a journal for the scientific world to see, we may request written permission from you and your parents/carer to use your photographs for this purpose. Your photographs will be stored in password-protected computers in the Glasgow Dental Hospital for a period of 10 years. Your facial photographs will be used for this research project and possible other future studies.

Did anyone else check the study is okay?

Before any research is allowed to happen, it has to be checked by a group of people called a Research Ethics Committee. They make sure the research is fair. This study has been approved.

What do I do now?

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Take time to decide if you want to take part or not and please ask us if there is anything you do not understand.

If you have questions, ask your parents to send us an email at

We will try to answer your questions.

Figure 70 - Information leaflet on Research project for research participants under 16 years

Date: 21st February 2024 Version 01 IRAS ID: 334720

Would you like to have a 3D video taken of your face?

My name is Jessica Monaghan, and I am doing a research project to look at how the muscles of the face move in children. I need willing volunteers aged from 13 to 17 years to have a harmless 3D video picture taken while making some facial expressions. This would take about 15 minutes.

If you are under 16 years old, your parent or carer will need to give their approval for you to take part.

Your images will be stored securely on NHS-approved computers. No other information about you will be stored. The project has been approved by a Research Ethics Committee.

A £10 voucher will be offered to all participants.

If you are interested in participating, please contacting me at:

The project is being supervised by:

Mr Philip Benington, email:

Mr Kurt Naudi, email:

Prof Ashraf Ayoub, email:

Figure 71 - Recruitment notice posted

Table 21 - Descriptive characteristics for the magnitude of UCLP landmarks to reach maximum smile

Landmark	Mean (mm)	Std Dev (mm)	Median (mm)	Range (mm)	Min (mm)	Max (mm)	Skewness
Cleft Side Cheilion	27.24	11.79	27.48	42.51	6.97	49.48	0.11
Non Cleft Side Cheilion	29.49	10.62	30.18	44.74	6.99	51.73	-0.01
Cleft Side Philtrum	6.84	4.05	5.96	17.75	1.59	19.34	1.38
Non Cleft Side Philtrum	7.59	3.68	6.7	15.22	1.48	16.7	0.77
Cleft Lower Lip	19.85	11.34	16.6	48.17	3.19	51.35	1.12
Non Cleft Lower Lip	18.04	10.24	15.1	40.35	4.72	45.07	1.1

Table 22 - Descriptive characteristics for Magnitude of the Control group landmarks to reach maximum smile

Landmark	Mean (mm)	Std Dev (mm)	Median (mm)	Range (mm)	Min (mm)	Max (mm)	Skewness
Left cheilion control group	37.22	17.46	32.65	65.31	15.44	80.75	1.07
Right cheilion control group	40.03	21.53	34.26	92.71	8.32	101.03	0.95
Left philtrum control group	14.44	9.94	11.29	42.98	4.31	47.29	1.71
Right philtrum control group	13.39	8.8	10.17	43.38	3.53	46.91	1.94
Left lower lip control group	26.88	19.35	21.92	76.64	7.92	84.56	1.63
Right lower lip control group	25.25	17.34	18.39	62.57	10.85	73.42	1.64

Table 23 - Speed comparison for UCLP cleft side and the left side landmarks for the control group

Landmark	Mean (mm/s)	Std Dev (mm/s)	Median (mm/s)	Range (mm/s)	Min (mm/s)	Max (mm/s)	Skewness
Cleft Side Cheilion	28.69	14.14	28.6	56.45	5.55	62	0.29
Left Cheilion control	63.58	38.72	53.91	164.33	20.21	184.54	1.661
Cleft Side Philtrum	7.24	4.52	5.98	19.11	0.83	19.94	1.17
Left Philtrum control	22.7	10.02	19.32	37.36	5.63	42.99	0.56
Cleft Lower Lip	20.98	11.72	20.66	45.89	1.66	47.55	0.55
Left Lower Lip control	39.08	22.31	28.46	92.8	13.09	105.89	1.47

Table 24 - Speed comparison for the non cleft side of the UCLP group and the right side landmarks for the control group

Landmark	Mean (mm/s)	Std Dev (mm/s)	Median (mm/s)	Range (mm/s)	Min (mm/s)	Max (mm/s)	Skewness
Non Cleft Side Cheilion	32.05	16.25	31.11	75.02	3.64	78.66	0.98
Right Side Cheilion	69.76	49.6	58.36	215.22	11.09	226.31	1.67
Non Cleft Side Philtrum	8.22	4.79	7.65	21.27	0.77	22.04	1.04
Right Side Philtrum	20.43	9.13	20.24	34.6	4.71	39.21	0.4
Non Cleft Lower Lip	19.22	10.95	20.2	40.14	2.46	42.6	0.52
Right Lower Lip	40.36	21.56	29.54	78.63	16.45	95.08	0.94

Table 25 - Mann Whitney U test to compare the cleft side in UCLP group and left side in control group for all three landmarks

		Ranks			Test statistics			
Landmarks	Side/group	No. of Subjects	Mean rank	Sum of ranks	Mann Whitney U	Wilcoxon W	Z	Asymp. Sign. (2-tailed)
Cheilion	Cleft side/ UCLP	31	21.42	664	168	664	-4.72	<0.001
	Left side/ control	34	43.56	1481				
Philtrum	Cleft side/ UCLP	31	18.45	572	76	572	-5.92	<0.001
	Left side/ control	34	46.26	1573				
Lower lip	Cleft side/ UCLP	31	23.68	734	238	734	-3.79	<0.001
	Left side/ control	34	41.5	1411				

Table 26 - Mann Whitney U test to compare the non-cleft side in UCLP group and right side in control group for all three landmarks

		Ranks			Test statistics			
Landmarks	Side/group	No. of Subjects	Mean rank	Sum of ranks	Mann Whitney U	Wilcoxon W	Z	Asymp. Sign. (2-tailed)
Cheilion	Non cleft side/ UCLP	31	23.06	715	219	715	-4.05	<0.001
	Right side/ control	34	42.06	1430				
Philtrum	Non cleft side/ UCLP	31	19.55	606	110	606	-5.48	<0.001
	Right side/ control	34	45.26	1539				
Lower lip	Non cleft side/ UCLP	31	22.42	695	199	695	-4.31	<0.001
	Right side/ control	34	42.65	1450				