DESIGN OF MAXILLOFACIAL IMPLANTS FOR COSMETIC AND RECONSTRUCTIVE PROCEDURES

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DESIGN OF MAXILLOFACIAL IMPLANTS FOR COSMETIC AND RECONSTRUCTIVE PROCEDURES

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SUMMARY:

Maxillofacial surgery can be used to help appearance and restore function. Often there is a need to provide additional volume with soft tissue properties. This works explores the use of a new biomaterial invented at GT with soft tissue properties as possible maxillofacial implants to provide volume. The implants are for restoring speech function in cleft palate patients presenting velopharyngeal insufficiency and providing volume to reduce the nasolabial folds in order to create a more youthful appearance.

We have developed facial implants for the nasolabial fold and lip plumping to address low efficiency of the current methods employed for dermal fillers by providing both long-term usage as well as removability. Furthermore, an insertion method and insertion tools were developed to facilitate the implantation for the surgeons.

Regarding the reconstructive aspects of the maxillofacial implants, we have developed a pharyngeal implant aiming to reduce the gap between the pharyngeal implant and the velum (soft palate) of 20% of patients presenting a cleft palate. This implant will allow the care team to delay the palatoplasty in order to not hinder palatal growth in patients.

The material used for the implants can also be used to better the current obturators by replacing the acrylic, posterior portion. The main current obturators are the nance obturator and custom acrylic obturators, deemed uncomfortable for the patients due to the hardness of the material. The design process for the implants and the novel obturator involved the optimization of material and shape, taking into consideration mechanical properties of the implants' surrounding tissues, the anatomy of each feature being enhanced as well as potential implantation modes.

Part 1: Cleft palate

Chapter 1: Background

1.1 Description of the condition

A cleft palate is an oral birth defect that happens during the early stages of a fetus' development, affecting the roof of the patient's mouth. The cause is currently unknown, but scientists believe it is a combination of genetic and environmental factors. Each year, approximately 2650 children are born in the US with a cleft palate. The cleft could be unilateral or bilateral, and it could affect the soft palate, the hard palate or both, depending on the severity. [1, 2]

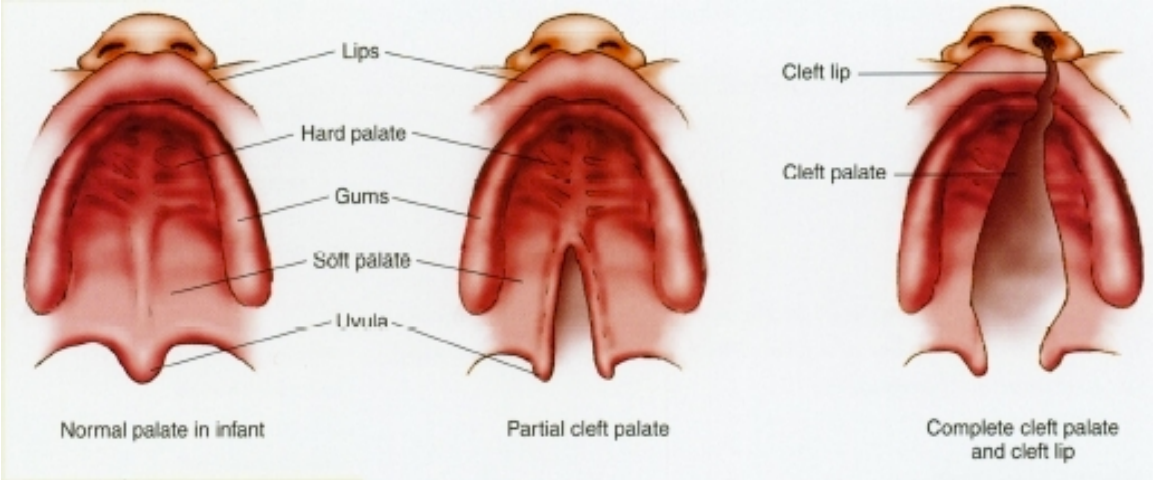

Figure 1: normal palate vs partial cleft palate and complete, unilateral cleft palate

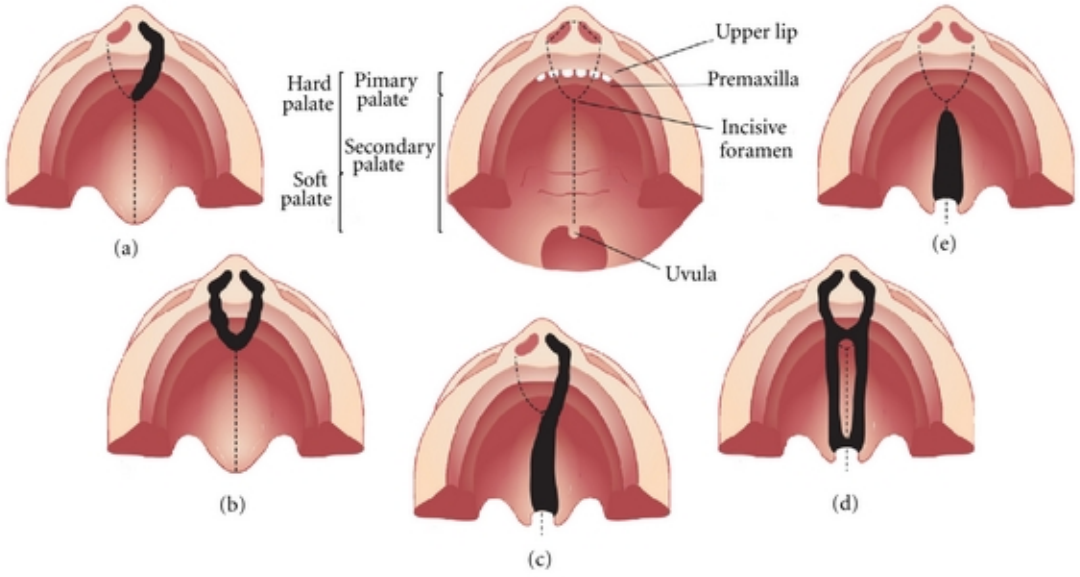

Figure 2: Representation of the most common types of cleft affecting the palate. (a) Unilateral cleft lip with alveolar involvement; (b) bilateral cleft lip with alveolar involvement; (c) unilateral cleft lip associated with cleft palate; (d) bilateral cleft lip and palate; (e) cleft palate only.[3]

1.2 Problems caused by the condition:

In a pediatric patient presenting with a cleft palate, speech production, dentition, feeding and maxillofacial growth are affected. Feeding is the most critical challenge faced by parents of babies born with cleft lip/palate. [4, 5] Not only appropriate feeding is important for the infants' adequate development, but also the volume of milk intake must be sufficient for adequate weight gain prior to surgical repair of the cleft lip and or palate. [4-6]

Studies have shown a significant difference in weight between babies with cleft palates and babies without, as well as levels of weight discrepancies depending on the type and extensity of cleft[7]. Babies with more extensive complete clefts suffer of poorer oral intake thus tend to weigh less than babies with smaller complete clefts, while babies

with incomplete clefts generally weigh less than babies with complete clefts. The reason behind the latter is that incomplete clefts are less often detected as early as complete clefts.[8] Parental and infantile frustration during the feeding process can also affect the parent-child bonding process.

Different feeding strategies have been developed to address this problem, depending on the type of cleft the baby is presenting. The ability to produce both positive and negative pressure for suction and release of the nipple during the feeding process is the most important criteria for infant feeding.

Cleft Palate only case:

In the case of a narrow cleft affecting only the soft palate, the baby is able to adjust and eventually develop sufficient suction for breastfeeding. When the hard palate is affected however, the patient is more likely to have long-term difficulty producing adequate suction because of a smaller palatal surface available for the tongue to apply pressure.[5] In this case, bottle-feeding is a better feeding option compared to breastfeeding. Table 1 describes the types of commercially available bottles for cleft palate patients.

Table 1: Types of nipples available for cleft palate feeding bottles [5]

Nipple Type	Pliability	Flow Rate	Shape	Hole Type
Preemie	Soft	Fast	Traditional	Hole and cross-cut
NUK-style	Soft	Fast	Broad, Flat	Hole on top surface of tip
Ross Cleft	Soft	Fast	Long, Thin	Large hole
Standard	Medium	Low	Traditional	Hole and cross-cut, several holes
Mead Johnson	Soft	Feeder regulated	Customized	Cross-cut
Haberman System	Soft	Feeder regulated	Customized	Slit

Figure 3: Mead bottle

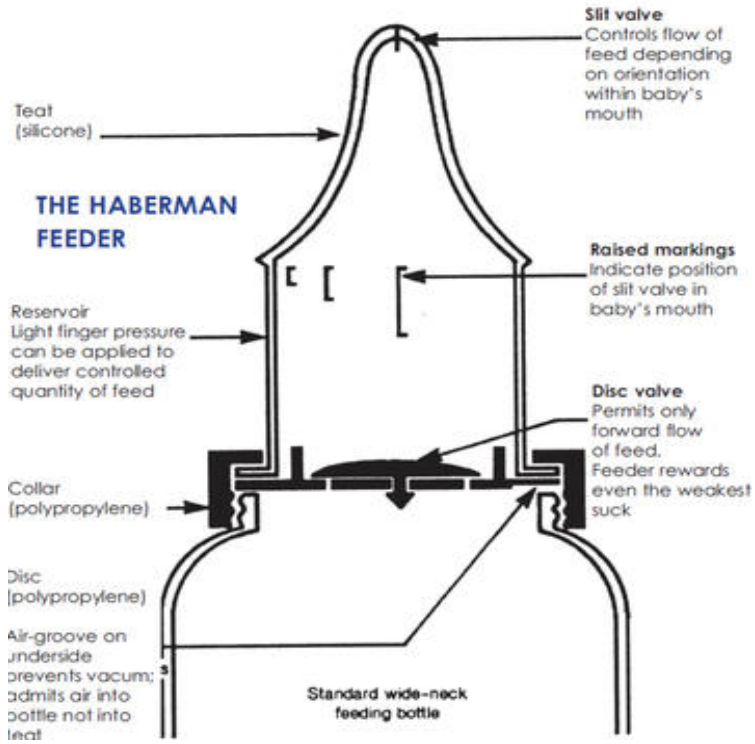

Figure 4: Details of a Haberman Feeder [6]

Cleft lip and palate case:

The cleft lip hinders infants from properly creating a seal around the nipple of the breast or the feeding bottle, which directly affects their ability to produce adequate pressure for suction or releasing of the nipple. Additionally, the patients with cleft lip and palate present larger palatal clefts, contributing to the intraoral pressure insufficiency. Breastfeeding is therefore of very little likelihood in patients presenting both cleft lip and palate. [5] Although there still is some difficulty present with the usage of feeding bottles, they are significantly better alternative for these patients.

In addition to feeding bottles, palatal obturators are used to create provide more area on the roof of the mouth to allow the tongue to produce more pressure during feeding.[9] Obturators are prosthetic devices made to fit in the roof of the mouth and cover the gap. Palatal obturators are typically made out of acrylic on a per patient basis, depending on each patient's anatomy. As the patients grow, the type of obturator changes from a full palatal obturator covering the entire palate to a partial palatal obturator, anchored at the molars and covering mainly the cleft. [5] These palatal obturators are risky for the patients because of the material qualities of acrylic: because of its hardness, it can cut the patient's tongue or create ulcerations on the patient's palate. There is therefore a need in the field for obturators to be made out of a softer material.

The second most critical concern for parents of infants presenting a cleft palate is the predisposition for a speech impediment as they grow. [10, 11]The speech production problem faced by many cleft palate patients is due to velopharyngeal insufficiency (VPI). The velopharyngeal valve plays an important role during speech production, primarily directing airflow and sound energy into the oral and nasal cavities. VPI is defined as an

inadequate physiological barrier between the naso-pharynx and oropharynx during speech, due to the dysfunction of the coordinated movements of the velum (soft palate) and a wider than usual posterior gap between the soft palate and the posterior pharyngeal gap [4, 5, 12]. In approximately 20% of cleft palate patients, the velum is unable to reach the pharyngeal wall for the proper production of sounds. [5]Unfortunately, in some cases VPI persists in patients even after palatoplasty (palatal closure). Studies have determined the factors that influence persistent VPI post-palatoplasty in order to predict the occurrence. The posterior gap between the velum and the pharyngeal wall and the width of the cleft at the hard palate level are the main criteria used for VPI prediction [13]. Platelet rich plasma and autologous fat injection on the pharyngeal wall is done in order to boost the wall's thickness and reduce the posterior gap between the velum and the pharyngeal wall, or a pharyngeal flap is inserted to reduce said gap [12, 14].

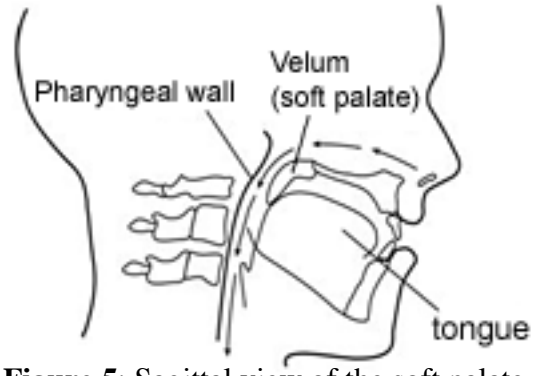

Figure 5: Sagittal view of the soft palate and pharyngeal wall

1.3 Surgical Treatment:

A palatoplasty, consisting of the repositioning of tissues and muscles in order to close the cleft and rebuild the roof of the mouth, is performed when the patient is deemed ready by the surgeon. This surgical treatment may occur in one or two steps, depending on the size of the cleft [15, 16]. Clefts deemed as particularly large are treated in a two-step manner, where the first surgery, the soft palate closure may occur as early as 3-4 months, followed by a hard palate closure, usually when the patient is 18 months old[15]. In cases where the physician considers the cleft small, the palatoplasty is usually accomplished at age 11 months. The timelines for surgical planning vary per patients, depending on whether they meet certain preoperational criteria such as hemoglobin levels of at least 10 g/dL, weight gain, and lack of infection.[11, 16] Palatoplasties occurring at a later stage are usually accompanied with a pharyngeal flap to better the speech production phase of the child's growth [17, 18].

The purpose of the palatoplasty is to create separation between the oral and nasal to facilitate both feeding and speech production post surgery. The benefits from this treatment are evidently significant, however, studies have shown that early palatal closure negatively affects longitudinal palatal growth[18, 19]. Additionally, the risk for maxillofacial growth abnormalities is increased. The palate usually reaches its optimal size at age 5, but waiting this long before performing the palatoplasty at this stage of the child's development has a significantly negative effect on the child's speech development, and potentially have some effects on the child's social and emotional development.

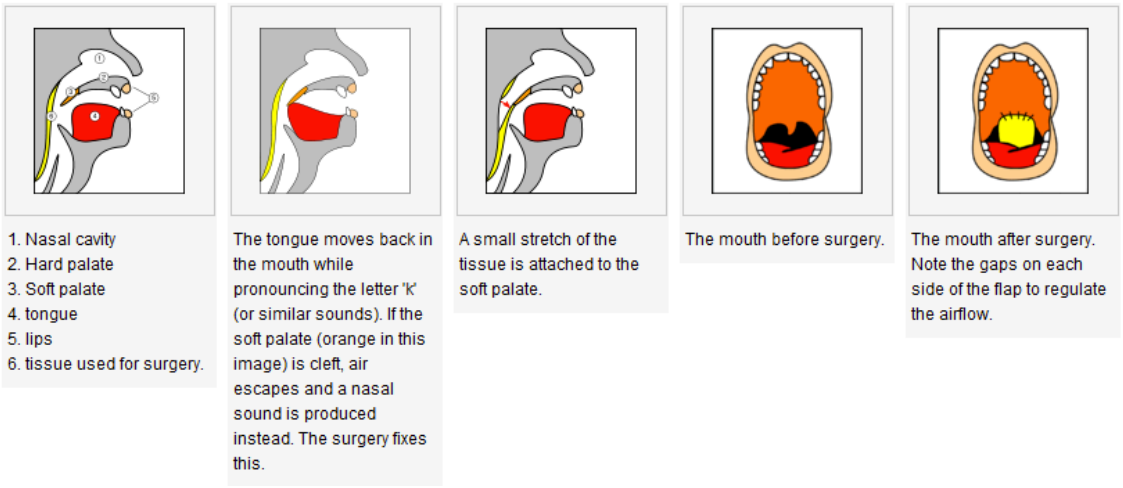

Figure 6: description of pharyngeal flap insertion in patients suffering of velopharyngeal insufficiency[14]

1.4 Deficiencies that need to be addressed:

Early palatoplasties affect the maxillary arch growth and can potentially lead to some maxillary development abnormalities, while delaying the procedure too far can tremendously affect the patients' speech and socio-emotional development[17, 20, 21]. There is thus a need for a form of treatment that would allow sufficient palatal growth, while still assisting the speech production at an early stage. Additionally, it is important to look at ways to reduce the risks associated with the obturators due to acrylic's hardness.

1.5 Proposed Solution

In order to address the deficiencies related to the timelines of surgical procedures and medical treatments of the cleft palate, this research came up with two separate devices: an implant that would be inserted into the pharyngeal wall, underneath the skin in order to shorten the velopharyngeal gap and a softer obturator to cover the palatal cleft.

Chapter 2: Market Analysis

2.1 Market overview

Every year in the United States, approximately 2500 children are born with a cleft palate or cleft lip and palate. The average cost involved in the treatment and accommodations of a patient with a cleft palate from birth to adulthood is $100,000. This device may reduce the cost of the cleft palate surgical treatment by one half, from potentially $20,000 to $10,000 [22]. This cost reduction could come from delaying and reducing of the number of surgical procedures performed during the typical treatment timeline. Additionally, because the implant will be ideally placed before the patient's speech pattern begins to develop, the cost of speech therapy may be significantly reduced. Speech therapy is estimated at $100/hour, and the number of hours needed strictly depend on the patient and the severity of the speech impediment.

1.2 Patient Profile

The patients that would be considered for the pharyngeal implant are the 20% of cleft palate patients suffering of velopharyngeal insufficiency, ranging from age 0 to 5 years. The majority of cleft palate patients wear palatal obturator during the course of their treatment; therefore the palatal obturator's design is applicable to a wide range of cleft palate patients.

Chapter 3: Design considerations

3.1 Design controls overview

Design controls specify the formal methodology followed during the product development process. Several regulatory agencies such as the Food and Drug Authority (FDA) and the Environmental Protection Agency (EPA) make the implementation of this process mandatory for designers and manufacturers of new products. The FDA offers specific guidance for design controls of medical devices. This process entails the definition of design input, obtaining design outputs, reviewing the design, verifying the design and validating the design and documenting all phases of the process with design history file [23].

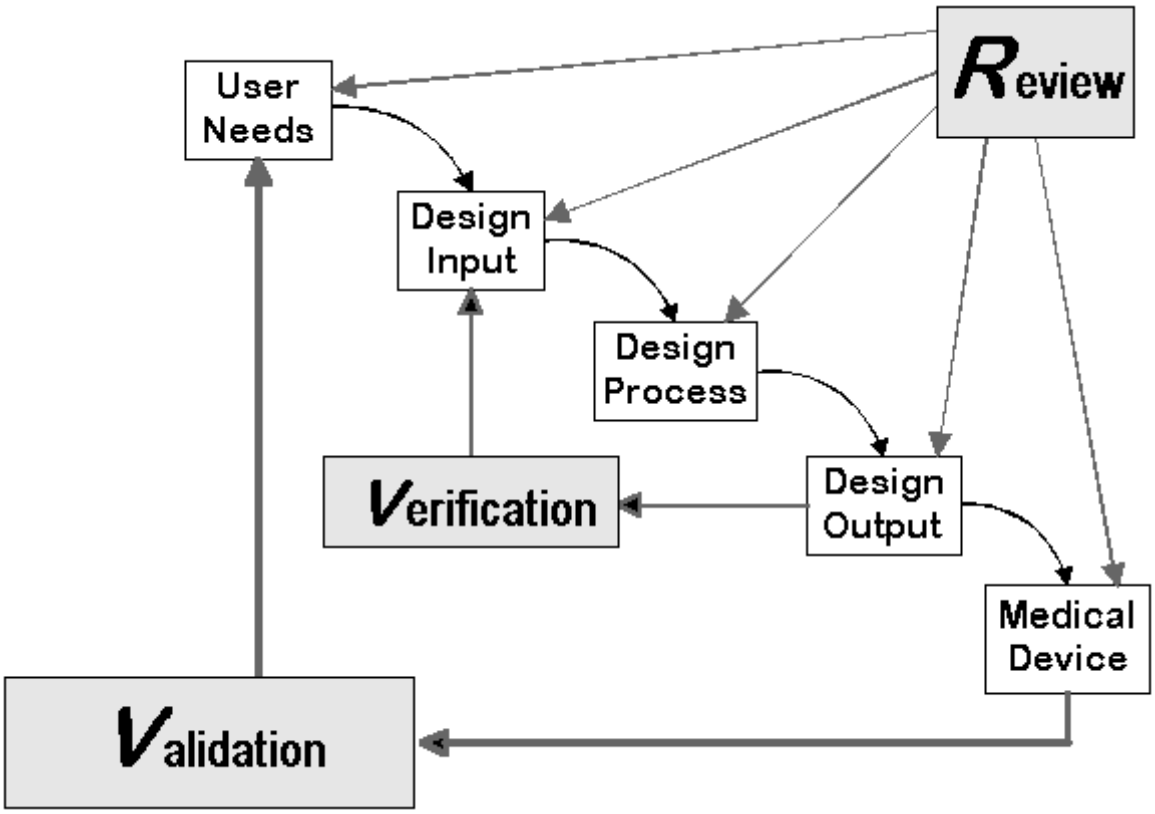

Figure 7: Steps of the medical device development process[24]

Design inputs are the starting line of the design of a product: during this part, the designer takes into consideration the end users' needs (patient and healthcare practitioner) and translates these needs into design criteria for the device for the device's functionality. Once the design inputs have been established, the designer comes up with product concepts that may be altered depending on the changes made to the design input of the device. The verification phase involves the different tests that need to be effectuated to verify that the device design meets the predefined criteria in the design input section. Lastly, the device validation phase involves making sure that the device will conform to user needs without having unwarranted adverse effects. This phase involves effectuating a device risk analysis, risk mitigation and potentially clinical trials, depending on the type of device. In the case of this research, the risk analysis and risk mitigation were the steps taken for the device validation. [25]

Design Input

In order to determine the design input for a device, the main customers' requirements are determined. Customers are defined as the end users of the devices being designed. It is important to note that for this research, two devices are being developed to assist with cleft palate problems: One implant to help with speech production, and a de novo palatal obturator.

Customer identification:

The primary costumers for the pharyngeal implant and de novo palatal obturator are the end users: the patient and the health care practitioner that will handle the implantation/insertion.

3.2 Customer needs:

The following tables describe each consumer's needs per device. Because certain needs may counteract with others, a Design Control process is used to minimize the risks for the devices and preserve the effectiveness.

Table 2: Customer needs for the pharyngeal implant

	Patient Needs
1	Pharyngo-palatal gap reduced, leading to better speech production
2	Safe device
3	Long life of device
4	Reduce cost of long term care
5	Minimized need of additional surgeries
6	No discomfort from implanted device
	Surgeon Need
1	Reduce frequency of treatment using device compared to current treatment
2	Wide range of device size to select from
3	Standardized method for selection of size
6	Device that is tactile
7	Diagram and procedures for best practices of positioning, delivering and implanting

Table 3: Customer needs for the palatal obturator

	Patient Needs
1	Oro-nasal fistula covered/filled while giving a more comfortable feel
2	Safe device
3	Removable device
4	Long life of device
5	Reduce cost of long term care
6	Minimized need of additional surgeries
7	No discomfort from implanted device
	Physician Need
1	Reduce frequency of treatment using device compared to current treatment
2	Wide range of device size to select from
3	Standardized method for selection of size
4	Device that is tactile
5	Diagram and procedures for best practices of positioning and delivering

The customers' needs were determined by surveying physicians as well as finding current problems in the field from published case studies. These customer needs are then translated into quantifiable and measurable engineering parameters using a quality functional deployment (QFD) chart. A QFD is defined as a structured approach used to defining customer needs and succinctly translating said needs into specific plans to produce the product to meet those needs [26]

The primary needs of the customers were evaluated and described in two main categories: ease of implantation and functionality after implantation.

The ease of implantation category covers the requirements related to the surgeons' needs. One of the main clinician goals is to increase the patient throughput without jeopardizing

necessary time in the hospital, therefore minimizing the time of the procedure by making the device easily implantable and making the insertion the least complex possible will help accomplishing this goal. Additionally, a set method for implant size selection should be implemented in order to minimize potential complications and improve patient satisfaction.

Functionality after implantation as a category encompasses the physical role the implant is meant to play. This therefore addresses needs of the patients, the surgeons, insurance companies and hospitals. For example, for a patient receiving a pharyngeal wall implant, the velopharyngeal gap must be shortened well enough in order to enhance speech production. In the same breath, such implants must not cause immune reactions, infections, or migrate from their site of insertion.

3.3 Linking Requirements to parameters

Once the engineering parameters were identified and consumer requirements specified, each parameter was evaluated to determine which consumer requirement it addresses in the respective QFDs. This work tested for those parameters, evaluating the functionality of each device. Elements such as the shape, size and softness (elasticity) of the pharyngeal implant and posterior portion of the palatal obturator, and how close the material could be to human adipose/muscle tissue in terms of mechanical properties were critical for the creation of each device. These criteria drove the evaluation of the devices important characteristics.

Table 4: QFD translating customer needs to design inputs for the pharyngeal implant

	Design Inputs										
Consumer Requirements	Elasticity	Shape	Height	Depth	Length	Biocompatibility	Removability	Tensile Strength	Tear Strength	Swellability	asepticity/sterility
Ease of Implantation											
Wide range of device size to select from			*	*	*						
Standardized method for selection of size		*	*	*	*						
Functionality after Implantation											
Minimized need for additional surgeries	*						*				
Improved speech production due to reduced Velopharyngeal gap			*	*	*						
Long life of device	*						*	*	*		*
Critical Functionality tests	1	-	-	-	-	-	-	2	3	4	-

Table 5: tests performed to verify properties of the pharyngeal implant

Test	**Type**
1	Compression Test
2	Tensile Strength Test
3	Tear Strength Test
4	Swelling Test

Table 6: QFD translating customer needs to design inputs for the palatal obturator

	Design Inputs										
Consumer Requirements	Elasticity	Shape	Height	Depth	Length	Biocompatibility	Removability	Tensile Strength	Tear Strength	Swellability	asepticity/sterility
Insertability											
Insertion causes minimal local trauma		*	*	*							
Safe device						*	*	*	*		*
Wide range of device size to select from			*	*	*						
Standardized method for selection of size		*	*	*	*						
Functionality after Implantation											
Improved speech production due to reduced oro-nasal communication		*	*	*	*						
Reduce risk of treatment using device compared to current treatment	*						*	*	*	*	
Long life of device	*						*	*	*		
Functionality tests	1	-	-	-	-	-	-	2	3	4	-

3.4 Design Inputs

The most critical design specifications for these devices are encompassed by the geometric characteristics, the mechanical property, and sterility. The tables below break every design characteristic into specific items and outlines to boundary for each.

Table 7: Design Inputs for the pharyngeal implant

Item	Design Parameter	Design Specification
A	Elasticity	The material used for the pharyngeal implant must have a modulus of elasticity less than 200 kPa and greater than 50 kPa
B	Shape	The pharyngeal wall implant must be a cube/block of the polymer that can be carved by the surgeon
C	Length	The length could range from 10 to 20 mm
D	Height	The height will be 5 mm
E	Depth	The depth will be 5 mm
F	Biocompatibility	The implant meets ISO 10993 requirements for implants
G	Removability	Remains intact and solid, does not dissolve in the body
H	Tensile Strength	The material used has a tensile strength of at least 25 kPa
I	Tear Strength	The material used has a tear strength of at least 30 mN/mm
J	Swellability	The material selected must neither swell by more than 10% in physiological conditions nor must it shrink
K	Asepticity/sterility	Implant meets tripartite sterility test requirements
L	Low fibrosis	The implant must not adhere or react to the surrounding tissue or lead to tissue ingrowth

Table 8: Design Inputs for the palatal obturator

Item	Design Parameter	Design Specification
A	Elasticity	The material used for the posterior portion of the obturator must have a modulus of elasticity less than 1 MPa and greater than 200 kPa
B	Shape	The pharyngeal wall implant must be a cube/block of the polymer that can be carved by the surgeon
C	Width	3-6 cm (patient specific)
D	Height	5-10 mm (patient specific)
E	Length	3-6 cm (patient specific)
F	Biocompatibility	The implant meets ISO 10993 requirements for implants
G	Removability	Remains intact and solid, does not dissolve in the body
H	Tensile Strength	The material used has a tensile strength of at least 25 kPa
I	Tear Strength	The material used has a tear strength of at least 30 mN/mm
J	Swellability	The material selected must neither swell by more than 15% in physiological conditions, nor must it shrink
K	asepticity/sterility	Implant meets tripartite sterility test requirements

3.5 Justification of design specifications

Pharyngeal Implant

- **Shape, Length, Height and Depth –** the pharyngeal wall implant is designed to be a block of polymer than can be carved and shaped by the surgeon based on the anatomy of the patient being treated. The dimensions of the block are to be as recommended from surgeons, and recorded dimensions of velopharyngeal gap in CP patients.
- **Asepticity/Sterility** – the implants must be sterile when inserted into the patient, and not lead to any infection

- **Biocompatibility –** The implant must be completely compatible with the human body in order to avoid any form of immune reaction or lead to dangerous consequences such as development of cancerous cells
- **Tensile and Tear Strength** – both were determined experimentally by pulling a sample implant from an extensometer using surgical forceps and recording the load. This was necessary because it is part of the criteria covered by the removability of the implant.
- **Swelling – The swelling ratio of the implants is determined by inserting blocks of the material used into saline baths, and measuring the samples' weight until a plateau is reached, in the order of days.** The implant pharyngeal wall implant should not show a swelling ratio of more than 10% because a significant increase in volume could lead to the tear of stitches during the early stages, and potential implant migration and partial airway obstruction
- **Compressive modulus of elasticity:** the implant must be firm and provide a base that is not too hard. Additionally, the pharyngeal wall is mostly composed of muscle and connective tissue; therefore it is best to use a material of elasticity similar to that of skeletal muscle tissue.
- **Low fibrosis:** The material selected for the implant must not adhere to the local/surrounding tissue in case of long-term complication. It is important that the implant has not adhered to the surrounding tissue if the need to remove it present itself, for example in the event of a potential local infection.

De Novo Palatal Obturator

- **Dimensions & shape** This obturator is patient specific, and the posterior part is what we are focusing on as part of this work. It is meant to be a block of polymer attached to a rigid acrylic frontal part by a metallic hook. The block of polymer is meant to be carved by the surgeon based on the dimensions and type of the cleft affecting the palate.
- **Asepticity/Sterility** – the implants must be sterile when inserted into the patient, and not lead to any infection
- **Tensile and Tear Strength**: The material used for the posterior part of the obturator must resist tear and tension from potentially repeated removal and patient-device interaction: material tensile strength greater than 25kPa, and tear strength greater than 30 mN/mm.
- **Compressive Modulus of elasticity:** The posterior part of the palatal obturator should be firm enough to resist recurrent placement and removal, but still be softer in compression than the current acrylic obturators. Additionally, the palate being mainly composed of cartilage, it is important that the elasticity range selected for the obturator is of the same order as that of cartilage (0.5-0.9 MPa) [27]
- **Dimensional Stability:** A significant change in the posterior part of the obturator will affect how it fits into the patient's cleft and may have consequences on the intraoral pressure necessary for speech production as well as swallowing, and may lead to ulcerations on the patient's palate.

Prior to deciding on designing two separate devices (pharyngeal wall implant and de novo palatal obturator), several concepts of a device that would work as a valve

separating the oral and nasal cavities, facilitating speech production as well as proper feeding for the patients.

Chapter 4: Concept Development

4.1 Materials Selection

Various biomaterials are researched and used in patient care. Because the FDA clears devices and not materials, it is simpler to choose a material used in previously approved devices. The main goal of this research was to design functional, solid and removable maxillofacial implants for eventual clinical use in the cosmetic and reconstructive fields of plastic surgery. Silicone, PMMA, Hard Tissue Replacement polymer, polyesters, biodegradable polyesters (Poly-L-Lactic Acid, Polyglycolic acid) Polyethylene, and polypropylene are some materials used in maxillofacial implants [28, 29].

The characteristics of the material to be used were determined by observing those of the surrounding tissues, as well as each type of implant's design constraints. Because this research aimed at coming up with removable long term implants, it was deemed important to select a non-biodegradable material. The table below compares and contrasts different materials currently used in maxillofacial implants. Based on each material's characteristics. The leading criteria that lead to selecting PVA as the material for the implant is its inertia/non-adhesion to human tissue. A solid implant is removable in case of potential long-term complications. For the obturator, it was the new design objective that implant be more elastic, since the main issue with acrylic obturators is hardness, which could potentially cut the patient's tongue or lead to ulcerations.

Table 9: List of materials used for maxillofacial implants and prosthesis and their characteristics

Material	FDA Approved	Toxic	Microspheres	Solid	Tissue Adhesion	Soft Tissue-like elasticity
PVA	Yes	No	No	Yes	No	Yes
PMMA	Yes	Yes	Yes	Yes	No	No
ePTFE	Yes	No	No	Yes	No	No
PET	Yes	No	No	Yes	Yes	No
Acrylic	Yes	No	No	Yes	No	No

Poly (vinyl) Alcohol can be made into cryogels with a wide range of mechanical properties similar to those of biological tissues. This material is also biocompatible and non-biodegradable [30]. A set of experiments were performed on a wide range of hydrogels at different PVA concentrations in order to determine the ideal hydrogel that would meet the implant's required properties. The following properties were evaluated for the cryogels: moduli of elasticity under compression, tensile strength, tear strength, and swellability.

Manufacturing of PVA cryogel

PVA cryogel is made through dissolution of high molecular granular PVA in normal saline, putting the solution in a mold of the desired shape and putting it through freeze-thaw cycles. After a few freeze-thaw cycles, the mixture transitions from being a viscous liquid to being a solid and the properties tend to plateau at approximately 6 cycles. Granular PVA used was obtained from Brenntag under the label selvol 165. The solute is mixed with the solvent (water, or saline, depending on the test) in an autoclave-safe container, sealed and autoclaved at [insert temp] for 25 minutes. The following formula and table prescribe the amount of PVA to use per weight concentration:

$$PVA(grams) = \frac{(\%concentration) * (mass\ of\ solute - H_2O, Normal\ Saline, etc)}{1 - (\%concentration)}$$

Table 10: Amount of PVA to use per 100 mL of H20 for selected concentrations

PVA %Concentration	PVA mass to use (g) per 100mL of H20
1.30%	1.32
2.50%	2.564
5%	5.263
7.50%	8.108
10%	11.111
20%	25
30%	42.87

After the PVA has been dissolved, the solution is poured/injected into the designated mold. It is important to make sure that there are no air voids/bubbles in the solution by letting the air rise to maintain the integrity of the parts being manufactured. The mold is then put in a freezer start the freeze-thaw process. Putting the hydrogels through freeze-thaw cycles increases its crosslinking, thus increasing its elastic modulus. When the hydrogel is completely frozen, it has a white coloration and is completely opaque. It is then thawed at room temperature. Thawed hydrogels are clear and somewhat cloudy. Once the first freeze-thaw cycle is completed, the mold is placed back into the freezer. For this research, the samples are put through 6 freeze-thaw cycles because this is the number at which a plateau is reached for the hydrogels in terms of cross-linkage[31].

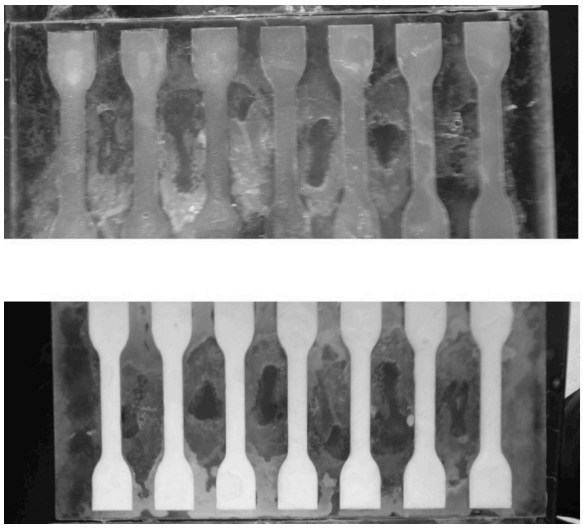

Figure 8: Comparison of thawed (top, cloudy, translucent) and frozen (bottom, white, opaque) PVA

4.2 Mold Fabrication

Multi-part acrylic molds were used for objects of more convoluted shapes that could not me created by book molding. This type of mold was used mainly for the cleft palate project. Based on the shape and size of each part of the product, acrylic sheets of different thickness were sourced from a local manufacturer, McMaster Carr. Each geometrical aspect of the product was drawn in AutoCAD and used to laser-cut the different pieces of acrylic that would then be stacked onto one another.

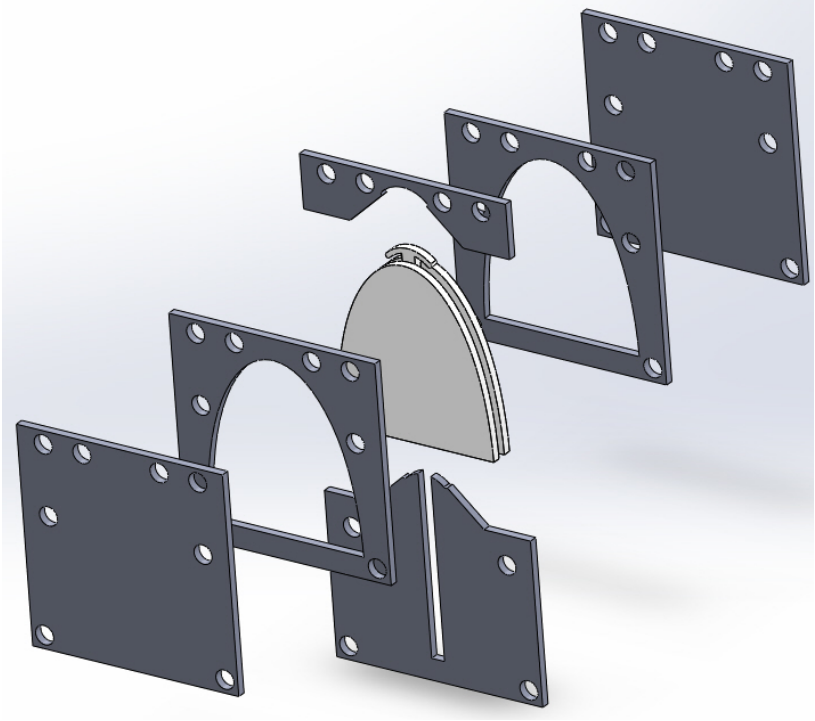

Figure 9: Example of pre-designed acrylic multi-part mold for naso-oral valve/obturator

4.3 Concept Evolution

Concept 1

The problems identified with the current methods of treatment of cleft palate patients were the main factors that shaped the bourgeoning of the original concept. As a pediatrician, being able to insert a valve-like device that would cover the cleft and impeach naso-oral communication, leading to better feeding and sound production, while delaying the surgical procedure in order to allow optimal longitudinal palatal growth would be ideal both in terms of cost efficiency, and improvement of patient care. This original concept involved two thin 2mm flaps joined by a bridge that would be of the thickness of the hard palate. The superior flap would fold and lay atop the hard palate, the bridge would fit into the cleft and the inferior flap would cover the roof of the mouth.

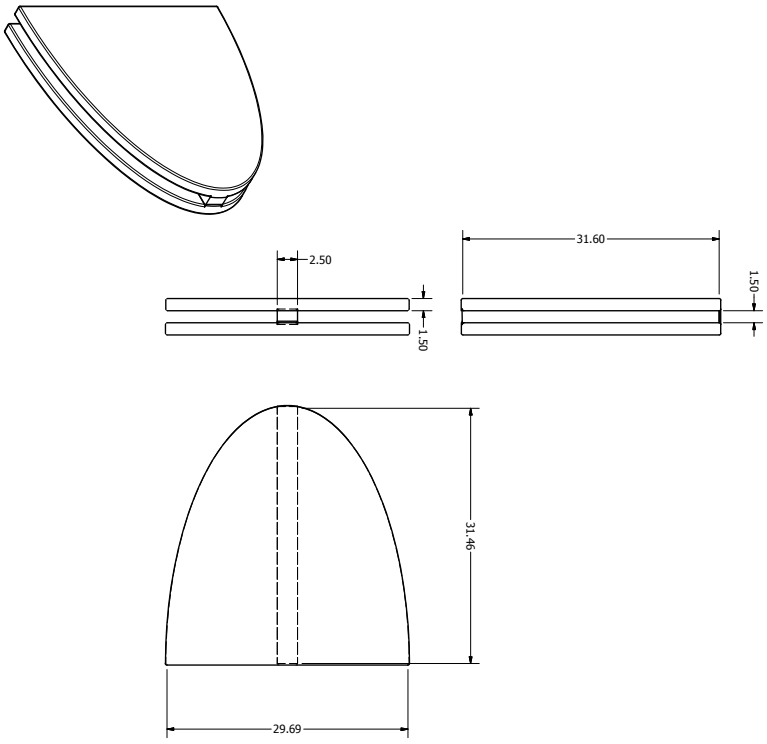

Figure 10: Concept 1: simple valve-like obturator for cleft palate patient (numbers in mm to 2 significant figures)

Concept 2:

Because of the varying anatomy of clefts based on their nature, changes were made to the original concept, adjusting the shape and dimensions of the bridge aimed to fit into the cleft. Data of dimensions of maxillofacial anatomy was obtained from past studies observing unilateral complete cleft lip and palate and incomplete cleft palate. An anterior knob was added to the bridge of the valve in order to ease up the removal.

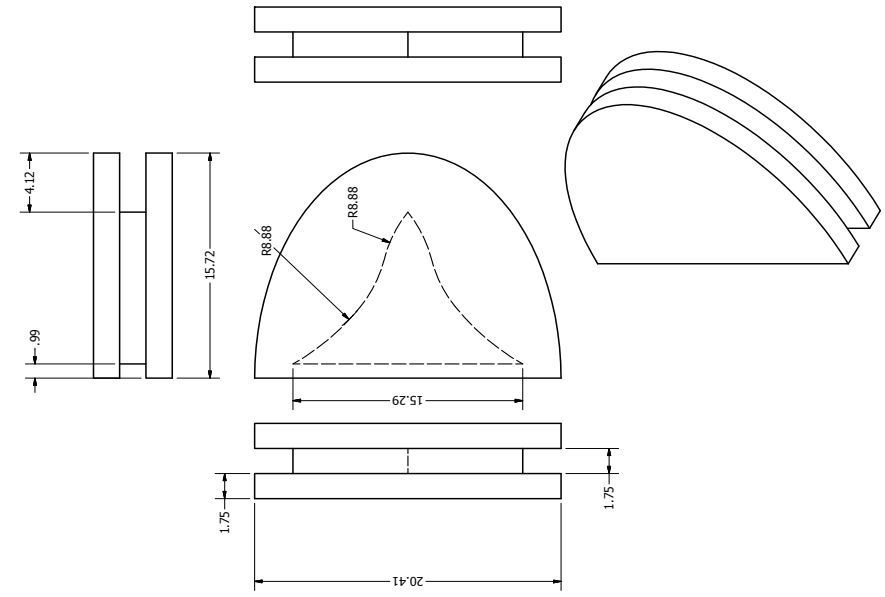

Figure 11: Concept 2: specific valve-like obturator for patients presenting an incomplete cleft palate (numbers in mm to 2 significant figures)

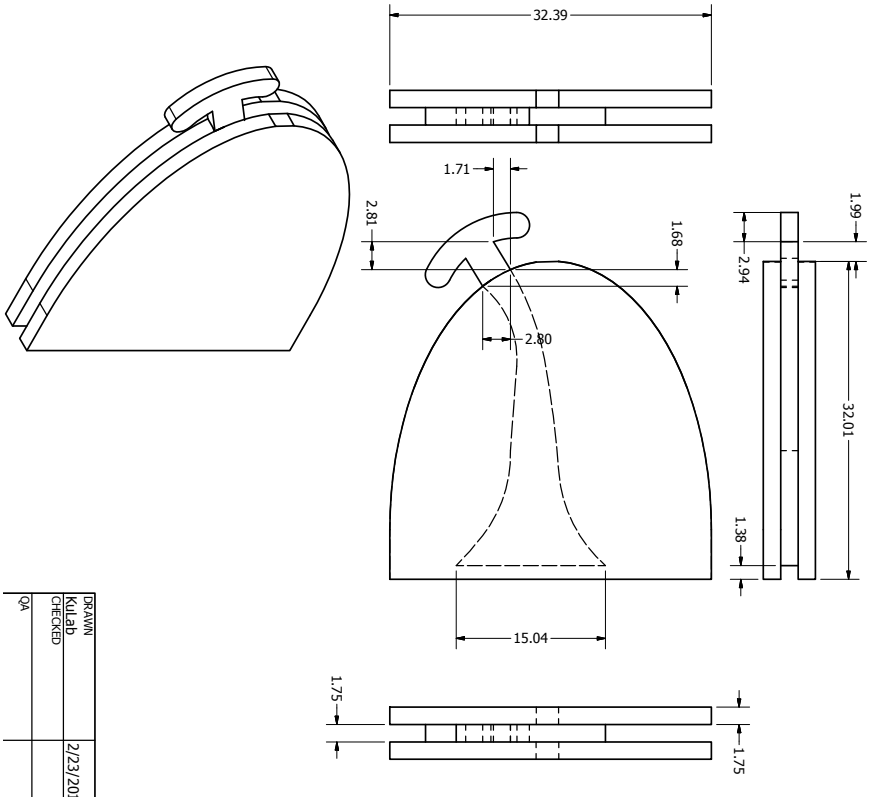

Figure 12: Concept 2: Specific valve-like obturator for patients presenting a complete, unilateral cleft palate (numbers in mm to 2 significant figures)

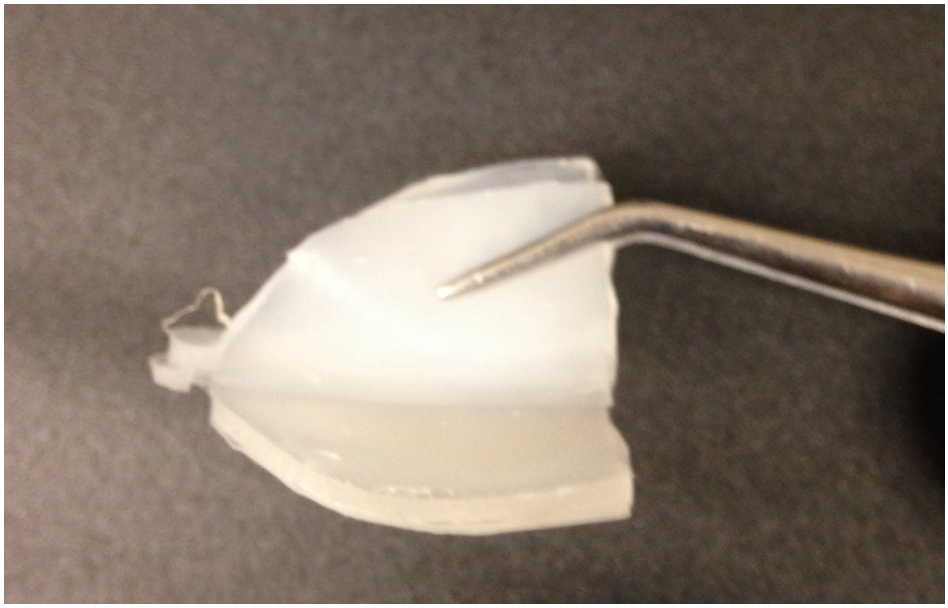

Figure 13: example of lab-fabricated PVA palatal obturator

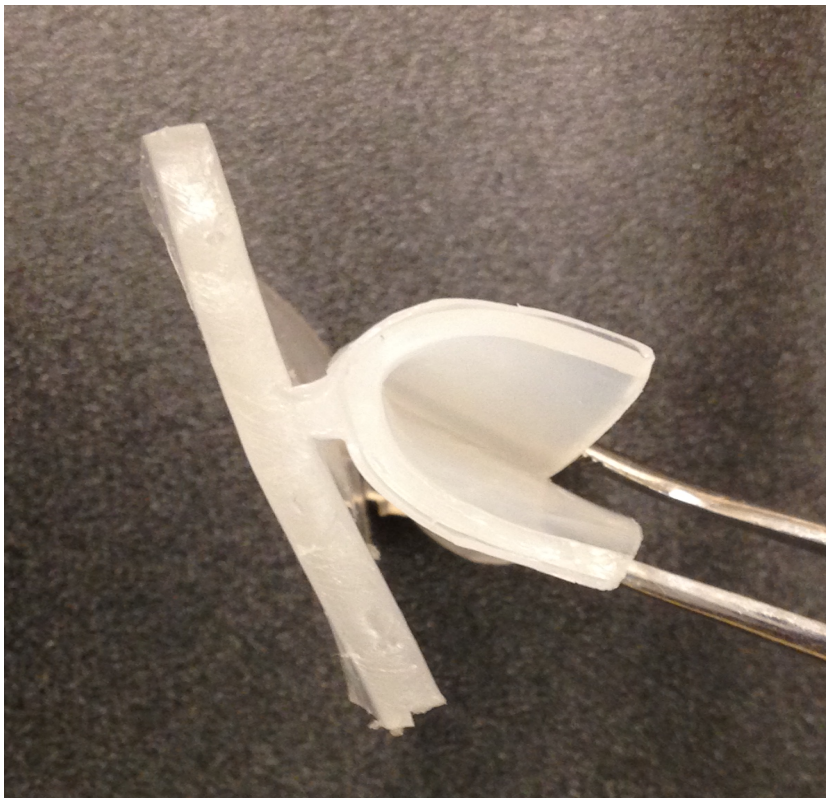

Figure 14: example of lab-fabricated PVA palatal obturator

Figure 15: example of lab-fabricated PVA palatal obturator (sample cut out manually with surgical scissors, hence ragged edge)

Concept 3:

After consulting a few clinicians, it was noted that a major anatomical concern with the previous concept was the presence of the nasal septum, a cartilaginous body that lies atop the hard palate. Having his would complicate the insertion of the valve, and the designed needed to take it into consideration. The superior flap of the valve was thus divided into two parts. This made the fabrication of the design even more convoluted. A more uniform design for this stage was to have a single flap with two posterior nodules between which the nasal septum would fit into.

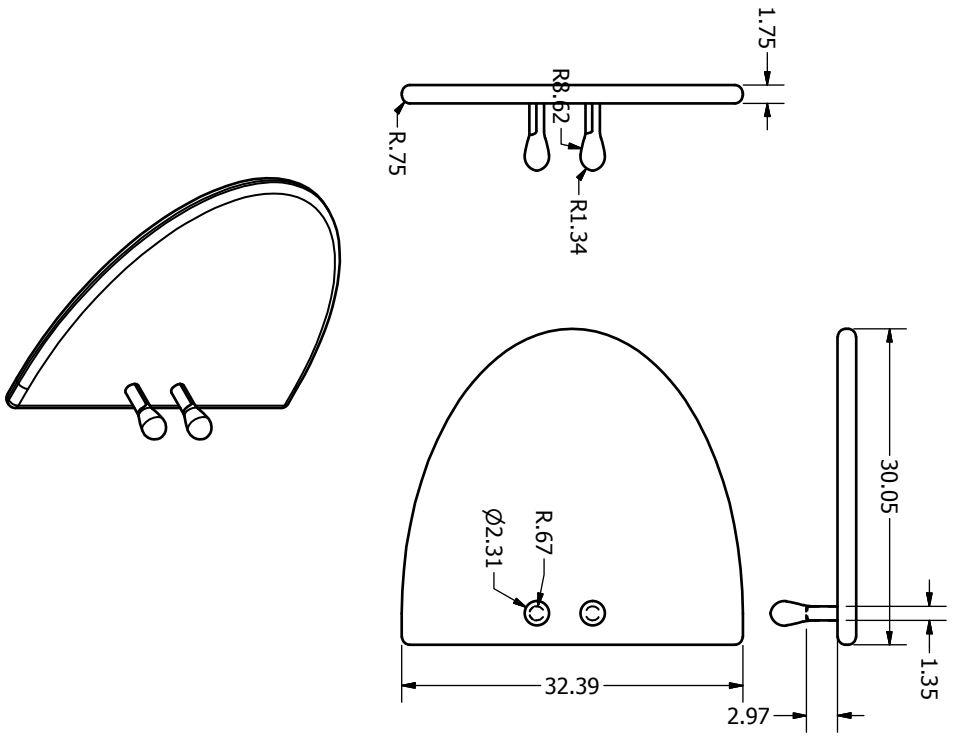

Figure 16: Concept 3: Uniform valve-like oburator with nodules (dimensions in mm, to 2 significant figures)

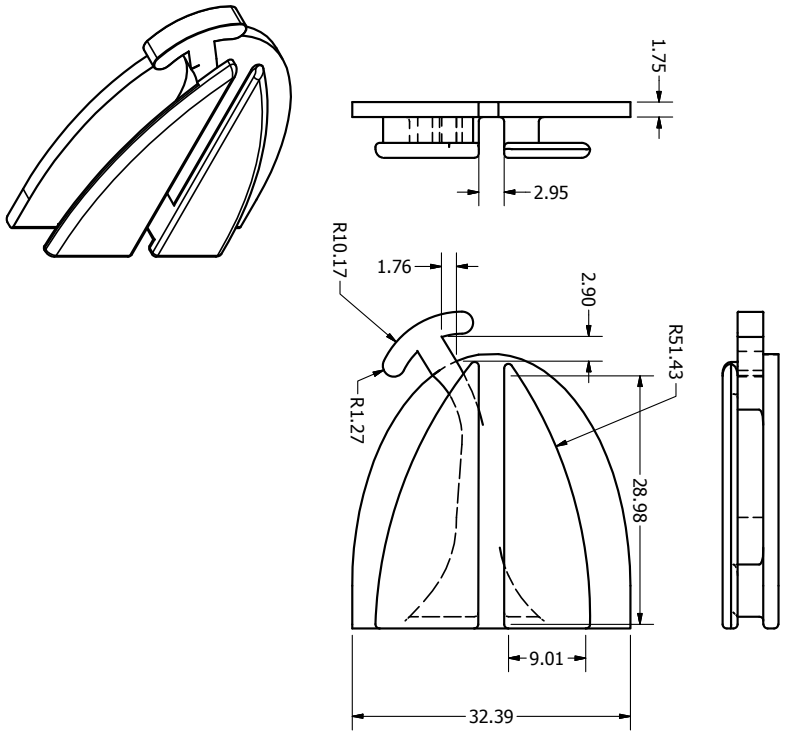

Figure 17: Concept 3: specific valve-like obturator for patients with unilateral cleft palate (dimensions in mm, to 2 significant figures)

Concept 4:

One of the major concerns from clinicians with the idea of the valve-like device was the risk of the patient accidentally aspirating the device, which could potentially lead to airway obstruction, and death in the worst-case scenario. Thoughts of sewing the flaps onto the soft palate, but because anesthesia would be required for this, the clinicians' preference is to simply operate on the patient and aim for palatal closure. However, because it is still a priority to delay the surgery on the palate until it has reached its optimal size, the clinicians' recommendations were to rather address velopharyngeal insufficiency, one of the main consequences of a cleft palate, and the discomfort caused by the current patient-specific acrylic palatal obturators.

This stage divided the project into two different products: a pharyngeal wall implant and a de novo palatal obturator.

The pharyngeal wall implant is designed as a block of PVA hydrogel with the elasticity of surrounding tissue (0.5-50kPa)[32] that can be carved by the surgeon based on the size of the velopharyngeal gap. Similarly, the palatal obturator's posterior acrylic part is to be replaced by PVA hydrogel. The softness and elasticity of this part would have a cushion-like effect on the cleft, an improvement from the current discomfort caused by acrylic. The different part of the obturator are held together by metal pins/wire, and because of PVA's softness, the posterior, U-shaped part of the metal wire would be threaded to enhance PVA-Metal adhesion after molding, and reduce the chances of the posterior part detaching from the obturator This block of PVA attached to the metal piece would be carved by the orthodontist to fit into the patient's cleft.

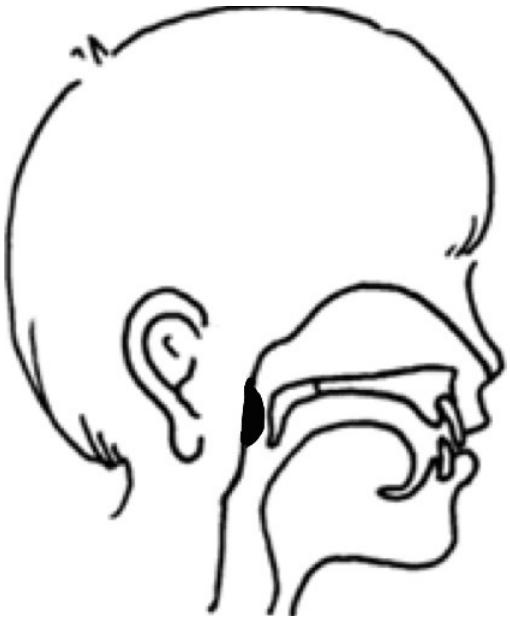

Figure 18: Display of pharyngeal wall augmentation via solid implant

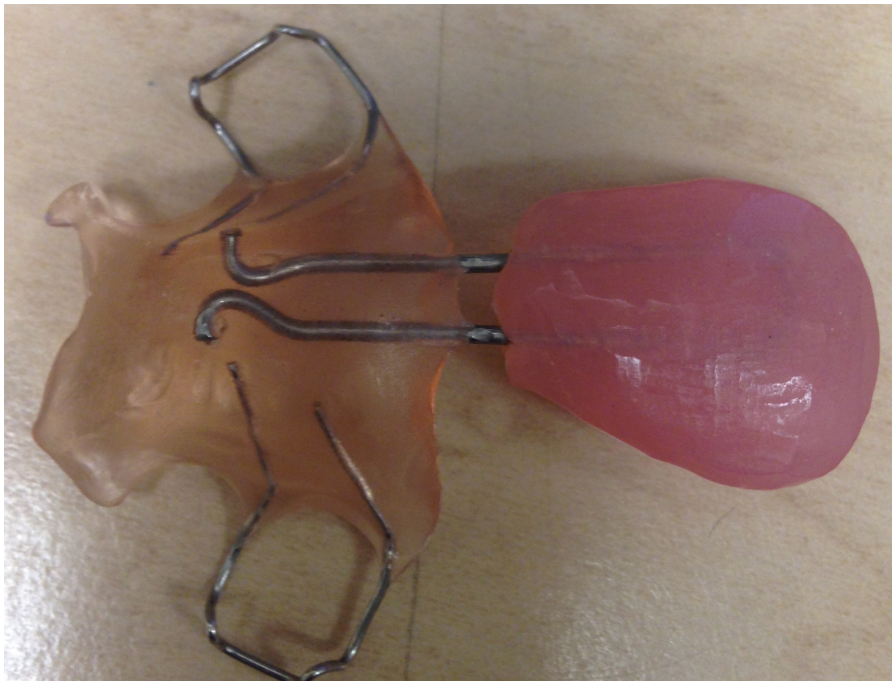

Figure 19: example of currently used acrylic obturator

4.4 Concept Selection

The selection of the final concept to address the problems this research aims to tackle was made using the following criteria: ease of fabrication, ease of implementation, likelihood of function without too high of a risk based on the recommendation of the surgeons consulted. The table below ranks each concept per category. The concept with the highest number is the chosen one.

Table 11: Grading of different concepts aiming to solve the speech problem caused by cleft palate

	Ease of implementation	Ease of fabrication	Likelihood to function without too high of a risk	Sum/Final Score
Concept 1	1	3	1	4
Concept 2	2	2	1	5
Concept 3	3	2	1	6
Concept 4	5	5	5	15

The table above shows a progression with each new iteration, but also a significant improvement with concept 4, which is the final concept being designed for this work. It entails, as aforementioned, a velopharyngeal implant to enhance speech production faculties, and the palatal obturator, creating a separation between the oral and nasal cavities.

Chapter 5: Risk Analysis

5.1 Overview of risk analysis

The risk analysis is an important portion of product development in many industries. With medical devices, it is even more important because these devices affect patients' lives through usage. A risk analysis is a mandatory portion of the FDA submission process for medical devices, and is very useful because it emphasizes the importance of safety of each medical device while indirectly minimizing costs related to potential recalls as well as lawsuits.

ISO 14971, FDA Guidance: Incorporating human factor into risk, FDA guidance: Premarketing Risk Assessment are some documents that can be used to draft a device's risk analysis. Identifying risks, evaluating them, determining control methods and re-evaluating them are the steps to thoroughly follow when drafting a risk analysis. When a risk cannot be completely eliminated, it is important to communicate such information to the end users, notably the insurance companies, hospitals, physicians and the patients. For Class 2 medical devices, the most commonly used approach is the FMEA (failure mode effect analysis). The goal with this method is to eliminate failures before they occur, and is focused on preventing defects, enhancing safety and increasing customer satisfaction. With the FMEA, each function of the device is evaluated and potential failure modes are brainstormed. The different effects of each failure modes are listed, and each is assigned a number for severity, occurrence and detectability [33]. For certain elements, it is not possible to assign a perfect level or occurrence or level of detectability, therefore an educated guess is taken. The next step is to calculate the RPN (risk priority number) per failure mode effect and prioritize them based on said RPN. Based on the risk

analysis rubric, the risks are addressed in order to reduce to RPN to an acceptable number.

Table 12: Detectability grading rubric[33]

Probability of detection	Description	Score
Very Low	Patient Unaware of product malfunction. Trained clinician unable to detect malfunction, surgical intervention may be required to detect malfunction	5
Low	Patient unaware of product malfunction. Trained Clinician unlikely to detect malfunction without specific technique	4
Moderate	Patient unlikely aware of malfunction. Clinician may require targeted investigation to detect problem	3
High	Patient may be aware of malfunction. Clinician aware of malfunction following routine exam	2
Very high	Patient fully aware of product malfunction	1

Table 13: Occurrence grading rubric [33]

Probability of occurrence	Description	Score
Likely	Incidence significantly more than 20%	5
Probable	Incidence approximately 5-20%	4
Possible	Incidence approximately 1-5%	3
Remote	Incidence less than 1%, occurrence contingent upon implant error, patient anomaly or unlikely event	2
Unlikely	Incidence less than 0.1%	1

Table 14: severity grading rubric[33]

Severity of failure	Description	Score
Very High	Death or serious injury likely without prompt medical intervention. Death may be imminent	5
High	Patient has moderate or chronic clinical symptoms in response to decreased performance (eg. continued swelling, ulcerations, redness, chronic pain)	4
Moderate	Patient may present with mild or intermittent clinical symptoms indicative of slightly reduced performance. Patient safety has not been compromised and product continues to function in intended manner (mild pain, redness, discomfort)	3
Low	Clinician may have an isolated test finding supporting decreased product performance but patient is asymptomatic/Patient may claim symptoms without clinical findings	2
Very Low	Neither patient safety nor product performance is affected	1

5.2 Pharyngeal Implant Risk Analysis

Table 15: Pharyngeal Implant risk analysis no 1

Design Function	Potential Failure Mode	Potential effects twitter of Failure Mode	Severity	Potential Causes of Failure	Detection	Current Design Controls	Occurrence	RPN	Recommended Action
Shortening the velopharyngeal gap	Implant migration	Implant progressing into GI track	3	Stitches from incision loosened	3	Insertion and securing method	1	9	Optimize the insertion and securing method
		Loss of function	3	Implant flattened/lost volume	3		1	9	
Dimensional Stability, Integrity	Dissolves or deteriorates	Migration of pieces, leading to progression into GI track	2	Hot beverages consumption	3	Suggestions/warnings to parent post surgery	2	12	N/A
	Implant distortion	Discomfort over time	3	Implant interaction with surrounding - pressure etc	1	Material properties	2	6	
	Implant split	Migration of pieces, aspiration - Airway obstruction	5	Patient poking suture lines with object	2	Suggestion`s/warnings to parent post surgery	2	20	
	Implant dries and shrinks in volume	Loss of function	2	Lack of local hydration of tissue	3	Selection of appropriate	2	12	
	Implant swells beyond acceptable measures	Partial obstruction of airways, migration	5	Implant hydration X exposure	2	Material properties	2	20	Material selection: pick known biocompatible material
Stay aseptic/Sterile	Bacterial growth and accumulation	Infection	4	Poor care pre-insertion	3	N/a	2	24	Mandatory surgeon training prior to implant purchase/procedure
	Contamination during surgical procedure	Infection	4	Careless insertion from surgeon	3		2	24	
		Infection and partial airway obstruction	4		3		1	12	
Size of the implant matching the need	Implant is too large	Partial airway obstruction	5	Untrained surgeon, careless selection of implant size	2		2	20	
	Implant is too small	Loss of function	2		3		2	12	
Correct orientation of implant	Surgeon misorients implant	Loss of function	2		3		2	12	
		Partial airways obstruction	5		2		2	20	

Correct placement of implant	Implant inserted in wrong tissue plane	Bleeding, infection	4		2		1	8	
	Implant inserted in wrong location on pharyngeal wall	Loss of function	2		3		2	12	
		Partial obstruction of airways	4		3		1	12	
Implant staying soft once implanted	Implant hardens	Discomfort	3	Cold beverage	1	Suggestions/warnings to parent post surgery	3	9	
Biocompatibility	Patient allergic to material used	Allergic reaction	3	Patient-specific	1	Selection of widely used material	1	3	N/A
		Anaphylactic shock	5		1		1	5	
Durability	Implant Creeping	Device failure	2	High temperature exposure	3	Material properties	1	6	N/A
	Implant Wear	Device failure	2	Repetitive loading	3	Material Properties	1	6	N/A
	Implant Fatigue	Device failure	2	Repetitive loading	3	Material Properties	1	6	N/A
	Implant corrosion	Device failure	2	Stress corrosion	3	Material Properties	1	6	N/A
	Implant yielding	Device Failure	2	High stress, repetitive loading	3	Material Properties	1	6	N//A

Risk Mitigation

The scores for each potential effect of failure mode based on severity, occurrence and detectability were determined after consulting a team of surgeons at Emory University School of Medicine Department of Surgery and a team of engineers at Georgia tech. Based on the first risk analysis that was done with this device, it was deemed important to address the potential failure modes that presented an RPN greater than 15. Those were the failure modes that could lead to patient death via airways obstruction or acute infection. Requiring appropriate training for the surgeons, designing implant insertion and securing method were the main recommended actions that would significantly reduce the chances of these failure modes occurring. A second risk analysis was done based on these recommended actions, and all RPNs were under 15, which was the goal set for this research (see table below). The highest risks after the second risk analysis was performed are the following:

- Implant too large, potentially leading to airway obstruction
- Incorrect implant orientation/placement, potentially leading to airway obstruction
- Implant contamination during surgical procedure, potentially leading to infection and airway obstruction

Table 16: Pharyngeal Implant second risk analysis

Design Function	Potential Failure Mode	Potential effects twitter of Failure Mode	Severity	Potential Causes of Failure	Detection	Current Design Controls	Occurrence	RPN	Recommended Action
		Implant progressing into GI track	3	Stitches from incision loosened	3		1	9	
Shortening the velopharyngeal gap	Implant migration	Loss of function	3	Implant flattened/lost volume	3	Insertion and securing method	1	9	Improving the insertion and securing method
	Dissolves or deteriorates	Migration of pieces, leading to progression into GI track	2	Hot beverages consumption	3	Suggestions/warnings to parent post surgery	1	6	
Implant to not significantly change in size and shape	Implant distortion	Discomfort over time	3	Implant interaction with surrounding - pressure etc	1	Material properties	2	6	
	Implant split	Migration of pieces, aspiration - Airway obstruction	5	Patient poking suture lines with object	1	Suggestions/warnings to parent post surgery	1	5	N/a
	Implant dries and shrinks in volume	Loss of function	2	Lack of local hydration of tissue	3	Sterilization of implants pre-packaging	1	6	
	Implant swells beyond acceptable measures	Partial obstruction of airways, migration	5	Implant hydration X exposure	2	Material properties	1	10	Material selection: pick known biocompatible material
	Bacterial growth and accumulation	Infection	4	Poor care pre-insertion	2		1	8	
Stay aseptic/Sterile	Contamination during surgical procedure	Infection	4	Careless insertion from surgeon	2		1	8	
		Infection and partial airway obstruction	5		2		1	10	
Size of the implant matching the need	Implant is too large	Partial airway obstruction	5	Untrained surgeon, careless selection of implant size	2		1	10	
	Implant is too small	Loss of function	2		3		1	6	
Correct orientation of implant	Surgeon misorients implant	Loss of function	2		3		1	6	Mandatory surgeon training prior to implant purchase/procedure
		Partial airways obstruction	5		2	N/a	1	10	

Correct placement of implant	Implant inserted in wrong tissue plane	Bleeding, infection	4		2		1	8	
	Implant inserted in wrong location on pharyngeal wall	Loss of function	2		3		1	6	
		Partial obstruction of airways	5		2		1	10	
Implant staying soft once implanted	Implant hardens	Discomfort	3	Cold beverage	1	Suggestions/warnings to parent post surgery	3	9	
Biocompatibility	Patient allergic to material used	Allergic reaction	3		1		1	3	
		Anaphylactic shock	5	Patient-specific	1	Selection of widely used material	1	5	N/a
Durability	Implant Creeping	Device failure	2	High temperature exposure	3	Material properties	1	6	N/A
	Implant Wear	Device failure	2	Repetitive loading	3	Material Properties	1	6	N/A
	Implant Fatigue	Device failure	2	Repetitive loading	3	Material Properties	1	6	N/A
	Implant corrosion	Device failure	2	Stress corrosion	3	Material Properties	1	6	N/A
	Implant yielding	Device Failure	2	High stress, repetitive loading	3	Material Properties	1	6	N//A

5.3 Palatal Obturator Risk Analysis

Table 17: Palatal obturator risk analysis number 1

Design Function	Potential Failure Mode	Potential effects of Failure Mode	Severity	Potential Causes of Failure	Detection	Current Design Controls	Occurrence	RPN	Recommended Action
		Progressing into the GI track	3	Looseness of obturator, patient mishandling	3		2	18	Design appropriate hooks to anchor posterior part
	Part migration	**Obstruction of airways**	**5**		**2**	Threaded metallic hook	**3**	**25**	
Posterior part to stay anchored to the frame	Soft/posterior part torn by metal hook	Product failure	3	Patient mishandling	3	Material properties	2	18	
		Progression into GI track	3	Patient consuming hot beverages	3		2	18	Select non-biodegradable material
Removability	Dissolves or deteriorates	Obstruction of airways	5	Sharp edges of the obturator, pressure	1		2	10	Remove obturator at night
Size of the posterior part matches the cleft/fistula	Posterior part too big	Ulcerations	3	Surgeon misjudgment	1	Selection of widely used material in humans	2	6	Surgeon training prior to obturator installation
		Allergic Reaction	3	Patient specific	1	Selection of widely used material in humans	2	6	Select known biocompatible material, test for potential allergies
Biocompatibility	Patient allergic to material used	Anaphylactic shock	5	Patient specific	1	Sterilization prior to insertion, daily cleaning	2	10	
Stay aseptic/sterile	Bacterial growth and accumulation	Infection	4	Poor oral hygiene, poor care of obturator	2	Obturator to be removed and cleaned daily	1	8	
Posterior part of implant to not significantly change in shape or size	Posterior part shrinks	Failure of device	3	Patient lets obturator @ open air	1	Obturator to be stored in a humid environment when not worn to prevent drying	2	6	Warnings to parents and patients
	Posterior part swells beyond acceptability	Ulcerations	3	Patient lets obturator sit in solution too long	1	Obturator to not be kept in solution beyond 10 hours	2	6	
	Posterior part distorts	Ulcerations, failure of device	3	Patient chews on, plays with obturator	1	n/a	1	3	
Durability	Wear	Device Failure	3	Cyclic loading, constant stress on obturator	1	Materials selection, warning to users	1	3	N/A
	Corrosion			Exposure to corrosive liquids	1	Materials selection, warning to users	1	3	
	Fatigue	Device failure	3	Cyclic loading, constant stress on obturator	1	Materials selection, warning to users	1	3	
	Yielding	Device failure	3	Patient bending, chewing, pulling obturator apart	1	Materials selection, warning to users	1	3	

Palatal Obturator:

This is a device that can be removed in a home setting by a caretaker or the patient himself. This therefore presents little alarming risk. However, because PVA is significantly less elastic than acrylic, there is a chance that the posterior part gets torn or slips off the metal anchor, which may lead to aspiration and potentially death via airways obstruction, with an RPN of 25. In order to address this risk, the metal anchor used is designed to have u-shaped hook in order to create more resistance in case the softer part is pulled. This would significantly reduce the occurrences, and lead to an RPN below 15.

After the risk mitigation, the potential failure modes that present the highest risk are the following:

- Deterioration of the obturator potentially leading to part migration and airway obstruction
- Patient allergic to material selected, potentially leading to an anaphylactic shock

Table 18: Palatal obturator risk analysis no 2

Design Function	Potential Failure Mode	Potential effects of Failure Mode	Severity	Potential Causes of Failure	Detection	Current Design Controls	Occurrence	RPN	Recommended Action
Posterior part to stay anchored to the frame	Part migration	Progressing into the GI track	3	Looseness of obturator, patient mishandling	3	Threaded metallic hook	1	9	Design appropriate hooks to anchor posterior part
		Obstruction of airways	5		2		1	10	
	Soft/posterior part torn by metal hook	Product failure	3	Patient mishandling	3	Material properties	1	9	
Removability	Dissolves or deteriorates	Progression into GI track	3	Patient consuming hot beverages	3		1	9	Select non-biodegradable material
		Obstruction of airways	5	Sharp edges of the obturator, pressure	1		2	10	Remove obturator at night
Size of the posterior part matches the cleft/fistula	Posterior part too big	Ulcerations	3	Surgeon misjudgment	1	Selection of widely used material in humans	2	6	Surgeon training prior to obturator installation
Biocompatibility	Patient allergic to material used	Allergic Reaction	3	Patient specific	2	Selection of widely used material in humans	1	6	Select known biocompatible material, test for potential allergies
		Anaphylactic shock	5	Patient specific	2	Sterilization prior to insertion, daily cleaning	1	10	
Stay aseptic/sterile	Bacterial growth and accumulation	Infection	4	Poor oral hygiene, poor care of obturator	2	Obturator to be removed and cleaned daily	1	8	
Posterior part of implant to not significantly change in shape or size	Posterior part shrinks	Failure of device	3	Patient lets obturator @ open air	1	Obturator to be stored in a humid environment when not worn to prevent drying	2	6	Warnings to parents and patients
	Posterior part swells beyond acceptability	Ulcerations	3	Patient lets obturator sit in solution too long	1	Obturator to not be kept in solution beyond 10 hours	2	6	
	Posterior part distorts	Ulcerations, failure of device	3	Patient chews on, plays with obturator	1	n/a	1	3	

Durability	Wear	Device Failure	3	Cyclic loading, constant stress on obturator	1	Materials selection, warning to users	1	3	N/A
	Corrosion			Exposure to corrosive liquids	1	Materials selection, warning to users	1	3	
	Fatigue	Device failure	3	Cyclic loading, constant stress on obturator	1	Materials selection, warning to users	1	3	
	Yielding	Device failure	3	Patient bending, chewing, pulling obturator apart	1	Materials selection, warning to users	1	3	

Chapter 6: Verification testing

6.1 Tensile Strength Test

Experiment protocol

The tensile strength and tear strength of each hydrogel are particularly important because it affects the removability of the implants, a critical design characteristic. The minimum tensile strength for each implant was 25 kPa determined experimentally by mimicking the action of pulling a sample attached to a load gauge, while the tensile strength of adipose tissue between 2 and 24 kPa [34], and is used as a determining parameter. The reason why adipose tissue is used as a reference point here is that current pharyngeal augmentations are performed by injecting adipose tissue or platelet rich plasma into the pharyngeal wall. The samples made (normal saline and 1.8% NaCl in the solution) were tested immediately after 6 freeze-thaw cycles, and did not undergo any drying or swelling.

The tensile strength tests were conducted using an extensometer (Instron materials testing machine). Once the dimensions (thickness and width) of the specimens were recorded, they were placed into the grips of the extensometer, and the original length of the specimens was also recorded. Because the grips are metallic and present a rough texture, damage of the specimen may occur so in order to avoid such event, 0.5 mm thin cardboard sheets were placed on the outer surfaces of the specimens' grip ends. The specimens were adjusted symmetrically to distribute tension uniformly across the sections, and the grip was tightened to prevent slippage. After the specimen is placed into the extensometer's grips, the test is launched using the software supporting the extensometer. The specimen is pulled until it breaks, or tears along the nick in the case of the tear strength test. The data recorded by the software includes the load is applied to the specimen continuously until yield, the extension of the gauge. This testing apparatus software also calculates critical information such as yield stress and maximum strain, based on the recorded load and the dimensions originally recorded. For verification purposes, the yield stress and maximum stress were calculated manually using the recorded loads, dimensions and extension from each test. The tear strength was calculated similarly, using the maximum load applied and the thickness of each specimen. All specimens were pulled at a rate of 500 mm/min[35].

Figure 20: Display of extensometer test for tensile strength

Stress Equation: $\sigma = \frac{F}{w \times t}$

Strain Equation: $\varepsilon = \frac{\Delta L}{L}$

Elongation Equation: $E = \varepsilon_{max} \times 100$

Results:

Samples of 1.3%, 2.5%, 5%, 7% and 10% and 20% weight PVA cryogel were tested in tension (n=3) to determine each tensile strength.

The tensile strength is the maximum stress a sample can bear in tension. The values were determined by following the ASTM D412-06a standards. The tensile strength of PVA samples within this concentration range (4.8-348 kPa) follows an exponential growth with respect to the weight percent concentration of polymer in the hydrogel solution. We

also compared the tensile strength of hydrogel samples depending on the amount of NaCl in the hydrogels, and samples made with 1.8% NaCl have a slightly lower tensile strength compared to those made with 0.9% NaCl tensile strength. The minimum tensile strength for these samples was set as 25 kPa.

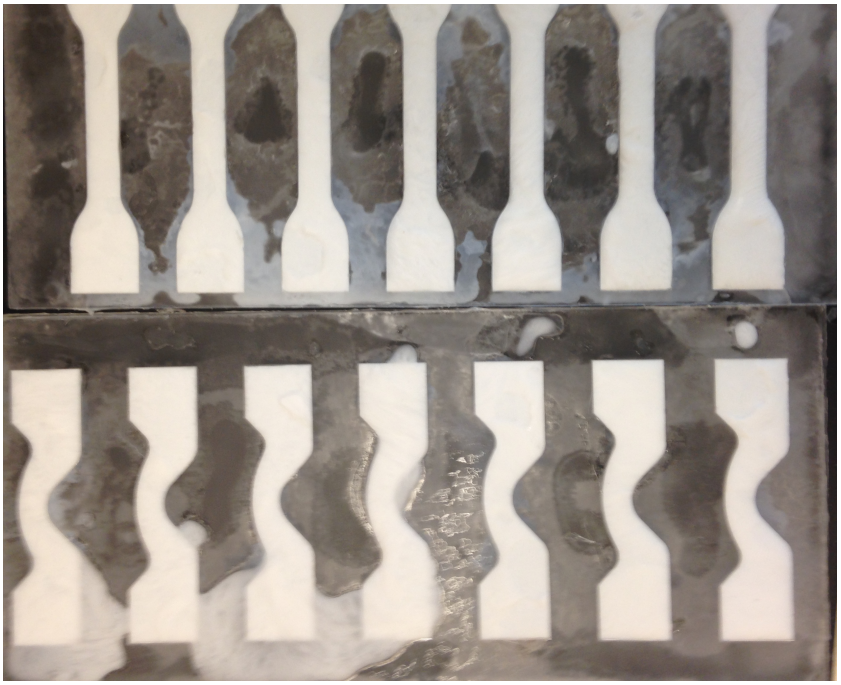

Figure 21: Tensile (top) and tear (bottom) strength test samples (white), following ASTM standards.

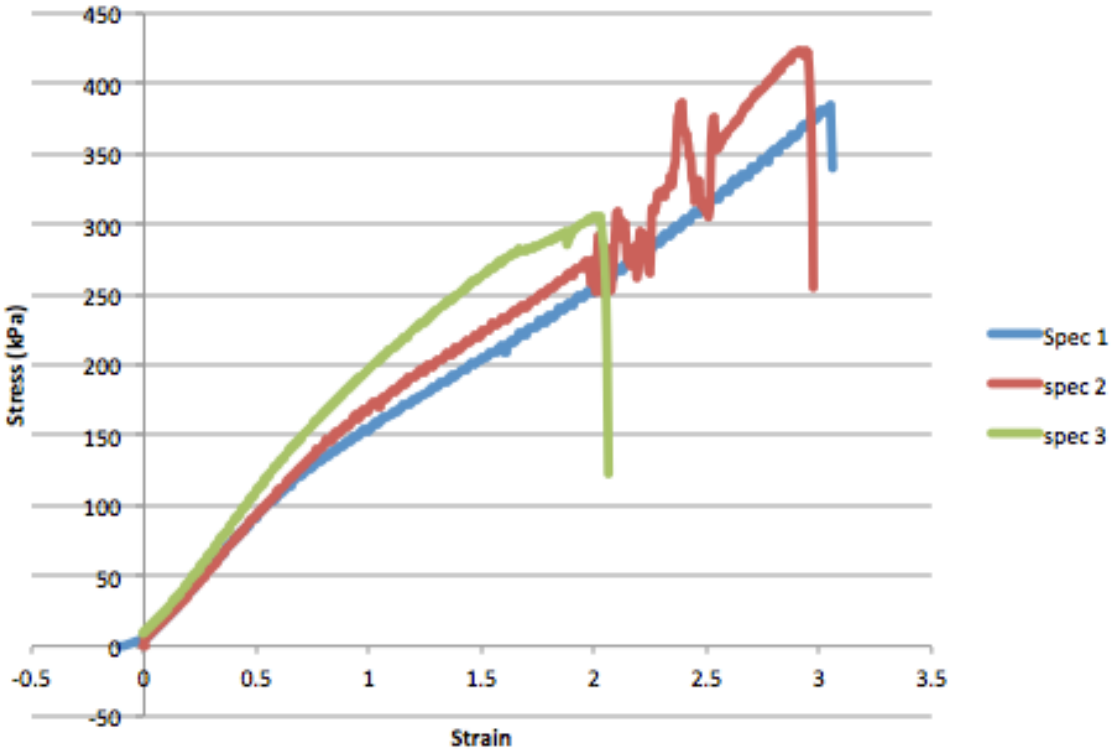

Figure 22: Sample stress-strain curve (20% PVA)

Table 19: Tensile strength of PVA samples made with 0.9% and 1.8% saline solution (not acceptable in grey: below 25 kPa)

PVA Concentration	Tensile Strength (kPa) for samples with 1.8% saline solution	Tensile Strength (kPa) for samples made with 0.9% saline solution
1.30%	N/A	4.8
2.50%	N/A	8.5
5%	28.33	33
7.50%	40.7	60.3
10%	71.3	109
20%	N/A	348

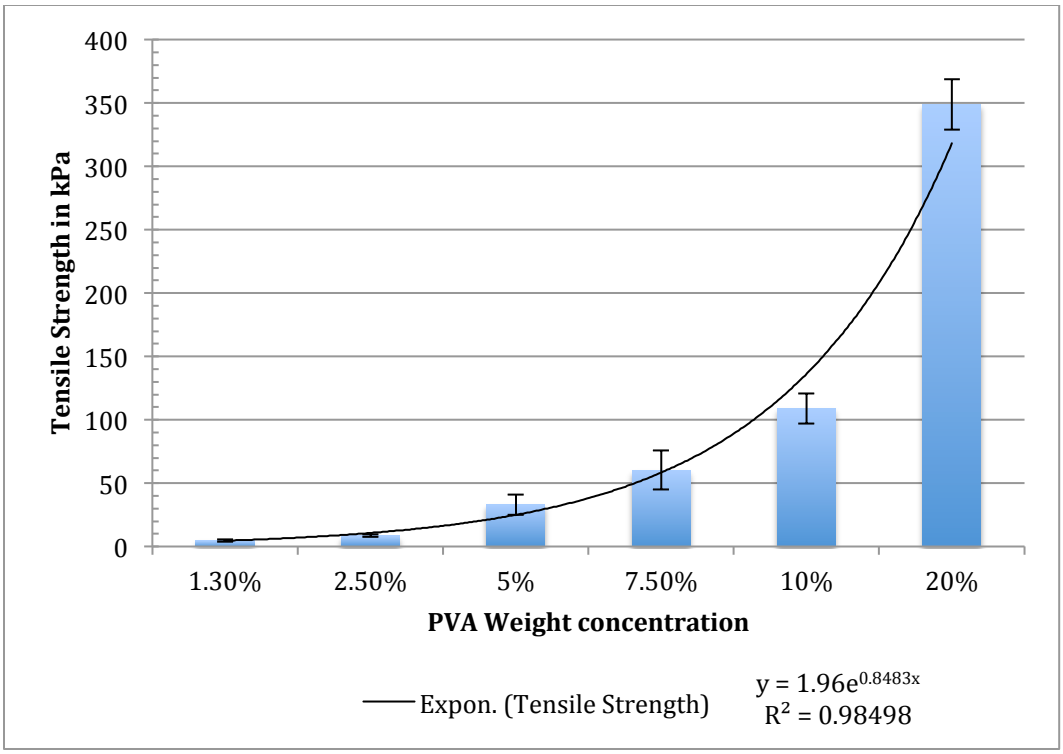

Figure 23: Tensile strength of PVA samples at different polymer concentrations (made with normal Saline)

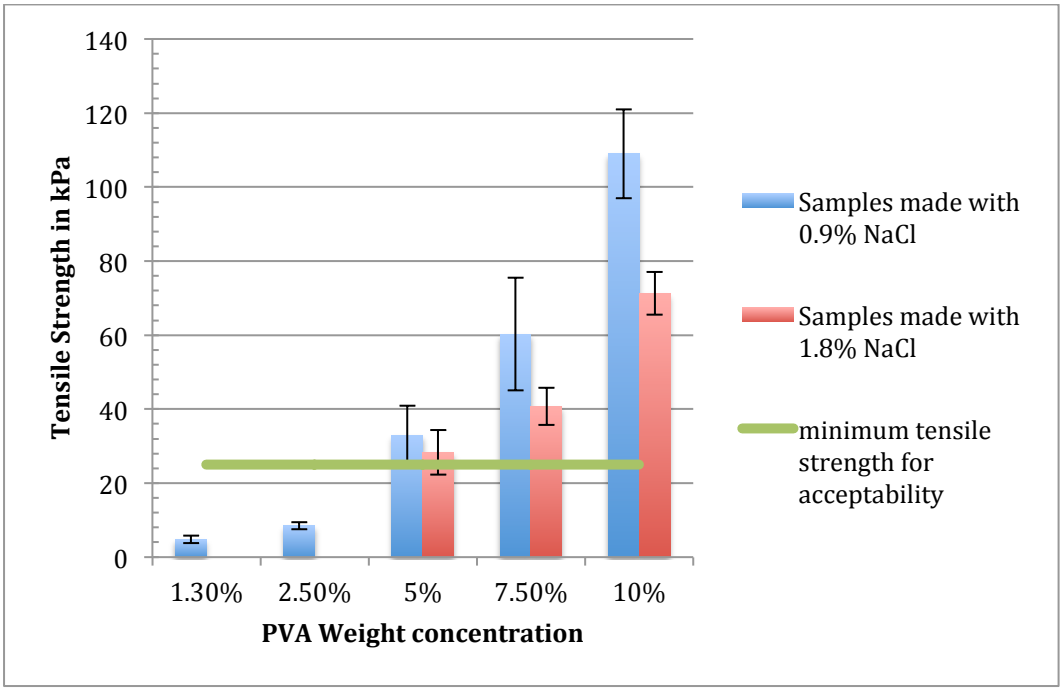

Figure 24: Tensile strength of PVA samples made with 0.9% saline and 1.8% Saline after freeze-thaw cycles

6.2 Tear Strength Test

Experiment protocol

The tear strength tests were performed following the ASTM D624-00 (Die B) protocol. Specific molds were manufactured out of acrylic, yielding dog-bone shaped samples. The tear strength tests were performed following the ASTM D624-00 (Die B) protocol. The acrylic mold manufactured for the tear strength tests yielded zig-zag shaped samples, per the standard prescription. Specifically for the tear strength test, a 1mm nick was made at the peak of each specimen's curvature. The samples made (normal saline and 1.8% saline) were tested immediately after 6 freeze-thaw cycles, and without any drying. Similarly to the tensile strength tests, the tear strength tests were performed using the Instron materials testing machine. The differences between the tear strength test and the tensile strength test protocols are the shape of the sample (see figure 20) as well as the data collected from the samples. For the tear strength test, the thickness of the specimens is measured with a caliper, before the extensometer pulls the specimen at a rate of 500 mm/s, and the testing apparatus' software records the load applied. The load at complete break is divided by the specimen's thickness, and the tear strength of the specimen is obtained.

Tear Strength Equation: $T_s = \frac{F_{max}}{t}$ (t= thickness, F_{max} = maximum load)

Results

The tear strength was determined following ASTM D 412 standards. It is a good measure of how well a material resists the growth of any cut under tension, and as aforementioned, is measured in N/mm for this study. We observe an exponential growth in tear strength as the weight percent concentration of PVA in the cryogel solution increases. Based on the results below, 5% PVA is more than four times stronger in tear

than 1.3%, while 10% PVA is almost 20 times stronger than 1.3%. The tear strength of samples of 1.3% and 2.5% PVA are significantly below the acceptability criteria (see table 19) whereas samples of 5%. 7.5% and 10% PVA meet this requirement.

Table 20: Tear Strength of PVA samples made with 0.9% and 1.8% Saline solution (N/A = data not available)

PVA Percent Weight	Tear Strength (N/mm) for samples made with 1.8% Saline Solution	Tear Strength (N/mm) for samples made with 0.9% Saline Solution
1.30%	N/A	0.24
2.50%	N/A	0.32
5%	0.789	1.05
7.50%	1	2.29
10%	2.23	4.1
20%	N/A	8.92

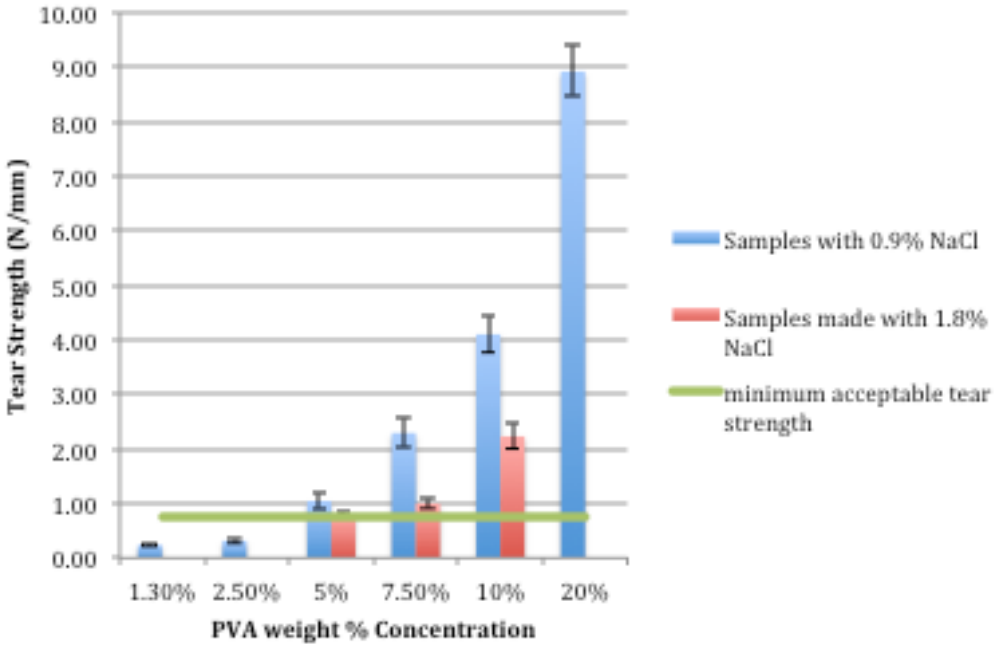

Figure 25: Tear strength of samples made with 0.9% saline and 1.8% saline after 6 freeze-thaw cycles

6.3 Compression Test

Experiment protocol

The compression test on hydrogels leads to determining the modulus of elasticity of the hydrogels at different PVA weight concentrations, in order to best mimic human tissue softness. This will help selecting which concentration will give the implants a more natural, comfortable feeling. There are different types of tests used to determine the softness of materials, and the modulus of elasticity is the most common measure used to quantify it. The samples made (normal saline and 1.8% NaCl in the solution) were tested immediately after 6 freeze-thaw cycles, and did not undergo any drying or swelling. The Instron material testing machine was used to perform the compression test, and the specimens tested were obtained by cutting out circle-shaped samples out of thick sheets of PVA cryogel cured in flat trays. Once the samples have been cut out, they are measured with a caliper (diameter and thickness), placed at the center of a flat support sheet (metal), and the head of compression machine is brought to right above the sample. The test is then started. Similarly to the tensile test procedure, the software assisting the testing apparatus records the load and extension of the gauge. Based on the raw data, the strain and stresses are determined, which leads to calculating the modulus of elasticity (figure 26).

$$\text{elastic modulus} = \frac{\text{stress}}{\text{strain}}$$

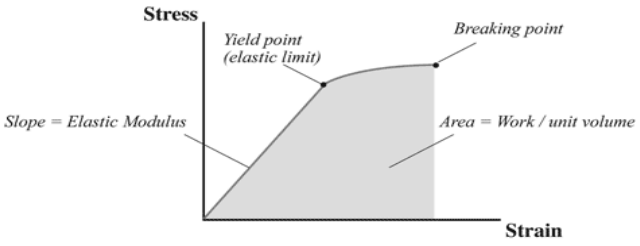

Figure 26: determining the elastic modulus of a specimen based from the Stress-Strain curve

Modulus of Elasticity

The compressive modulus of elasticity is determined by observing the stress-strain curve of each sample tested in compression and determining the slope of the region of the curve considered to be elastic. The values are averaged per samples to obtain the final modulus of elasticity. The compressive elasticity of PVA at different concentrations follows a linear growth with a high coefficient of correlation (R = 0.97), increasing with the weight concentration of polymer in the solution.

Results:

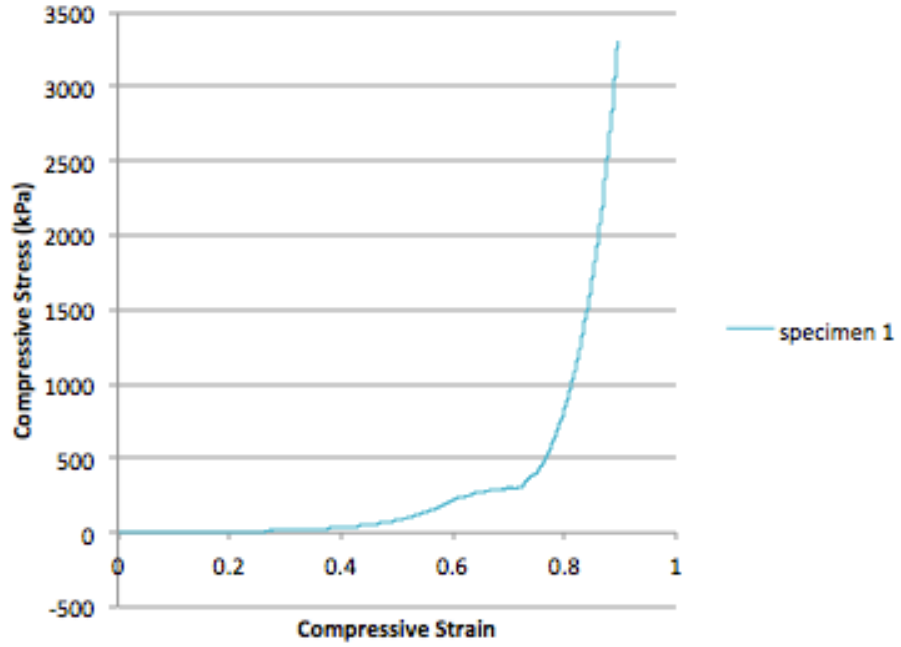

Figure 27: Sample stress strain curve for compression test on PVA samples used to determine compressive modulus of elasticity

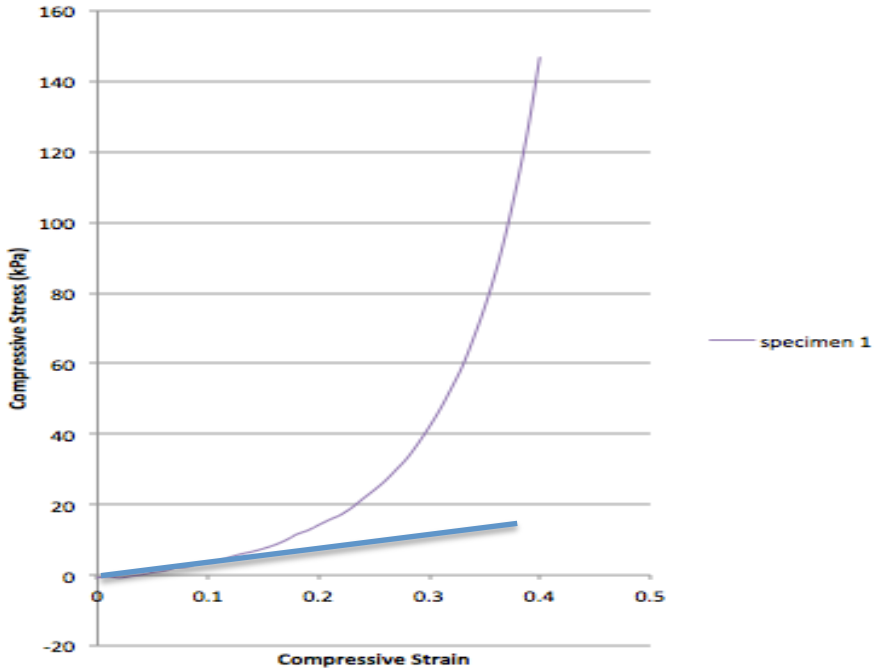

Figure 28: Sample stress strain curve for compression test on PVA samples (lower stress). The slope of the blue line (linear.elastic portion) is the modulus of elasticity of the specimen

Table 21: modulus of elasticity of PVA samples made with 0.9% saline, and projected modulus of elasticity of PVA samples made with 1.8% Saline

Concentration	Young Modulus kPa (samples made with 1.8% Saline Solution)	Young Modulus kPa (samples made with normal 0.9% Saline Solution)
1.30%	N/A	7.73
2.50%	N/A	11.65
5%	46.21	51.35
7.50%	55.04	64
10%	68.72	80
20%	N/A	240

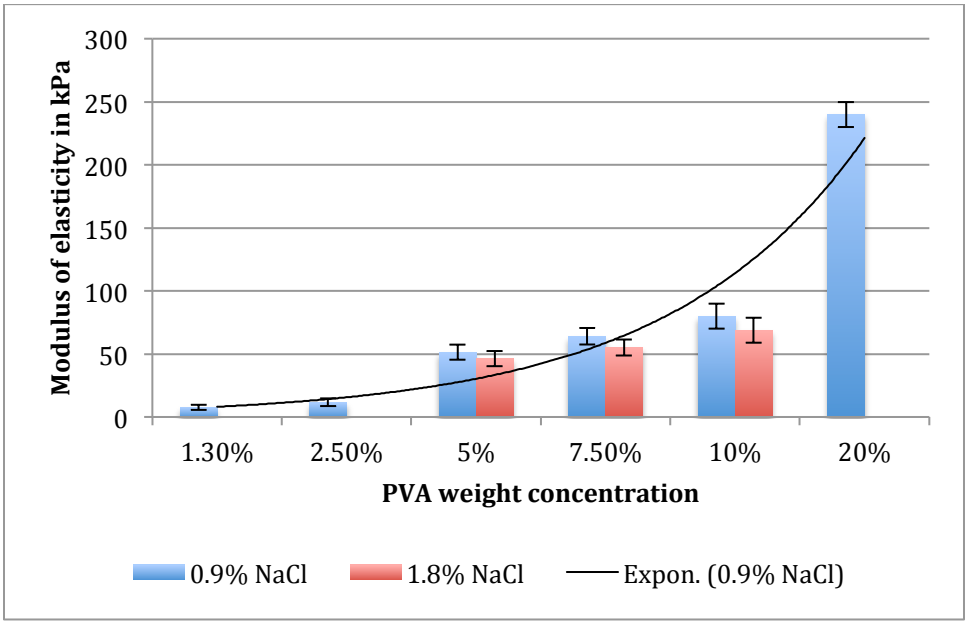

Figure 29: Compressive elasticity of PVA samples made with 0.9% saline, acceptable Elasticty ranging between 1 and 55 kPa , based on adipose tissue elasticity.

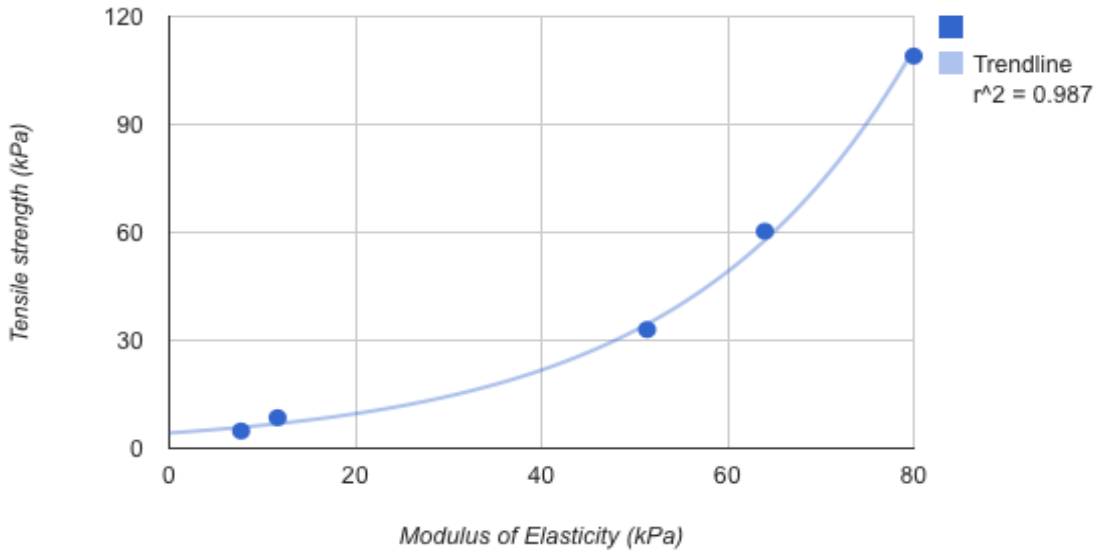

Figure 30: Correlation curve between tensile strength and compressive elastic modulus of PVA samples, R = 0.99.

6.4 Durometer Hardness:

Experiment protocol

Another tool used to quantify/qualify the softness of the hydrogels in this project was the Shore Durometer Type A [36]. Durometers are use to determine the hardness of materials, and the type A durometer specifically for soft rubbers and elastomers. The durometer's needled is pressed into the material of a minimum thickness of 6.4 mm for at least 15 seconds, and in the case of an electronic durometer, the number appearing on the screen is the hardness.

Results

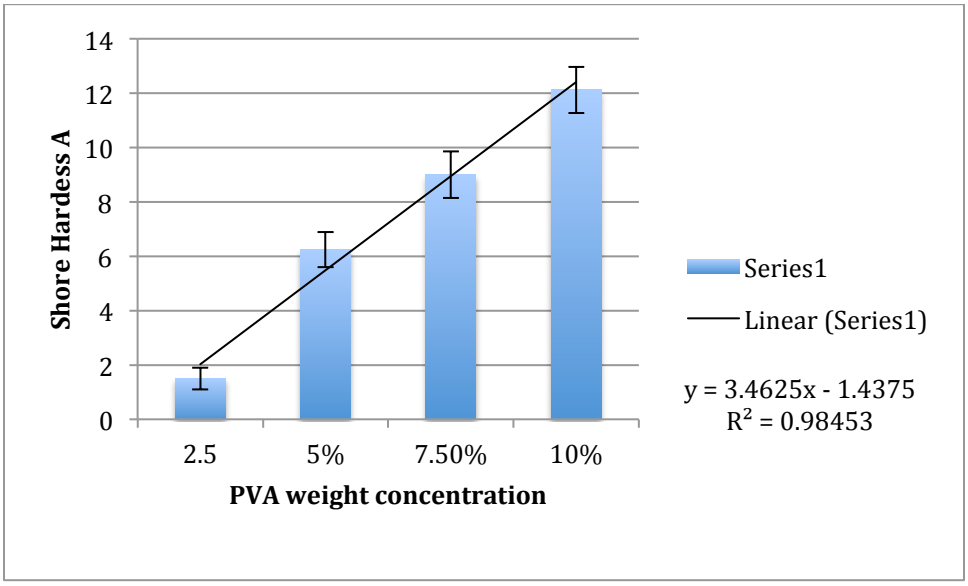

Figure 31: Shore A durometer hardness per PVA concentration (no difference recorded with changes in salt content)

Shore durometer hardness, used to quantify the hardness of soft elastomers was used to supplement the elasticity criteria selected as an end point to determine the ideal PVA concentration for each implant. On scale A, the hardness of PVA follows a linear growth with respect to the polymer concentration in the hydrogel solution.

6.5 Swellability

Experiment protocol

Hydrogels tend to swell when submerged in water. This is an important characteristic because the customer (surgeon and patient) would like to know how much swelling to expect after the implant has been inserted. Additionally, because water content changes the mechanical properties of the hydrogels, the swelling can be used to design the most suitable implant. For example, implants of a higher elastic modulus (and PVA content) may be easier to insert, but may not feel as natural as needed. If the implant can swell to a level or hydration that can significantly lower its elastic modulus, this may help with material selection. One can change the concentration of polymer in an implant by starting with a certain concentration, or starting with a lower concentration and drying the product after casting. For example, PVA samples can be made at a set concentration C1, and then densifying the sample by drying the samples in an oven at a controlled temperature of 70 degrees Celcius. The dried concentration C2 may be calculated by weighing, assuming that only water is evaporating. A target weight can be set, based on the desired concentration for the dense sample. After the dense sample can be placed in either normal saline or water. As the implant absorbs water, it swells. Swelling is then defined as the pre-set water content of the sample was simply based on what concentration of PVA yielded the adequate softness for the implants.

For example, 2.5% PVA samples (water content 97.5%) were dried in the oven and progressively weighted until they lost sufficient amounts of water to become 7.5% PVA (92.5% water content). After being dried, the samples were submerged in a normal saline and then weighted to observe a change in weight. The measurement is then

reported as the increase in weight over time. The increase in weight is attributed to water absorption or an increase in water content.

Alternatively, one can observe the water increase in samples that are not initial dried. The other samples observed in swelling (Swelling B) did not go through the drying process, but rather were submerged in normal saline immediately after the freeze-thaw cycles, and observed over the course of 48 hours.

PVA Swelling

PVA is a hydrophilic polymer, and its cryogels tend to grow in volume when surrounded by a hydrated environment. They also shrink in volume when exposed to a dry environment. Few factors affect the swelling of PVA hydrogels, including the osmotic pressure and the crosslinking of the hydrogels. It was observed by this study that an increased concentration of PVA in the hydrogel solution would lead to more swelling. Additionally, more swelling is observed in hypotonic solutions compared to isotonic solutions for hydrogels. Swelling is defined as the ratio between the change in weight and the original weight of the sample.

Results:
Dried samples (Swelling A):

After drying 2.5% PVA samples into 7.5% PVA and submerging them in a normal saline bath, we observed swelling in the 0.9% material and 1.8% material of approximately 7%.

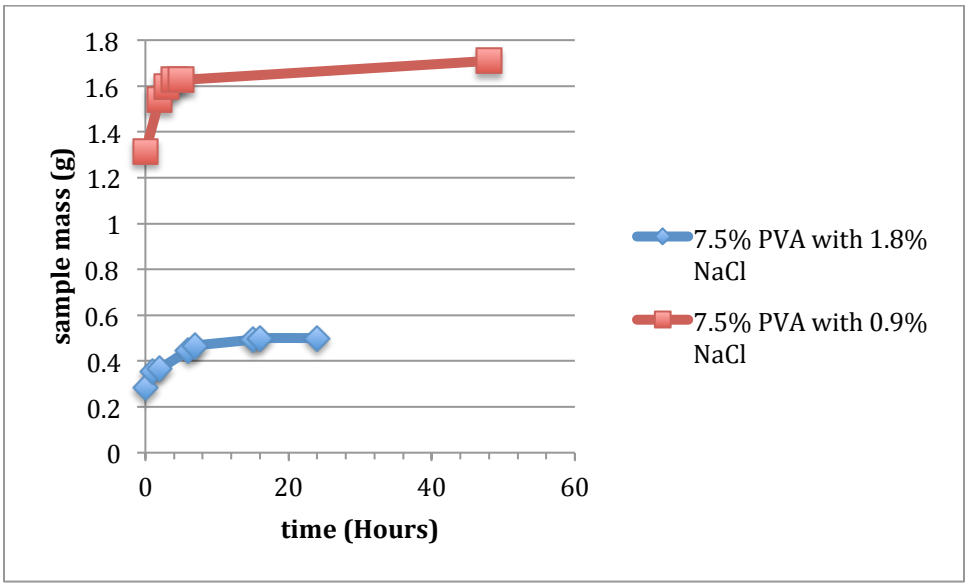

Figure 32:Mass of 7.5% PVA samples over time during swelling A (samples weigh respectively 0.3 and 1.31 grams in average)

In this experiment, the weight of samples was measured until a plateau (less than 0.2% swelling per hour) was reached for each case. Looking at the trend of the increase in weight over time appears somewhat misleading, thus the water content of the samples was calculated by adding the change in in weight of the sample to the original water content and dividing the result by the original sample weight, and plotted in order to depict the difference between the two types of samples.

$Water\ Content = \frac{\Delta w + w_0}{w_i} \times 100$; Where Δw is the change in weight of the sample, w_0 the original weight of the water in the sample and w_i the original weight of the entire sample.

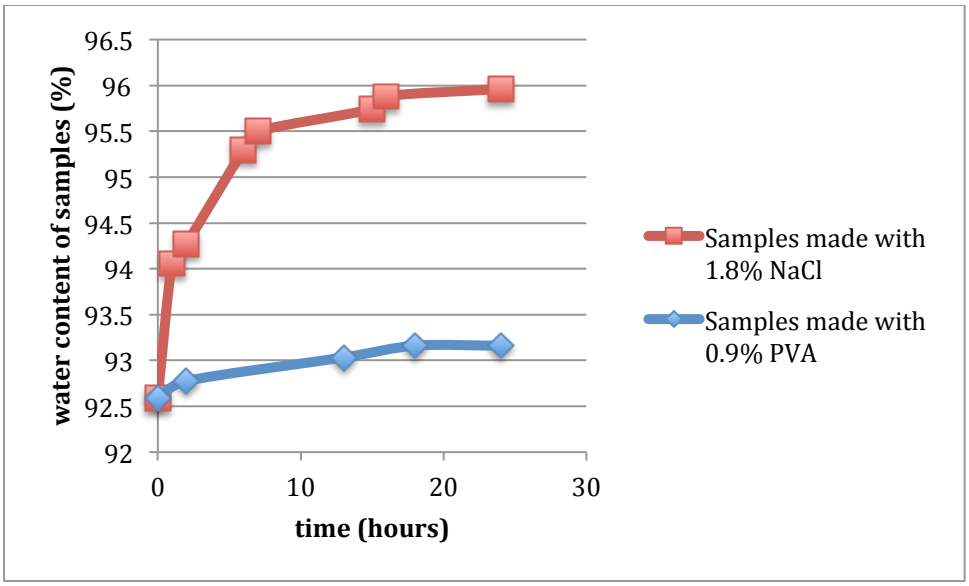

Figure 33: Water content for 7.5% PVA samples made with 1.8% Saline solution and 0.9% saline solution then placed in normal (0.9%) saline

Undried samples (Swelling B):

Additionally, samples of higher PVA concentration present increasingly more swelling (see table and chart below).

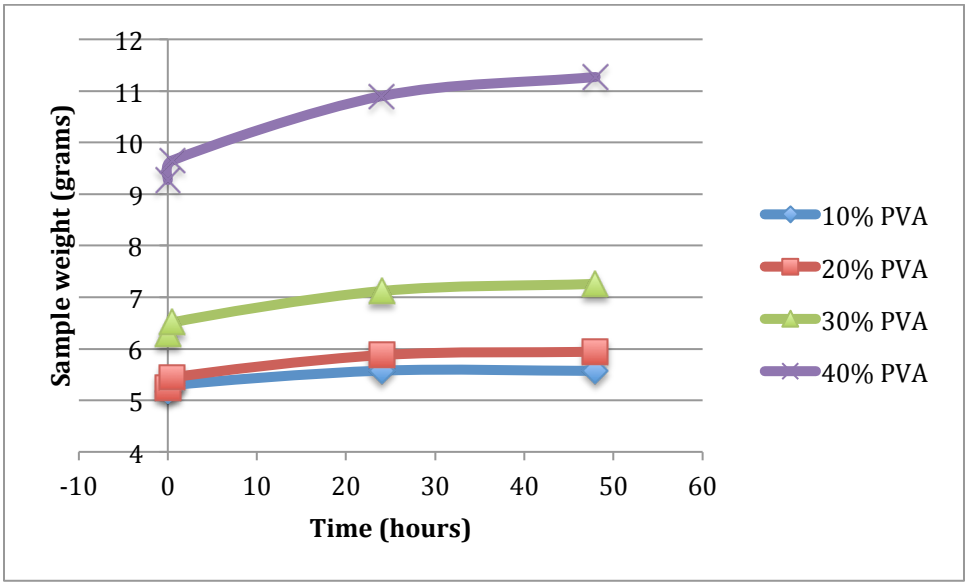

Figure 34: Swelling of PVA samples with normal saline in isotonic setting (raw data)

Table 22: Mass increase from water uptake during swelling for PVA samples after 6 freeze thaw cycles (Swelling B) from 10% to 40% in isotonic normal saline

PVA concentration	Percent swelling
10%	10%
20%	14%
30%	15%
40%	20%

Chapter 7: Discussion

7.1 Device description:

This work led to the design of two separate devices: an implant destined to boost the pharyngeal wall and shorten the velopharyngeal gap, and a palatal obturator. As aforementioned, the pharyngeal wall implant is in the form of a sterile block of PVA that the surgeon will be able to carve in order to match the patient's velopharyngeal anatomy. This implant will allow the patient's speech production to develop normally. Additionally, the palatal obturator, designed to have a softer posterior part, is a device that will not only help with speech production, but also feeding of the patient. The posterior part is currently designed to be a block of PVA attached to the anchoring metal, and will also be carved by the physician based on the size, shape and type of cleft the patient presents.

7.2 How the devices addressed the unmet needs

Combining the implantation of the pharyngeal implant and the usage of palatal obturators in patients presenting a cleft palate allows the team in charge of treatment to delay the palatoplasty, while still having a solution of speech production and feeding. Delaying the palatoplasty until the patient is about 5 years old allows optimal maxillofacial growth and

reduces chances of other related maxillofacial defects as mentioned above. This implant therefore serves as a buffer for the care team. Additionally, the problem of discomfort due to the hardness of current acrylic obturator is addressed by selecting a material with mechanical properties closer to those of human soft tissue compared to acrylic.

7.3 Comparison with other devices – Competitive Advantage

Pharyngeal Implant

The pharyngeal implant is designed to be a block of PVA the surgeon can carve to match the size and shape of the velopharyngeal gap. Posterior wall augmentation and Pharyngeal flap are the most common surgeries for velopharyngeal insufficiency in cleft palate patients. In both surgeries, autologous tissue is commonly used to fill the void[37-40]. However, in the past, synthetic materials including silicone (silastic), Teflon, proplast and collagen were used as implants. These were deemed undesirable in the long term due to post-operative complications and FDA restrictions [41, 42]. Porous polyethylene, commercialized by Medpor, is mostly used for craniofacial cartilage-like implants such as chin, nasal and mallar because of its stiffness. The lining of the pharyngeal wall is however soft tissue; therefore, use of a softer material for such implants would be better according to the surgeons consulted. Additionally, because of its texture, porous PET allows tissue ingrowth and is not favorable for removal in case of complications, unlike smooth-textured PVA[43] . The table below compares Medpor's PET mechanical properties to those of PVA hydrogels at concentrations deemed acceptable for the velopharyngeal implant.

Table 23: Comparing properties of PET, Silicone and low concentration PVA hydrogels

	Modulus of elasticity (MPa)	Tensile Strength (MPa)	Tear Strength (kN/mm)	Tissue Growth	Recorded Implant Migrations
Porous PET (medpor)	227-307	23	45	Yes	Yes
Silicone	2.07	6.55	1.03	No	Yes
Smooth 5% PVA	5.135×10^{-2}	3.3×10^{-2}	1.05×10^{-3}	No	N/A
Smooth 7.5% PVA	6.4×10^{-2}	6.03×10^{-2}	2.29×10^{-3}	No	N/A
Smooth 10% PVA	8×10^{-2}	1.09×10^{-2}	4.1×10^{-3}	No	N/A

De Novo Palatal Obturator:

The current material used for palatal obturators is acrylic. Table 22 shows acrylic's mechanical properties compared to the PVA hydrogels considered for this device [10%, 5%, 7.5%], acrylic is of much higher elasticity. Surgeons were surveyed and they suggest that a softer material, closer to adipose tissue be used for the posterior part of the obturator so that it is more comfortable, less painful for the patients. Therefore, selecting a hydrogel that fits within the adipose tissue elasticity range would be a better fit compared to acrylic.

Table 24: Comparing Silicone and Acrylic's mechanical properties with acceptable concentrations of PVA hydrogels

	Modulus of elasticity (MPa)	Tensile Strength (MPa)	Tear Strength (kN/mm)
Acrylic	3.2×10^{3}	75	N/A
Silicone	2.07	6.55	1.03
20% PVA	$2.\times10^{-1}$	3.48×10^{-1}	8.67×10^{-2}
30% PVA	8×10^{-2}	1.09×10^{-1}	4.1×10^{-2}

7.4 Limitations

The cleft palate part of this research focused on a preliminary design for both the pharyngeal wall implant and the de novo palatal obturator. In the case of the obturator, the research does not cover all the different types of obturators, but rather solely the two-part obturator that are used in patients with incomplete clefts. Additionally, due to time constraints, the foreseen step of cadaver testing to determine the most appropriate implantation method was not possible for the pharyngeal implant. Additionally, the fabrication of both the velopharyngeal implant and cleft palate implant did not follow strict guidelines, leaving room for improvement for future work.

In terms of tests performed on the material to be used, certain tests suggested by the FDA for implants were not performed, also due to time and resources constraints. The following tests were not performed: cytotoxicity test, sensitization test, hemocompatibility, pyrogenicity, genotoxicity, carcinogenicity, and biodegradation. These tests are usually performed in animal studies, which was out of the scope for this research.

Chapter 8: Part 1 Conclusions

It is important to note that with lower the concentration of PVA, the elasticity and tensile strength diminish. The tensile strength of PVA at 2.5% weight concentration is 8.5 kPa, below that of 5% PVA (33 kPa) as well as the set lower boundary for this criterion, 25 kPa. Based on this tensile strength criterion and the trendline obtained from the experimental tensile strength data, PVA at a percent weight concentration of 3% or above would meet this requirement. Lower weight concentrations of PVA (10%) have a swelling ratio of 10% or less in isotonic solutions, and said concentrations also meet the tear strength criteria of 30 mN/mm. Furthermore, it is important to highlight that PVA samples made with twice the amount of NaCl (1.8% Saline solution) show less modulus of elasticity, tensile strength and tear strength than similar parts made from 0,9% saline, while their swellability is significantly higher. Based on the types of PVA samples tested, the ideal weight percent concentration range for the pharyngeal implant would be 5% to 10% made with normal saline.

Because of constant removal and insertion of the obturator into the patient's mouth, it is important that the posterior part of the obturator is more elastic than the pharyngeal implant. Based on the experimental data and the literature[35], PVA cryogels within the 20% and 30% range in concentration and made with normal saline would be ideal for this device.

Part 2: Facial implants

Chapter 9: Background

9.1 Market Overview

Over the past 10 years, there has been an increase of approximately 205% in the number of soft tissue fillers procedures performed in the United States only, reaching a high of 2 million procedures. Long term fillers (PMMA, PLA) constituted 20% of the total number of procedures, while HA constituted 75% of the procedures. Having to get HA injections routinely (approximately every 6 months) can become an inconvenience for patients, but the current long term fillers being irreversible confine them to this very choice. In 2013, more than 2.5 billion dollars were spent on injectables, with nearly 1.9 billion on skin rejuvenation. Based on this data, the potential consumer base for the facial implants designed is about 500,000 procedures per year. The table below shows the number of procedures performed per the top 3 soft tissue filling injectables.

Table 25: Statistics on the number of procedures performed per type of dermal filler in 2015[44]

Dermal Filler Product	Brands	Number of Procedures in 2014
Hyaluronic Acid	Juvederm Ultra, Ultra plus, Perlane, restylane,Bellotero,Voluma	1,697,621
Poly-L-Lactic Acid	Sculptra	53,159
Calcium Hydroxylapatite	Radiesse	133,058
Total		**1,883,838**

Consumer identification

The primary consumers for the facial implants are the end users: the patient and the health care practitioner that will handle the implantation. The figure below shows a distribution of dermal fillers procedures per age groups. Patients 40 years and older are the significant majority of the target consumers.

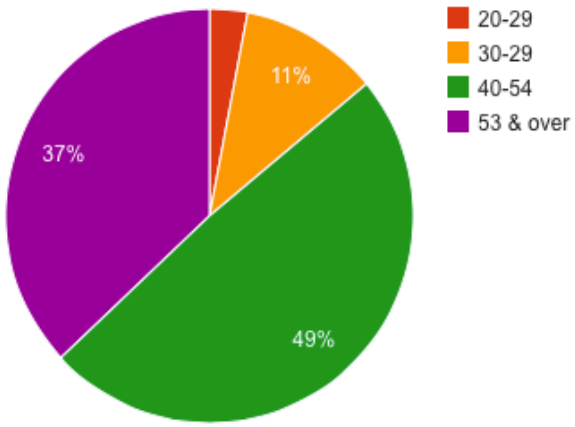

Figure 35: Age distribution of procedures involving soft tissue fillers [44]

9.2 Overview of facial implants and soft tissue fillers

Facial implants are solid, biocompatible implants that are specially formed to enhance a patient's facial structure based on their needs. The most popular facial implant procedures are malar augmentations, mentoplasties, and lip augmentations.

There are however, less invasive, non-surgical procedures that pertain to enhancing facial features, mainly to restore youthfulness. Dermal fillers are injectables that remove wrinkles, soften facial creases and enhance the youthful aspect of the face. Figure 31 depicts the different facial sites typically candidates for dermal fillers. According the American Society of Plastic Surgeons, softer tissue fillers are mostly used for lip

plumping, perioral, nasolabial folds and worry lines, while harder materials are used for cheek and chin augmentations[44].

Hyaluronic acid (HA), calcium hydroxyapatite (CaHa), poly-L-lactic acid and collagen are the main temporary wrinkle fillers, while Polymethylmethacrylate (PMMA) and Polylactic Acid (PLA) are semi-permanent (removable) wrinkle filler in the form of microspheres. [45-47]

Hyaluronic acid is found in the extra cellular matrix and is naturally absorbed [48] by the body 6 to 9 months after the injection, and calcium hydroxyapatite is naturally found in the bone matrix as well as in the teeth. CaHa microsphere start degrading 9 to 11 months after injection. PMMA is a more permanent solution; composed of 20% PMMA microspheres and 80% collagen [49-51]. These fillers are used to smooth wrinkles, correct folds and volume losses. PLA for example was cleared by the FDA for restoration of volume for HIV patients suffering from fat loss (lipoatrophy) [52]. Although the long-term dermal fillers lessen the patients' "injection fatigue," these fillers are not removable, which gives the surgeons less room for error in terms of volume selection

Figure 36: Different candidate sites for facial volume filling procedures

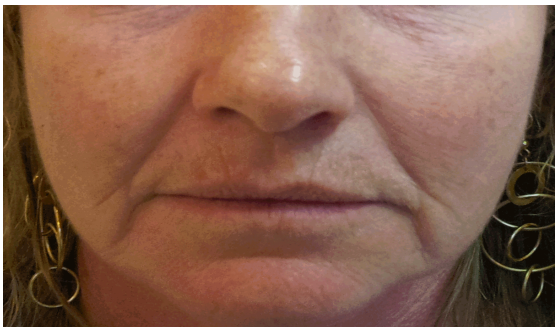

Figure 37: Nasolabial folds close-up

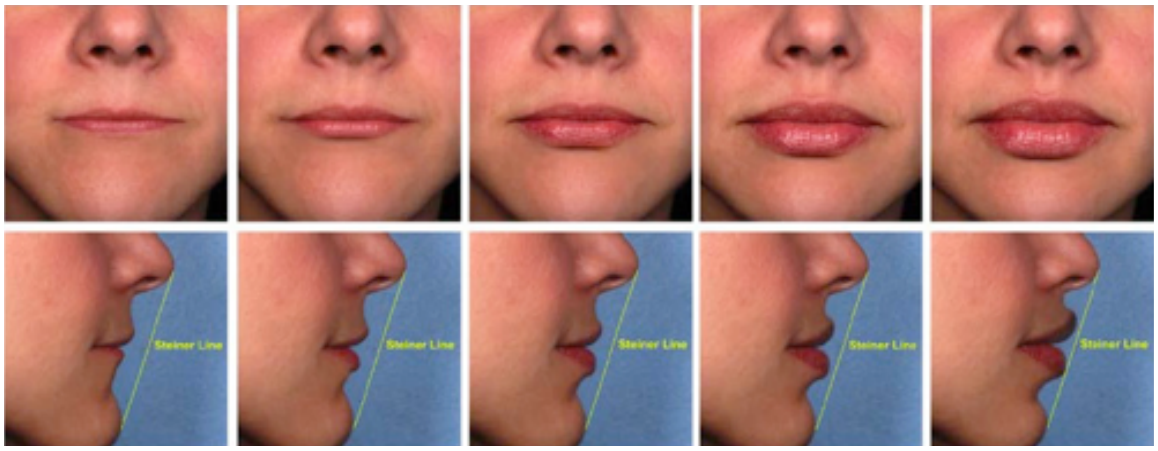

Figure 38: Lip plumping result with existing products

9.3 Existing products

The main softer tissue filler volume augmentation of the face are collagen, fat, Calcium Hydroxylapatite (CaHa), Hyaluronic Acid, Poly-L-Lactic Acid (PLA), Poly(Methyl Metacrylate). Additionally, the products used for solid implants include silicone, expanded Polyetrafluoroethylene (ePTFE, Gore-Tex) and porous polyethylene (PET), commercialized (PET, MedPor).

Table 26: Recently issued patents by USPTO involving soft tissue fillers [35]

PAT. NO.	Title	Inventors	Date of issue
8,932,637	Injectable and swellable microspheres for tissue bulking	Vogel et al.	1/13/2015
8,889,123	Compositions and soft tissue replacement methods	Van Epps et al	11/18/2014
8,846,094	Peripherally administered viscous formulations	Lyons et al	9/30/2014
8,822,676	Hyaluronic acid-based gels including lidocaine	Lebreton; Pierre F.	9/2/2014
8,815,228	Alloplastic injectable dermal filler and methods of use thereof	Boutros, Ayman	8/26/2014
8,883,185	Hydrogel implants with varying degrees of crosslinking	Bennett; Steven	11/11/2014
8,801,659	Injection device for soft-tissue augmentation fillers, bioactive agents and other biocompatible materials in liquid or gel form	Mudd et al.	8/12/2014
8,795,694	Microparticles comprising PCL and uses thereof	Super et al.	8/5/2014
8,865,879	Chitosan beads and filler comprising such beads	kiehm et al	10/21/2014
8,778,333	Injectable microspheres for tissue construction	Vogel et al.	7/15/2014
8,853,184	Polysaccharide gel formulation having increased longevity	Strompoulis et al.	10/7/2014

Hyaluronic acid ((C14H21NO11)n) is the most popular soft tissue filler, also labeled as dermal filler. HA is a chemical naturally found in the extra-cellular matrix, with a half-life of approximately 1-2 days. For that reason, HA[53] has been crosslinked with various chemicals to increase its longevity to approximately six months. HA lasts relatively longer in areas surrounded by less muscle than others, such as under the eyes (ie periorbital lines, tear through) and less in areas such as the lips. HA has been deemed safe for facial injections, and is currently commercialized under 4 FDA approved brand names: Restylane, Juvederm, Hylaform and Elevess. [44]

Collagen fillers are derived either from human skin or animal skin (bovine or porcine). Human-derived collagen formulas are commercialized under a few brands, including Cosmoplast and Cosmoderm. Zyderm and zyplast are brands of purified bovine collagen, while Evolence is derived from porcine fat. Animal-derived collagen must be tested for potential allergy reaction prior to injection. Artefill, a hybrid form of bovine collagen mixed with PMMA comes in the form of injectable microspheres. Because the body reabsorbs the injected collagen, the innovative part of Artefill is that the microspheres stimulate collagen production. [54]

Calcium Hydroxylapatite ($Ca_5(PO_4)_3(OH)$) is the heaviest of all dermal fillers. It is often used to correct moderate to severe creases such as the nasolabial fold and frown lines. Calcium Hydroxylapatite is biosynthetically produced, thus the risk of allergic reaction is lower compared to animal-derived collagen because it contains no animal byproducts. [47, 50, 55]

Poly L Lactic acid (PLA) is a synthetic material injected in the face leading to collagen production. It is a biodegradable material that was previously used for suturing. This is injected in the deep dermis with a special technique called tunneling. Even distribution of the PLA is important to avoid the formation of granulomas and potential inflammation. The only FDA-approved brand of PLA is Sculptra Aesthetic.[47]

Polymethyl-methacrylate (PMMA) is made of approximately 20% PMMA microspheres and 80% collagen gel. Once the initial collagen is broken down, the PMMA makes the body produce collagen in the target area to fill the space under the skin. Because PMMA injections are long term, surgeons tend to underfill the void during the first injection and

progressively fill it over a series of injections.. The only FDA approved PMMA brand is Artefill.

9.4 Deficiencies that need to be addressed

The main problem being targeted by this work in the plastics area is the lack of long term, removable facial implants for soft tissue fillers. This problem needs to be addressed because currently commercialized longer-term soft tissue fillers are not removable, giving very little room for correction to the surgeons after insertion. This work therefore addresses this by designing sufficiently soft implants for nasolabial folds and lip plumping, while preserving removability properties that harder implants present.

Chapter 10: Design considerations

10.1 Customer needs

The table below describes the patient and the surgeons' needs.

Table 27: Customer needs for facial implants

	Patient needs
1	**To fill targeted facial void/crease**
2	Long life of device (2+ years)*
3	Reduce additional surgeries*
4	Enhances targeted feature/rejuvenates targeted feature*
	Surgeon Need
1	Reduce risk of treatment using device compared to current treatment*
2	Wide range of device size to select from
3	Standardized method for selection of size*
4	Device that is tactile
5	Minimal number of incisions*
5	Diagrams and procedures for best practice of positioning, delivering and implanting

* - Would like to have: The main goal of this work is to design a long term removable implant, and the other needs are additional needs that will give the product an edge over the current competition

10.2 Linking requirements to parameters

After determining the patients and surgeon needs, a QFD was effectuated to translate said needs into technical criteria that would then be defined as design inputs.

Table 28: QFD for facial implants

	Design Inputs											
Consumer Requirements	Shape	Size of superior end	Size of inferior end	Length	Volume	Biocompatibility	Removability	Tensile Strength	Tear Strength	Swellaility	aseptcity/sterility	Insertabilithy
Minimal number of incisions												*
Implantation causes minimal local trauma		*	*	*								*
Safe device							*	*	*	*		
Wide range of device size to select from					*	*						
Standardized method for selection of size		*	*	*	*	*						
Functionality after Implantation												
Enhances targeted feature	*	*	*	*	*	*						
Long life of device	*							*	*	*		
Verification Tests	**1**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**2**	**3**	**4**	**5**

Table 29: Different tests used to verify the implants' design inputs

Test	**Type**
1	Compression Test
2	Tensile Strength Test
3	Tear Strength Test
4	Swelling Test
5	Cadaver Test

10.3 Design Inputs

The most critical design specifications for these devices are encompassed by the geometric characteristics, the mechanical property, and sterility. The tables below break every design characteristic into specific items and outlines to boundary for each.

Table 30: Design Inputs for Facial Implants

Item	Design Parameter	Design Specification
A	Elasticity	The material used for the facial implants fold implant should have a modulus of elasticity less than 55 kPa
B	Shape	The facial implant's shape ranges between being a truncated cone and cylindrical, with an ellipse as the base
C	Insertability	Implant easily insertable not only by surgeons, but also dermatologists
D	Size of superior end	The superior end of the implant must be no wider than 6mm
E	Size of inferior end	The inferior end/tip of the implant must be at least 2mm wide, and no wider than 4mm**
F	Length	The length should range from 25 to 50 mm**
G	Volume	The volume of the nasolabial fold implant could range from 0.25 to 5 mL**
H	Biocompatibility	The implant meets ISO 10993 requirements for implants
I	Removability	Remains intact and solid, does neither dissolve nor degrade in physiological conditions
J	Tensile Strength	The implant should have a tensile strength of at least 0.5 N
K	Tear Strength	The implant should have a tear strength of at least 0.5 N
L	Swellability	Implant must neither swell by more than 20%, nor shrink in physiological conditions
M	Asepticity/sterility	Implant meets tripartite sterility test requirements

10.4 Justification of Design Inputs

- **Elasticity** – For this work, one of our main goals is to make solid, removable implants that would still feel natural to the patient and not cause any discomfort. In order for this to be attained, the implant's modulus of elasticity must fit within the adipose to skeletal muscle tissue range of elasticity: 0.05 kPa-50 kPa[32]
- **Shape** – samples of the cylindrical/truncated cone shapes gave the targeted features (nasolabial fold and lips) a very natural, yet enhanced look.
- **Volume** – the recommendations for current volume fillers indicate no more than 5 ccs per treatment for nasolabial folds and lip implants, hence 5 ccs being the upper limit of implant volume
- **Superior and inferior ends** – The inferior end of the implant must be wider than 2mm because the wider tip lessens the chances of the implant bending/curling once implanted. On the other hand, the superior tip must be less than 6mm wide because one of the surgical goals is to keep the incision for the insertion as small as possible.
- **Tensile and Tear Strength** – both were determined experimentally by pulling a sample implant from an extensometer using surgical forceps and recording the load (0.5 N per pull). This was necessary because it is part of the criteria covered by the removability of the implant.
- **Removability** - in order for the implants to be fully removable, they must not deteriorate under temperatures the body may be exposed to (stay intact up at degrees Celsius) not break/tear under stress due to facial movements
- **Asepticity/Sterility** – the implants must be sterile when inserted into the patient

- **Biocompatibility –** The implant must be compatible with the human body in order to reduce risks of immune reaction or lead to dangerous consequences such as development of cancerous cells

Chapter 11: Concept development

11.1 Material Selection

As the need for a volume filling implant in this design was similar to that of the pharyngeal implant for cleft palate patients, the same material, Polyvinyl Alcohol was selected. The wide range of mechanical properties, biocompatibility and non-biodegradability as well as its proven longevity in the human body [30] are factors that influenced this material selection.

11.2 Mold Fabrication

For a large portion of this project, 3D printed 2-part book molds were used to create parts for testing. The two parts of a book mold fit into each other through a male-female, and once pulled apart after curing, the object obtained is of the image of the mold's crevices. In order to obtain the 3D printed molds, the product aimed to fabricate was first drawn using a CAD software (Autodesk inventor). From the CAD file of the object, a negative mold is derived and spit the longitudinal plane of the object. This mold CAD file is exported into a mesh file (STL), and processed through the 3D printer's software: Makerbot. The 3D printer used [insert specs] and the material used for printing is PLA.

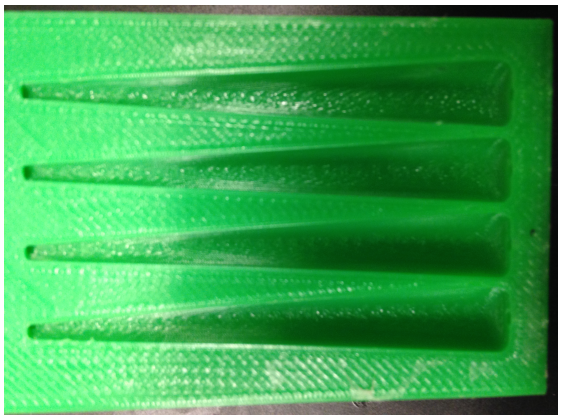

Figure 39: Examples of 3D printed mold (half) for nasolabial fold implant

11.3 Concept evolution

Concept 1: separate designs for nasolabial fold and lip implant:

The first concept design for the facial implants was mostly based on the shape of the features aimed at for correction or enhancement. For the nasolabial fold, the design involved a triangular prism that would reduce the depth of the crease due to its shape. This prism was aimed to be produced in a generic size and adjusted in length and width by the surgeon based on the length and depth of the patient's nasolabial fold.

For the lip implant, the design was more complex because of the shape of the upper lip. This design was made by connecting smoothly two cone-like solids with a thinner cupid bow, per the anatomy of the human lip. See figure 36.

The prototypes for both implants were made by injecting PVA hydrogel solution into each implant's respective, two-part mold 3D printed PLA molds and putting them through 6 freeze-thaw cycles. After the last freeze-thaw cycle, the implants were carefully removed from the molds and the flash lines (extra material due to book molding) were cut out using surgical scissors. The same method creating the implants by injecting PVA hydrogel solution into two-part molds was used for all the concepts.

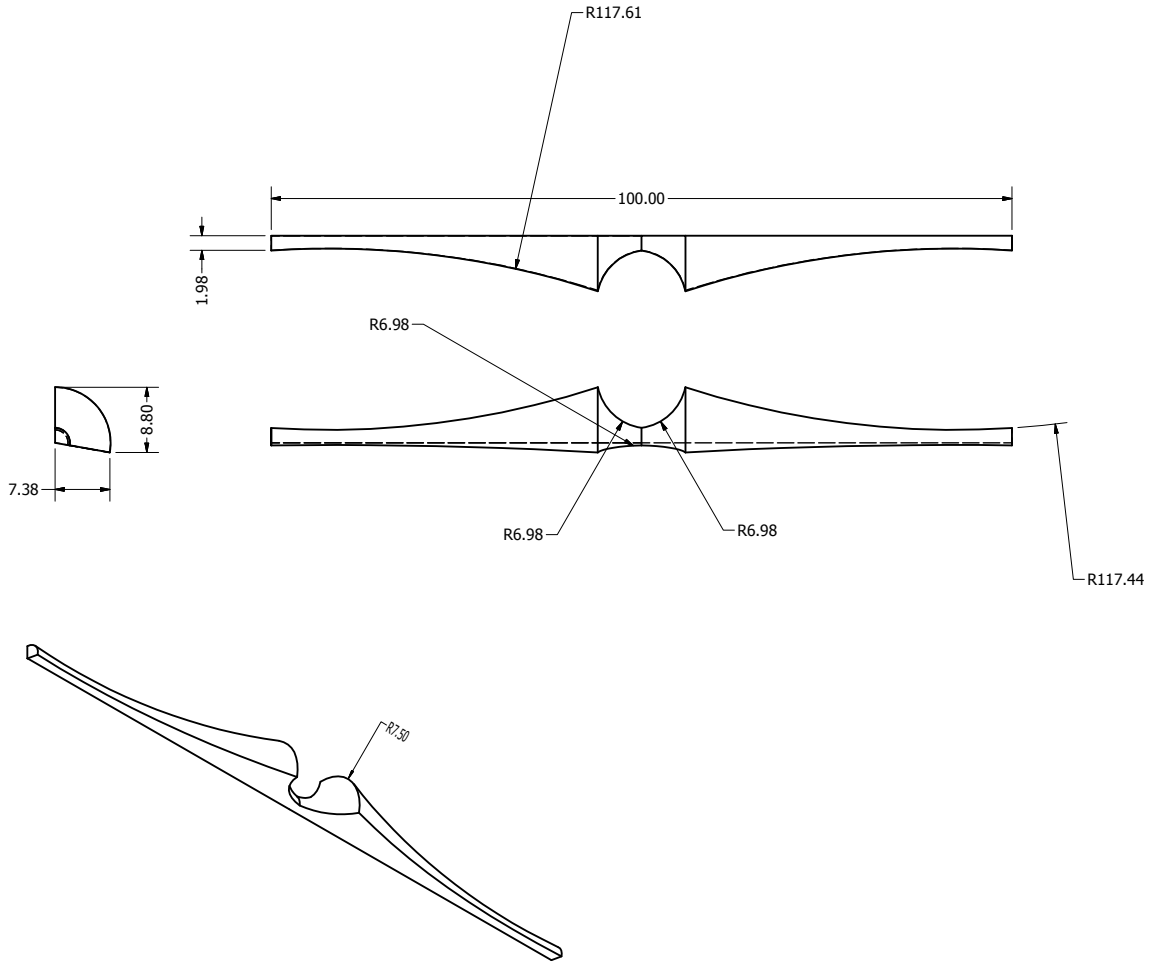

Figure 40: Design of lip implant (concept 1) (numbers in mm)

Concept 2: Simple Cone for nasolabial fold and Lip Implants

The second concept was influenced by the need to lessen the number of incisions made during the insertion of the implants, therefore limiting it to only one. This meant splitting the lip implant into two symmetrical components that would be inserted from the midpoint of the inner midpoint of the Cupid's bow. This trend of thought lead to designing a cone that would be used for both the lips and the nasolabial fold with varying sizes depending on the patient's need. A cone is more appropriate than the original prism

for the nasolabial fold as well because the depth of the crease tends to diminish with inferior progression from the alarfacial groove.

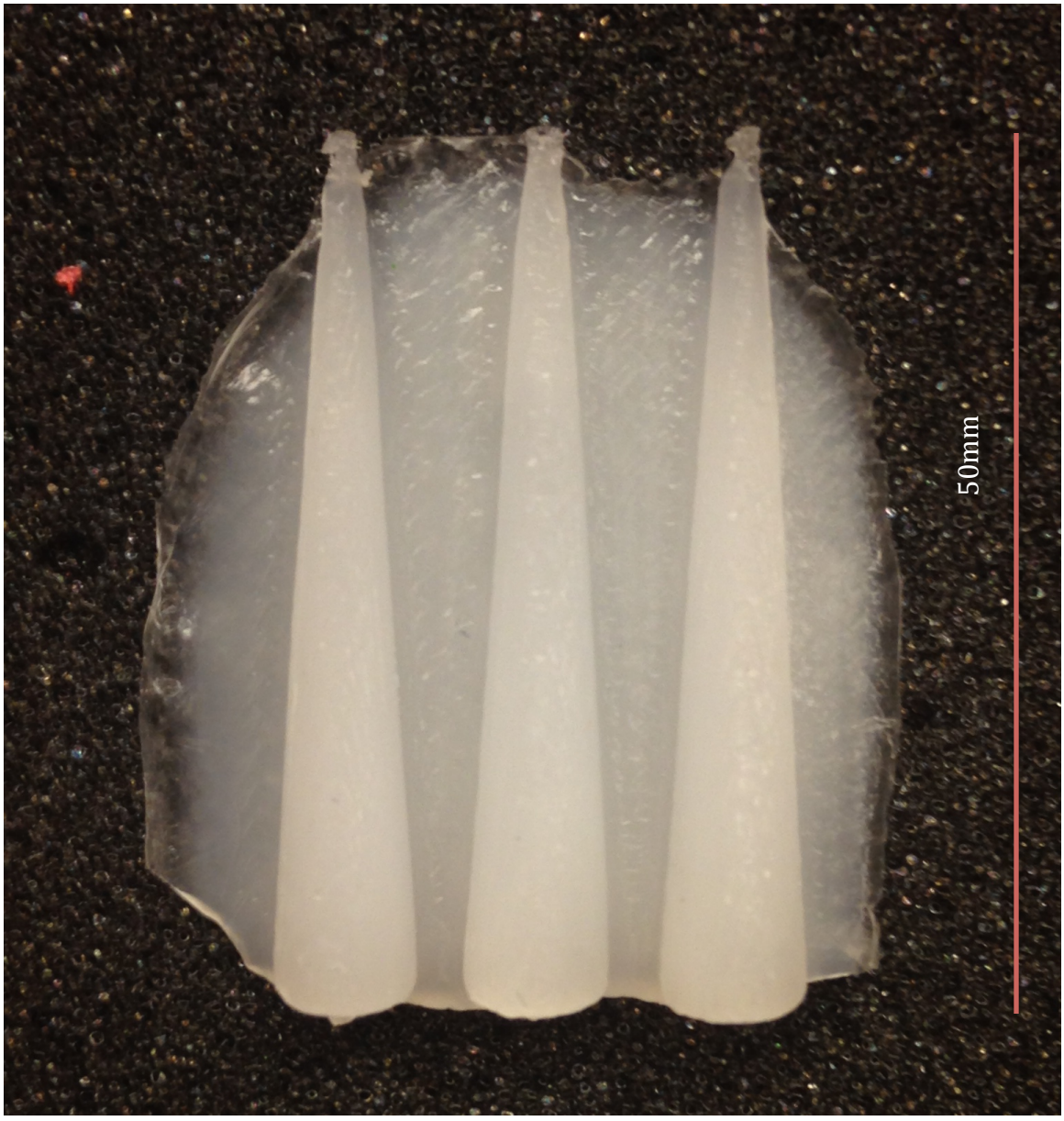

Figure 41: Image of conical PVA implants post removal from mold with flash material after 6 freeze thaw cycles.

Concept 3:

The third concept was influenced by the need to secure the implants once inserted in order to keep it from moving, as implant migration is one of the major concerns with solid implants. In order to address this, a loop was added at the base of the cone (previous design). The purpose of the loop was for it to be sutured into the skin, and to also allow seamless removal, should it be necessary after insertion of the implant. After testing, it was found that the loop was not needed because of the implant's surface smoothness and the way it fit into the dilated pocket made removal easy reducing chances of migration, which is a concern with many of the current implants and dermal fillers [56-58].

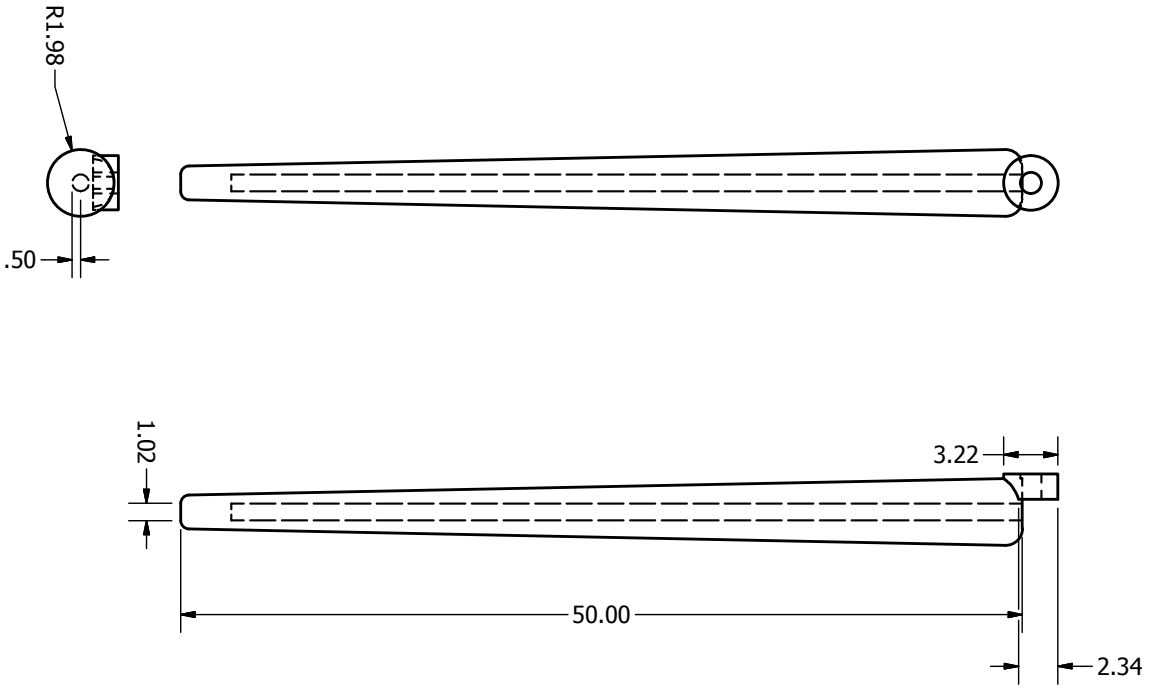

Figure 42: Concept 3- Design of facial implant with removal loop (dimensions in mm, to 2 significant figures)

Concept 4:

After a few experiments, it was determined that disrupting the fibrous tissues that connect the skin and the facial muscle in the case of the nasolabial fold had a stronger effect on reducing the depth of the fold than inserting the implant itself, therefore, the implant for the nasolabial fold, although kept at a conical shape, was designed to be flatter serve as a placeholder to prevent more fibers to connect the skin and the facial muscles. The lip implant on the other hand, still serves as a plumping agent and keeps the conical, volume-filling shape. The Implants also have a 1 mm centric channel that allows insertion with a specifically designed pin. With this final concept, the loop at the base of the implants no longer is.

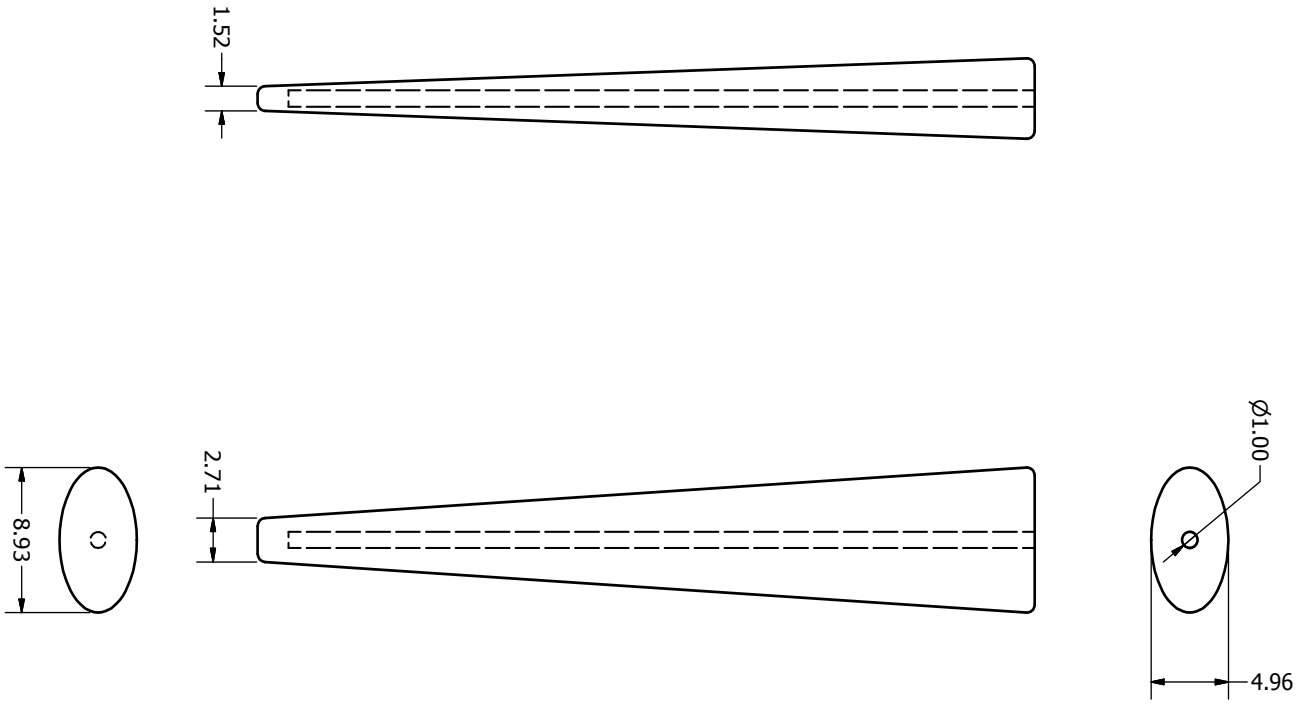

Figure 43: Concept 4 – flattened cone design for nasolabial fold implant (dimensions in mm, to 2 significant figures)

11.4 Concept selection

In order to determine which concept was the most ideal for the soft tissue filling implants being designed, a few criteria were considered: ease of implantation, ease of fabrication, and enhancement of targeted feature. The table below shows each concept and its score based on the aforementioned criteria.

Table 31: Comparison of different concepts for the facial implants

	Ease of implantation	Ease of fabrication	Enhancement of targeted feature	Product
Concept 1	1	1	4	4
Concept 2	2	4	5	40
Concept 3	3	4	5	60
Concept 4	5	5	5	125

The latest concept (concept 4) is easier to implant and fabricate because of the nature of the respective molds as well as the way each implant respectively fits the volume filling purpose. The nasolabial implant, because of its flatter nature is easier to insert after the pocket has been created rather serves as a solid that keeps the disrupted fibrous tissue from connecting the skin and the facial muscle tissue, while the lip implant has a more rounded base to assist with its plumping purpose.

11.5 Implantation Mode

Through this research, an emphasis was placed on making sure that the implants designed would be easily implanted not only by surgeons, but also dermatologists in order to increase the throughput of potential users. Although in vivo work is an important part of product development in medical devices, using similar methods in cadavers sufficed to determine the best method of insertion. The different cadaver testing iterations made it possible to tweak the design concepts for the best possible fit. The first step in cadaver testing was making a small incision (2mm) and using a surgical dilator to create a subcutaneous pocket for the implants. Although it was possible to insert the implant after having created a pocket with a smooth-surfaced dilator, it was difficult to do so partly because of the nature of the tissue. The surgical dilators' inability to create appropriate pockets lead to using screws as dilators because of their ability to disrupt different types of fibers. Different types of screws were used (thread height, spacing, etc) and all were able to create a pocket for the implant. This important finding helped designing the insertion kit for the implants.

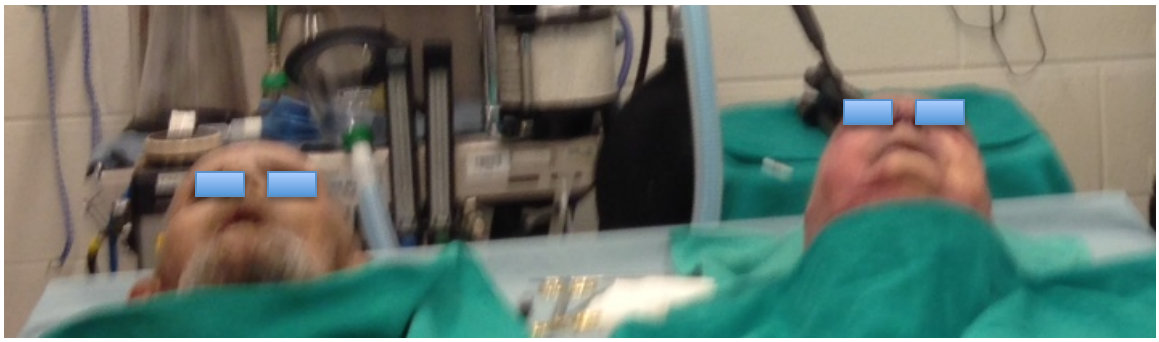

Figure 44: Cadaver testing set up.

11.6 Insertion Kit design

Dilator

Because of concerns such as level of trauma post-surgery, the screws' characteristics such as threat height, sharpness of the threads and nature of the tip (blunt vs punctilious) were taken into consideration when designing an implant-specific medical-grade screw. The number of threads on the screw was also considered important because one of the primary goals of this design is to make the insertion of the implants as simple as possible for the surgeons and dermatologists. The number of threads per dilator would impact the dilation time but also the effectiveness in fiber disruption. The goal with this dilator is to create a pocket of a similar shape and to that of the implant with a buffer amount of space to reduce potential pressure on the implant. The dilator's design went through two iterations.

The first set of dilators was designed by adding threads similar to those of an industrial wood screw to the original CAD design of the implant. Two dilators were designed, one with a total of 10 threads and another one with a total of 5 threads. See figure 43 and 44. A surgeon on a cadaver subsequently tested the dilators; he was able to create a pocket with both dilators, however he found that less spacing between the threads was better. Another important point from this test was that it was neither necessary for the dilator to be threaded from the tip to the base, but rather only halfway through its shaft, nor was it imperative for the dilator's basal half to be conical, or of the shape of the implant. The basal half of the implant could simply be cylindrical, similarly to self-taping screws and flat-headed screws. These findings lead to a second iteration for the dilator's design, described by the above characteristics.

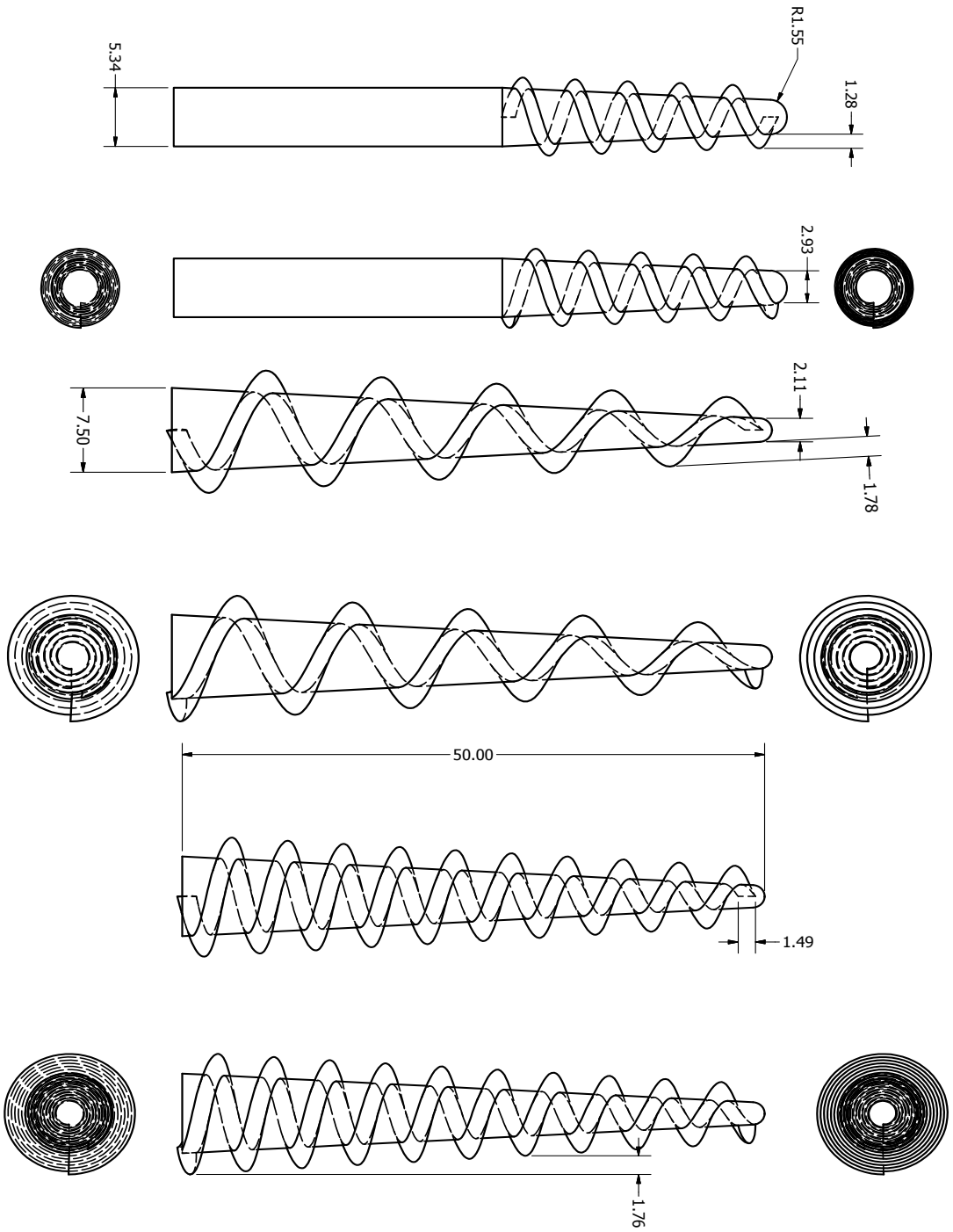

Figure 45: Different designs of dilators for the implant pocket (5 threads, half of the dilator textured, 5 threads, entire dilator textured, and 10 threads from top to bottom)

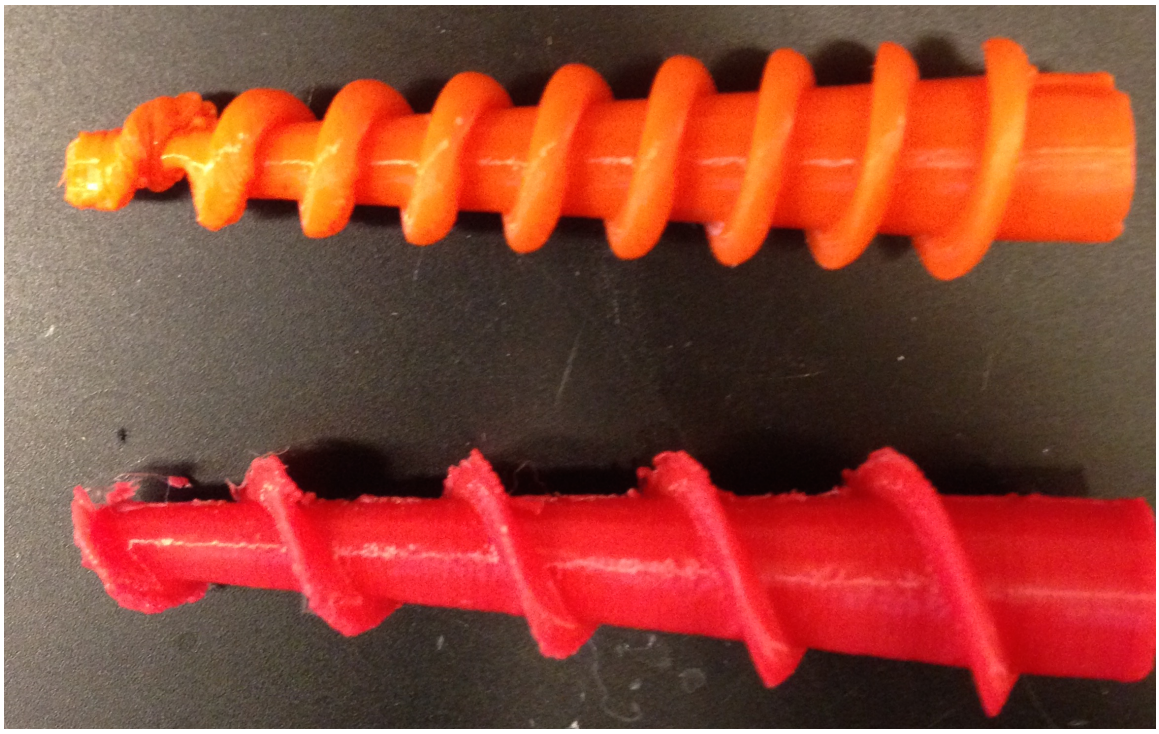

Figure 46: Examples of 3D Printed Dilators for implant pockets

Placeholder:

The placeholder is a plastic solid, in the shape of the implant used to keep the tissue from collapsing on itself after the pocket has been created using the dilator, while the surgeon prepares the implant for insertion.

Implant Inserter:

Keeping the implant sterile during the insertion is a very important part of the procedure; therefore it was deemed important to create an inserter that would not only make the implantation simple, but also shield the implant from potential contact with the external environment. This inserter consists of a 1 mm plastic/metal pin that fits in the implant's channel, a ball-like handle and a plastic sleeve with a flange on the implant end. Once the implant is inserted into the pre-dilated pocket, the surgeon/dermatologist would apply a small amount of pressure on the sleeve for the flange to press against the patient's skin,

while pulling the pin out by its ball-like handle. The surgeon/dermatologist would then dispose of the pin and the sleep, and proceed with gluing or stitching the incision.

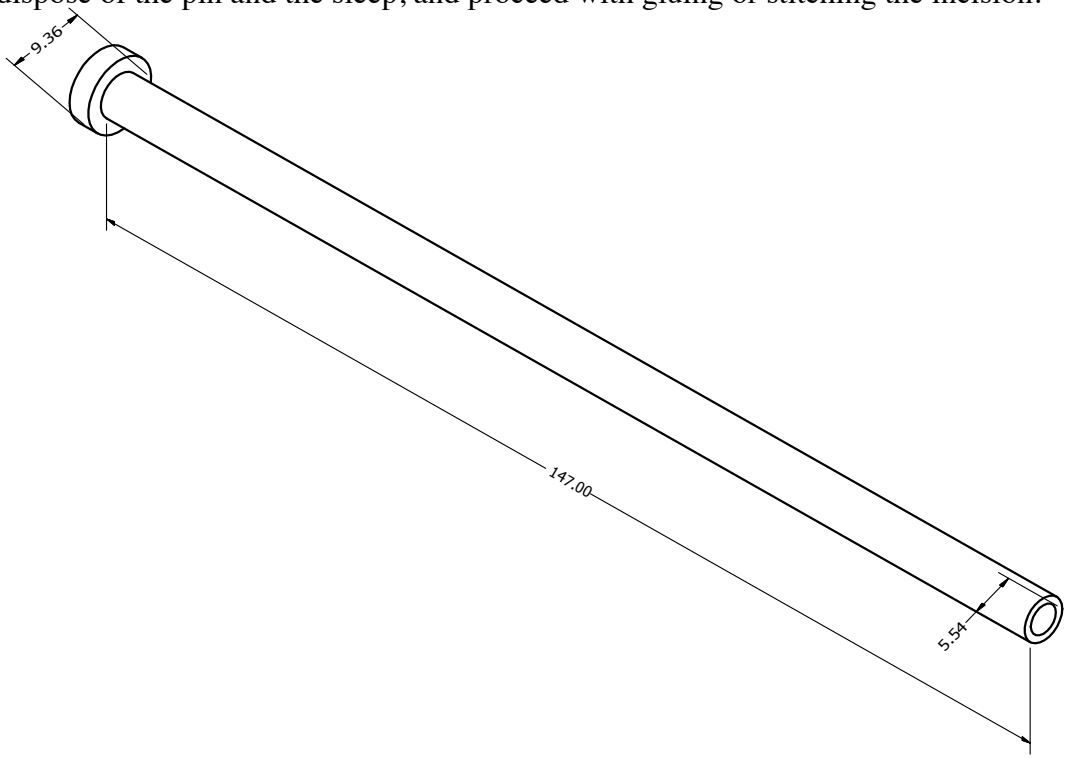

Figure 47: design of the handle for the implant inserter (dimensions in mm, to 2 significant figures)

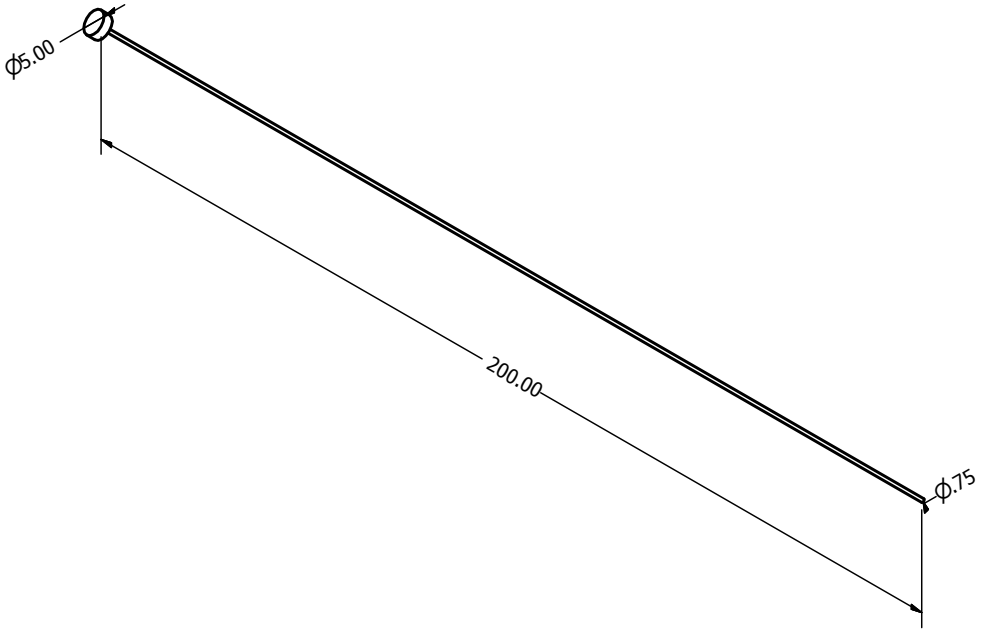

Figure 48: Design of implant needle, meant to fit into the inserter (dimensions in mm, to 2 significant figures)

Table 32: Risk analysis for facial implants

Design Function	Potential Failure Mode	Potential effects of Failure Mode	Severity	Potential Causes of Failure	Detection	Current Design Controls	Occurrence	RPN	Recommended Action
Implant to Stay in place	Implant migration	Pain	3	Implant moved by facial muscles' movement	1	Small pocket for insertion	2	6	Select a material not so likely to deform under the stress caused by facial muscle movement
		Redness	3		1			6	
N/A		Trauma during insertion	1	Surgeon not gentle during procedure	1		2	2	Infuse the implant with lidocaine solution prior to insertion
Removability	Dissolves and deteriorates	Migration of pieces	2	Implant moved by facial muscles' movement	2		2	8	Select a material not so likely to deform under the stress caused by facial muscle movement
		Lack of esthetics	3		1		2	6	
		Lessened removability	4		2		2	16	
Stay aseptic/Sterile	Causes infection	Need to remove the implant	4	Poor care pre-insertion/exposure to organisms	1		2	8	Clinicians performs insertion with caution
Give facial feature more volume	Dries out	Less volume than expected	1	N/A	3		2	6	
Biocompatibility	Patient allergic to material used	Allergic reaction	3		1		2	6	Select known biocompatible material, test patient for potential allergy
		Anaphylactic shock	5		1		2	10	
Implant staying soft	Implant hardens	Discomfort	3	Cold weather exposure	1	N/a	2	6	Warn patient about potential hardening
Size of the implant matching the need	Implant too large	Lack of esthetics	3	Surgeon misjudgment	1	N/a	2	6	Implement surgeon training video as requirement prior to purchase of implants
		Pain	3		1		2	6	
		Ulceration	3		1		2	6	
Implant to not significantly change in shape and size	Implant swells beyond what is acceptable	Pain	3	Excessive hydration of local tissue, larger implant pocket	1	Implant pocket of correct size	2	6	N/a
	Implant dries	Device failure	3	Lack of local hydration of tissue	1		2	6	
	Implant distortion	Lack of esthetics	3	Interaction with surroundings (pressure, etc)	1		2	6	
		Pain	3		1		2	6	
Durability	Implant creeping	Pain, device failure	3	Repetitive loading, high temperature exposure	1		1	3	N/A
	Implant wear	Device failure	3	Repetitive loading due to facial muscle movement	1		1	3	N/A
	Implant corrosion	Device Failure	3	Biological corrosion	1		1	3	N/A
	Implant fatigue	Device failure	3	Repetitive loading due to facial muscle movement	1		1	3	N/A

The majority of risks involved with potential failure modes of facial implants are cosmetic, and not likely to lead to patient death. These include implant migration, distortion, and shrinkage. The level of severity, occurrence and detectability for each risk was determined based on the aforementioned grading rubrics and consulting a team of engineers as well as two surgeons. More dangerous failure modes such as infection may occur, however, due to the combined low occurrence and severity, the RPN for this potential failure mode is below 15. With proper pre-insertion care from the surgeon, these facial implants present low risk for the patient.

Chapter 13: Verification testing

13.1 Material Properties tests

The following tests were performed to demonstrate the design inputs and risk mitigations:

- Compression Test
- Swelling Test

For tests above, please refer to Part I,

- Tensile Strength and Tear Strength:

From part 1, the material properties were determined, and based on the tensile strength of each type of PVA, we determined the tensile strength of the implants in terms of force. The average cross-sectional area of the implant was determined to be 51.5 mm^2 and the average thickness 5.18 mm. the cross sectional area and the thickness of the implant were respectively multiplied my the tensile strength in Pascals and N/mm, and these were then determined specifically for the implants. The table below displays both the tensile strength and tear strength of the implants in terms of force.

Table 33: Tensile and Tear strength of the facial implants (PVA samples with Normal Saline) Both the minimum tensile strength and tear strength were set at 0.5 N.

PVA Concentration	Tensile Strength (N)	Tear Strength (N)
1.30%	0.25	1.28
2.50%	0.45	2.27
5%	1.7	8.80
7.50%	3.10	16.1
10%	5.60	29.1

13.2 Cadaver Insertion Test

The cadaver tests were performed to verify the insertability of the implants designed. Three iterations were effectuated in order to each time better the insertion method, and this also led to the design of the implant insertion tool kit.

During the first test, a small incision (1mm) was made using a surgical scalpel, and a channel for the implant was created using a surgical dilator. Inserting the implant into said channel proved itself to be difficult and required two to three iterations prior to succeeding because of the tissue collapsing on itself.

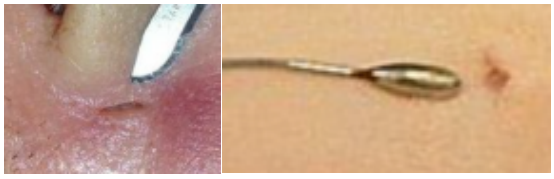

Figure 49: Left: Incision made with scalpel pre implant insertion, Right: Surgical dilator used for implant pocket

During the second test, industrial metal screws and bolts were used to dilate the implant channel, which facilitated the implant insertion.

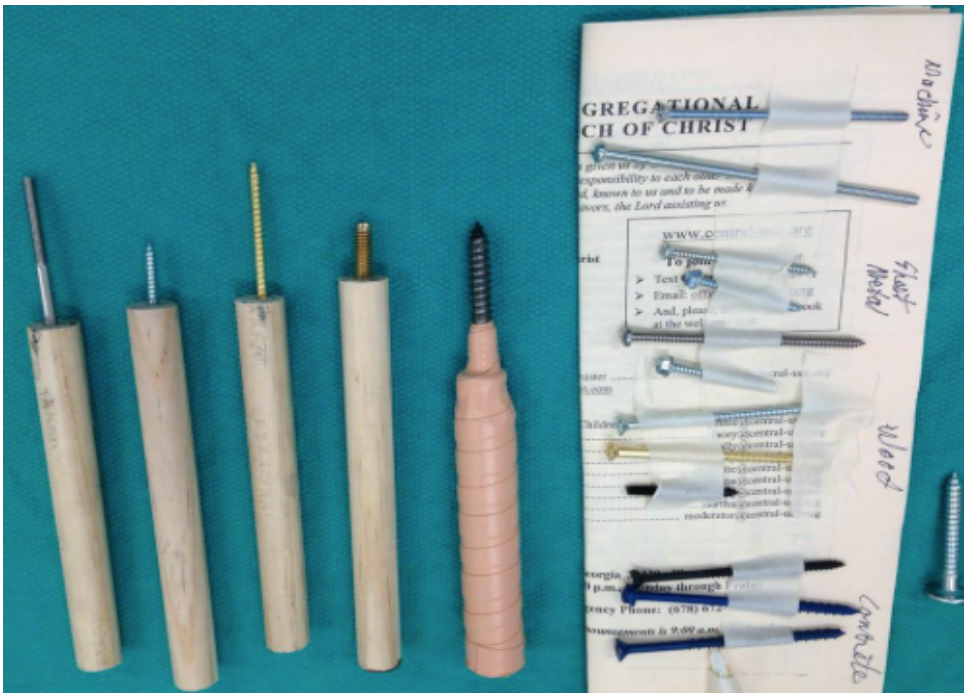

Figure 50: Set of industrial screws used for cadaver testing (dilation of implant pocket)

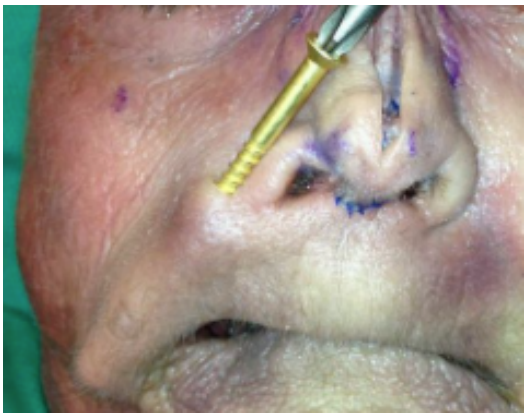

Figure 51: Dilation of implant pocket using industrial screw

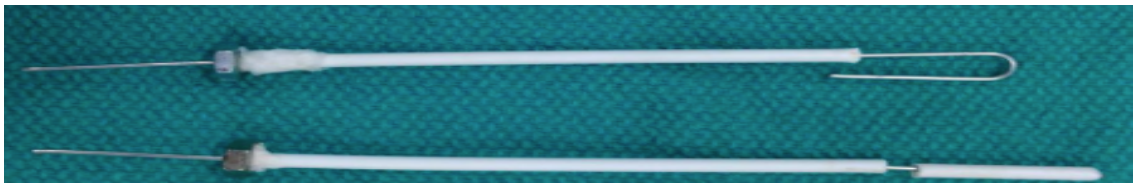

Figure 52: prototypes of inserters for facial implants

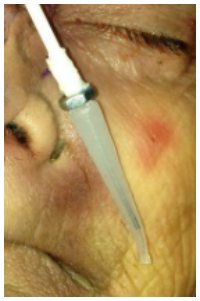

Figure 53: Nasolabial fold implant upon dilated NLF pocket

Chapter 14: Discussion

14.1 How the device addressed the unmet needs

The facial implants designed through this work for the nasolabial fold and lip implant are novel in the sense that, unlike the current devices commercialized and used as dermal fillers, they are removable solids involving less risks and potential complications, and are also long term implants because of the non-biodegradability of the material selected, PVA cryogel.

14.2 Comparison with other devices – Competitive Advantage

For facial implants, the FDA recommends a set of criteria to be met with respect to the following material properties: Tensile strength, tear strength, yield elongation and modulus of elasticity. It can be argued in the case of our research however; that elongation is not an important criterion because of the type of interaction the implants designed will have with their respective surroundings. The more important criteria from

the list above are the modulus of elasticity, a quantitative description of material softness, the tensile strength and lastly the tear strength.

Mechanical properties of popular biomaterials used for facial implants were surveyed and listed for reference in table 31. PET, ePTFE and silicone are the most popular biomaterials used for facial implants.

Table 34: Mechanical properties of popular polymeric materials used in facial implants

	Modulus of elasticity (MPa)	Tensile Strength	Tear Strength (kN/mm)
Polyetrafloryethylene (Gore-Tex)	6	12	179
porous PolyEthylene (medpor)	227-307	23	45
Silicone	2.07	6.55	1.03
PMMA	1800-3100	47-79	N/A

Modulus of Elasticity:

The modulus of elasticity is the most important mechanical property when it comes to facial implants because the softness or hardness of the implant, depending on the feature being enhanced has a tremendous impact on whether the implant feels natural to the patient, while maintaining the intended shape. It was found in the literature that the modulus of elasticity of adipose tissue ranges from .5 to 50 kPa, [32]with subcutaneous adipose tissue being the softest and omental adipose tissue being the most elastic. Meanwhile, skeletal muscle tissue's elasticity ranges from 21.2 to 28.2 kPa at the passive state [59]. PVA weight percent concentrations between 1% and 5% fit within the range of adipose tissue elasticity. PMMA for example, common soft tissue filler, is known to have an elasticity ranging from 1800 to 3100 MPa [35]. PMMA's elasticity is significantly higher than that of the surrounding soft tissues in the case of dermal fillers, making it too hard.

Tensile Strength:

Because the majority of current soft tissue volume fillers are injectable microspheres, they are neither removable, nor are they tested in tension. Tensile strength is an important criterion for the design of these implants as it translates into their removabilty. An estimate of the load applied to the implants under tension during removal was obtained by measuring the load applied to implants clamped to an extensometer while pulling the implant using surgical forceps, mimicking the action of pulling the implant out of its pocket. Based on experimental data (table 18) PVA weight percent concentration of 5,7.5 and 10% meet the 0.5 N minimum tensile strength. Using the exponential trendline obtained from the data, a minimum PVA weight percent concentration of 3% is required to meet the 0.5 N minimum tensile strength.

Tear Strength:

The minimum tear strength for soft tissue volume filling implants was also determined experimentally, Using the same estimate of load from tension and dividing it by the average thickness of the implant. This yielded a tear strength of 0.5 N, which is met by samples of concentrations 2.5% and above.

Durometer Hardness:

Durometer hardness is a criterion suggested by the FDA for implants fabricated with rubbery materials . This is tested following ASTM D2240 standards. The shore A scale, typically used for soft rubbers was selected to test these implants. However, because the results being on the lower end of the scale, it was determined that for future reference, the lower scale “00” would be more adequate. The company Nusil Technology has developed an ultra soft low consistency silicon elastomer MED 4286, intended for soft

tissue implants, and this material has a shore 000 hardness of 55, and a tensile strength of 45 psi (310 kPa)[60]. Certain studies have also studied the correlation between Shore A hardness and modulus of elasticity, and come up with empirical equations relating the two variables. The table below compares the expected hardness for each concentration based on the experimentally obtained elasticity:

Table 35: Comparison of expected durometer hardness based on elasticity and

PVA Weight % concentration	Experimental Hardness	Expected Hardness
1.3%	N/A	3
2.5%	[1.1,1.9]	4
5%	[5.6,6.9]	8
7.50%	[8.15,9.85]	9
10%	[11.27,12.97]	10

After performing a T-test to determine whether the expected hardness was within the 95% confidence interval of each experimental value, it was determined that only 7.5% PVA values matched those. The variations and differences here can be attributed to the error from manual calculation of the elasticity of each hydrogel specimen.

Hydrogel Swelling:

Based on experimental data, it is observed that PVA hydrogels made with higher polymer concentration in the solution swell more over time. The maximum swelling vs weight percent concentration curve is a linear curve. It was observed that samples of lower concentration reach their swelling plateau (less than 0.2% swelling per hour) at approximately 10% of swelling. Additionally, a change in the solute used to make the hydrogel significantly affects the swelling of the specimens. Doubling the amount of Sodium Chloride in the hydrogel to 1.8%, making the swelling experiment a hypotonic solution increases the amount of swelling for the specimens. Both trends concur with data

in previous studies where the change in osmotic pressure affects the nature of the hydrogels' swelling, and hydrogels of higher polymer content swell significantly more than those of lesser polymer content [61].

Design of Implants and Insertion Method

Dermal fillers are shapeless injectables, and meant to simply fill the spaces in which they are inserted. However, the design of these implants can be compared to that of Gore-Tex and ADVANTA ePTFE implants. Gore-Tex and Advanta implants are noodle-like cylindrical tubes of ePTFE, consisting of two layers of the material at different levels of porosity. The shape and size of the implants impact the insertion procedure. For example, the ePTFE implants used for lip plumping are the full length of the patient's lip, and the insertion method involved making two incisions, at both extremities of the lip in order to thread the implant from one extremity to the other [62, 63]. The facial implants designed for this research allow a simpler insertion method by reducing the number of incisions to just one mid-lip incision is made in a way that each implant can be inserted towards both extremities of the lip using the special dilator and inserter. Likewise, the insertion of the implant into the nasolabial bold only requires one incision instead of two like that of the ePTFE implants. Another important aspect of the insertion method of these implants is that the threading of the dilator allows for a safety net that prevents potential puncturing of the facial artery, which is an occurrence with injection of common dermal fillers. Injection fatigue also being a problem with dermal fillers such as HA due to the recurrent treatments, these implants bring a convenience element to the table.

14.3 Limitations

The mechanical properties of the hydrogel are determined by following ASTM standards and methods used in previous research studies. For Tensile and Tear strength, the ASTM D638 and D624 standards were followed with a slight deviation. However, the extensometer used did not have auto-tightening grips, so the samples were clamped manually.

Additionally, it was noticed during experimentation that if not tested immediately after taken out of the mold, samples tend to lose some of their water content most likely due to gravity. This concern was addressed but once the samples were made, the potential water losses during the freeze-thawing process were not accounted for. Additionally, the swelling experiment that was performed did not account for technicalities such as the **ratio** between the volume of the bath and the volume of the hydrogel samples being submerged, as done in other studies observing swelling of hydrogels which could have affected the swelling **ratio** of the samples.

Certain mechanical tests were not performed such as creep, wear, and cyclic loading for fatigue because we do not expect the implants to be subjected to high enough loads that would cause these forms of mechanical failures.

Chapter 15: Part 2 Conclusions

Based on the data obtained from mechanical testing and the preemptively set boundaries, it can be concluded that the ideal ranges for samples made out with normal saline, as a solute is 3-5% weight percent. The samples made with 1.8% NaCl swell more, therefore should there be a significant (>10%) difference in volume between the implant itself and the dilated pocket, these should be the implants used. Based on their mechanical properties, the ideal range of PVA concentrations for implants made with 1.8% NaCl is 5-7.5%.

Part 3: Thesis Discussion

Chapter 16: Similarities and differences between cleft palate and facial implants

The pharyngeal implant and facial (nasolabial and lip) implants designed through this research share some similarities but also present some strict differences, regarding primarily the role of each implant. Although they are both intended to fill respective voids/crevices in the targeted patients' anatomy, the pharyngeal implant's purpose is substantially constructive and non-cosmetic, and would lead to improving the patient's speech production. Meanwhile, the facial implants, also volume filling implants, serve a cosmetic purpose. Additionally, due to the different areas of the body targeted for each implant, the pharyngeal implant presented higher risks based on each one's first risk analysis: 6 potential failure modes with RPNs greater than 15, while the all the potential failure modes for the facial implants had RPNs below 15.

The molding techniques for each product differ: The facial implants specific shape requires specific casting into a pre-made mold, while the pharyngeal implant's generic cubical shape is molded using a simple tray of said shape. Furthermore, because the obturator includes a metallic frame as part of its design, the posterior polymeric part needs to be casted over the metallic frame during the molding process.

The mechanical properties of these products also differ based on each one's purpose. The facial implants, designed to be soft tissue fillers are the softest of the 3 products, and the range of PVA concentrations is 3% to 7.5% for the facial implants. Meanwhile, in order to provide a firm base that is not too hard, the pharyngeal implant's range of PVA concentrations is 5% to 10%, whereas the obturator's range is 20% to 30% to allow repeated removal and reinsertion without potential damage of the posterior part.

Aside from functional differences, one of the important differences between the facial implants and the pharyngeal implant is that the facial implants are preliminarily sized in a wide range, while the velopharyngeal implant's size is determined on site based on the patient's anatomy, and then carved out of a block of polymer by the physician.

Chapter 17: Regulatory Pathway

In the United States, the Food and Drug Administration is in charge of clearing or approving medical devices prior to commercialization and public usage. Based on their classification, purpose and risk, medical devices can different paths: Investigational Device Exemptions (IDE), Premarket Notification (510(k)), Premarket Approval Application (PMA) or Humanitarian Device Exemption (HDE). [64]

In order to follow the 510(k) path, devices' applications must show substantial similarities to FDA approved predicate devices, while the HDE path is reserved for devices that would benefit patients presenting diseases that affect 4000 people or less per year in the USA.

This work focused on the design of solid, removable facial implants. Because there exist previous similar devices classified as 510(k)s (see table 33), the products designed by this work can go through the 510(k) clearance pathway. It is important to note that, because only approximately 2650 babies are born in the United States with a cleft palate (<4000), both the pharyngeal implant and the obturator can follow the HDE pathway for FDA approval. For the HDE device clearance process, the devices are not required to prove effectiveness, but rather only limited risk. The following table lists all the relevant categories for maxillofacial implants as class 2 devices.

Table 36: FDA Product categories relevant to maxillofacial implants

Product code	Specialties	Description	Uses	Example	Material
ESH, JOF, MIB	ENT	Synthetic Polymer material (polymer, synthetic pife, silicon elastomer, polyethylene, polyurethane)	Space-occupying substance	Nose, Calf, Chin, Gluteal and pectoralis implants, Used to close esophagus defects	Synthetic polymer material
KHK	ENT	Polymer, ENT collagen material			Collagen
MCK	ENT	Voice amplification device	Voice amplificating implant	Laryngeal prosthesis (Taub design)	Silicon rubber
LMH	General and Plastic Surgery	Wrinkle filler	To fill facial wrinkles to rejuvenate appearance	Artefill	PMMA/PLA microspheres
NRO	General and Plastic Surgery	Surgical lip implant			
ESF, KDA, ODE	General and Plastic Surgery, ENT	Space-occupying implant material			

Chapter 18: Analysis of Potential Devices Mechanical Failure

Mechanical tests performed on the material were limited to compression, tensile and tear strength. There are however many other different forms of mechanical failure that can be tested for, including creep, fatigue, wear and yielding.

Creeping manifests itself in solid materials by their slow movement or deformation over long times due to mechanical stresses exceeding the elastic limit. Wear is caused by surface friction from shear forces. Fatigue is are specifically due to cyclic loading that exceed the Yield strength. Studies have evaluated PVA implants response to cyclic loading and wear in the case of cartilage implants (30-60% PVA). In these cases, it was shown that the thickness of the implant, the concentration of PVA and the surrounding material affect the level of wear occurring [30]. For example, implants shed more wear particles when cyclically loaded, creating shear forces with stainless steel than with articular cartilage. Given that significantly less loading on the implant is expected compared to the shoulder and the knee, **it was deemed not important to perform tests that would observe these forms of mechanical failure; and the same observation was made for facial implants.**

Creeping of the previously used PVA implants was not a concern highlighted by studies regarding mechanical failure [30].

Similarly for the obturator, the posterior part should be surrounded by tissues of similar elasticity (cartilage), and the tongue. The tongue is a muscle, which is less elastic than cartilage and less likely cause wear on obturator. Corrosion is a form of damage that could happen to the obturator when exposed to corrosive liquids, and this can be addressed by warning the users to keep the obturator away from such liquids.

Chapter 19: Part 3 Future work

Based on the discussion regarding each device designed by this research, there is work to be done prior to FDA clearance for each device and implementation into commercially available devices. Regarding the pharyngeal implant, PVA having been proven to be a biocompatible material, the next step to take for this implant is to develop an efficient insertion method into the pharyngeal wall; which can be done via cadaver testing, similarly to that of the facial implants insertion method development.

Regarding the obturators, their fabrication can be improved using current technologies. Because the shape of and size of the cleft vary per patient, it has been found difficult by physicians to streamline the fabrication of the devices. Using 3D imaging and 3D printing, molds for the obturators can be fabricated at the bedside based on the patients' anatomy, reducing the current window of error due to casting of molds since this process involves attempting to immobilize the patient, which is a complicated task when it comes to patients that don't easily follow directions (patients under 5).

Regarding facial implants, the designs having been improved and insertion method developed, the next step to take is starting the FDA clearance process. An important question regarding the FDA clearance process also needs to be addressed, which is whether the implants and the insertion kit should be marketed as a single device, or if the implants should be approved separately from the tools required from the insertion kit, and this will be the regulatory team's decision.

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