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Laryngeal Soft Tissue Fixation Device

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Client: Dr. Seth Dailey, UW School of Medicine and Public Health

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Abstract

Damage or scarring to the vocal folds causes severe limitations to their pliability, inhibiting proper phonation. Previous treatments such as implants and injections have proved unsuccessful. Negative aspects of these procedures include extrusion, limited biocompatibility, and do not address lamina propria damage. A newly developed surgical procedure is to be utilized for this type of vocal fold repair. This procedure utilizes a local vascularized tissue flap for the augmentation of Reinke's space. Proposed designs to secure the tissue flap in place include an improved corkscrew, barbed nail, soft tissue glue, and gecko tape method. After evaluating these design options, we have chosen to pursue the barbed nail and soft tissue glue designs. The designs will be obtained or fabricated and tested in canine larynges to determine the strength and duration of tissue flap attachment. Successful attachment of the soft tissue flap within the vocal fold will improve and possibly restore vocal function.

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BACKGROUND

MOTIVATION

Damage or scarring to the vocal folds causes severe limitations to their pliability, inhibiting proper phonation (Sulica). More specifically, when the lamina propria, a histological layer of the vocal folds, becomes scarred or injured the freedom of tissue motion is impaired. Therefore the tissue becomes stiff, preventing oscillation (Gray). Oscillation is also inhibited when fixation occurs between the lamina propria and the underlying tissues. In addition, asymmetric scarring of one vocal fold can cause inconsistencies between the vocal folds. For example, increased tension or a linear depression in one vocal fold can prevent the medial edge of the damaged vocal fold from meeting the opposite vocal fold (Schweinfurth). Incomplete closure of the vocal folds often causes patients to have a breathy voice and vocal fatigue. Other symptoms of scarring include hoarseness, thin, high-pitched voice, and poor volume and projection (Schweinfurth). Many of these symptoms have a significant effect on the daily lives of individuals with damaged vocal folds, providing a strong incentive for the creation of a method to correct for vocal fold damage and scarring.

ANATOMY

Anatomically, the vocal folds can be found within the larynx (figure 1). They are anteriorly connected to the thyroid cartilage and posteriorly attached to the arytenoid cartilage (figure 2). The neuromuscular control of the arytenoids causes the abduction (opening) and adduction (closing) of the vocal folds.

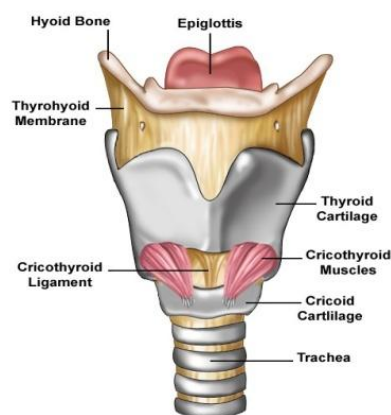


Figure 1.Anterior view of the larynx (Biology Corner)

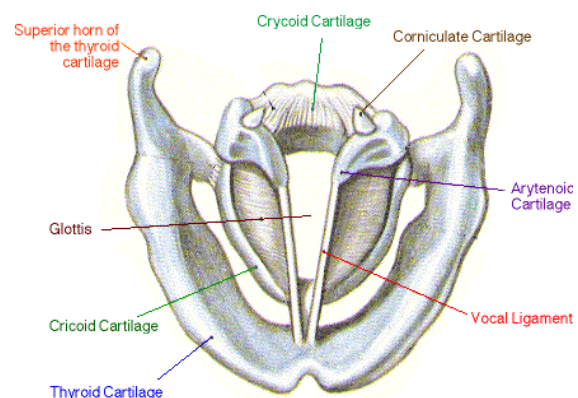


Figure 2.Transverse plane of the larynx viewed from above to show the anatomical location of the vocal folds (Singing voice).

FUNCTION

The primary function of the vocal folds is to protect the airways (Reeve). During respiration the vocal folds are open, allowing for air to pass into and out of the body. The ability of the vocal folds to constrict the airway leads to phonation. Phonation begins as the positive air pressure from the lungs forces the vocal folds open momentarily. The high velocity air causes a decrease in pressure by the Bernoulli effect, bringing the vocal folds back together again (Reeve). Subglottic pressures increases again and the process continues. The air compressions and refractions caused by the vocal folds create sound. Pitch is determined by the rate at which vocal folds come together and separate over a period of time. The exact number of repetitions is known as the frequency. Higher frequencies are perceived as higher pitched while lower frequencies result in a lower perceived pitch (Reeve).

The vibrating frequency of the vocal folds relies heavily on the integrity of the underlying layers of tissue, specifically the superficial layer of the lamina propria (Sulca). The histology of the vocal fold contains five layers with the superficial layer of the lamina propria being the closest layer to the epithelium at the free end of the vocal fold (figure 3)(Balasubramanian). The superficial layer of the lamina propria is often referred to as Reinke's space. A thin layer of epithelial cells acts as a supportive and protective boundary between the lamina propria and the airway. Below the superficial layer lie the intermediate and deep layers of the lamina propria. Finally, the vocalis muscle lies underneath the lamina propria. The superficial layer of the lamina propria is composed of loosely packed fibers offering minimal resistance to vibration (Balasubramanian). This layer contains a negligible amount of elastic and collagenous fibers whereas the intermediate layer has a higher concentration of connective tissue and the deep layer has a dense collection of elastic and collagenous fibers. The composition of the intermediate and deep layers of the lamina propria serves to provide protection to the vocal folds from mechanical damage (Balasubramanian).

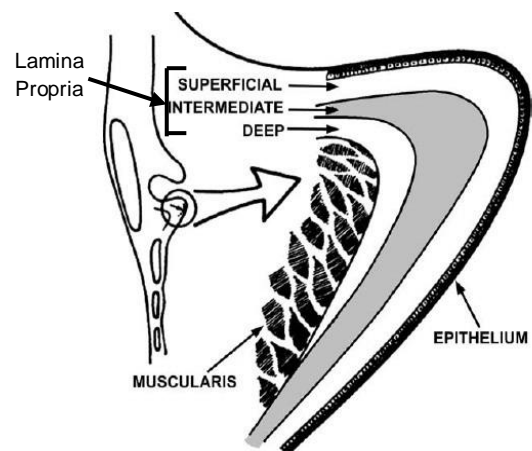


Figure 3. Histological layers of a vocal fold (Balasubramanian)

SURGICAL PROCEDURE

The proposed method for the treatment of scarred vocal folds uses a local vascularized flap for the augmentation of Reinke's space (Dailey). The soft tissue flap used in this procedure is known as the composite thyroid ala perichondrium flap (CTAP). A thin layer of tissue is removed from the anterior surface of the thyroid cartilage. The tissue was perforated along the contralateral oblique line, allowing for the removal of only half of the tissue found on the anterior face of the thyroid cartilage. The flap is left attached to only the inferior edge of the

thyroid cartilage. In addition to the perichondrial tissue, adjacent adipose tissue was left attached to the distal end of the flap (figure 4). The adipose tissue was removed from the anteromedialpreepiglottic space. The adipose tissue is the desired tissue to be inserted into Reinke's space, while the perichondrial tissue functions as the vascular tissue for the adipose tissue. By inserting the adipose tissue into the lamina propria, it serves to restore function to the damaged or scarred vocal folds. This is possible due to the similar viscoelastic properties of the lamina propria and adipose tissue. Viscosity determines the amount of energy required for tissue oscillation. As damage and scarring occur to the vocal folds tissue viscosity increases, increasing the amount of energy required for oscillation (Gray). By inserting adipose tissue into the damaged Reinke's space, the original properties of the region can be restored.

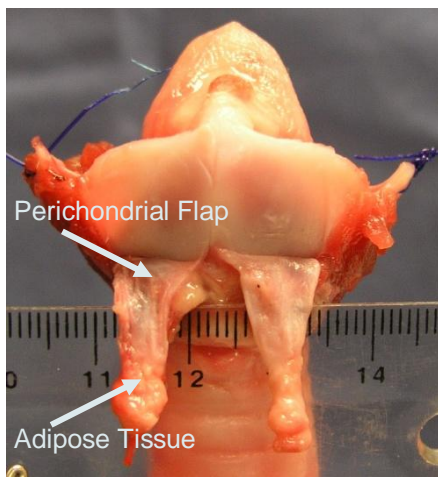


Figure 4.Removal of the perichondrial flap with attached adipose tissue from the surface of the thyroid cartilage (Dailey)

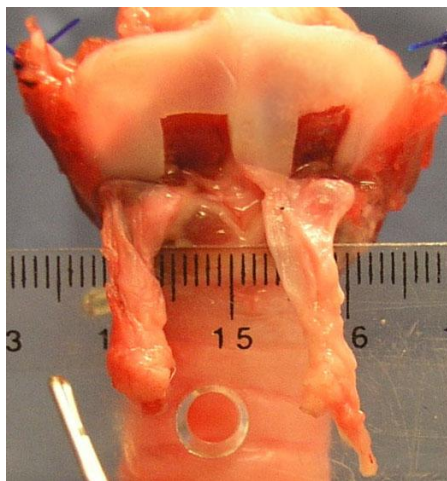


Figure 5.Minithyrotomy, the procedure used to gain access to Reinke's space by creating a window through the thyroid cartilage (Dailey)

Once the tissue flap is removed, access to Reinke's space is achieved through a minithyrotomy, as described by Gray. Entrance to the lamina propria is achieved by creating a 4 mm window in the thyroid cartilage, slightly off the midline along the inferior edge (figure 5). This procedure lines up the direction of dissection in the anterior-to-posterior orientation, avoids incisions through the epithelial layer of the vocal folds, and provides access for microscopic instruments with the surgeon's hand in close proximity to the tissue of interest (gray). It is especially important to note the advantage of leaving the epithelial layer intact as the larynx is subject to a plethora of bacteria that passes through the esophagus. When the epithelial layer in the larynx is severed, severe and even lethal infections can occur at the incision site. Therefore, a minithyrotomy is an advantageous approach to the insertion of the tissue flap used for the augmentation of Reinke's space.

Once access has been gained to Reinke's space, dilation of the space needs to occur to allow for insertion of the soft tissue flap. This process is achieved with the use of a set of titanium dilators of various diameters (figure 6). Dilators are inserted through the window created by the minithrotomy, starting with the smallest diameter and progressively growing to the dilator with the largest diameter. This method is used to expand the tissues in the lamina propria in order to create an adequate amount of space for the insertion of the flap and the materials required for the appropriate fixation of the flap. Once the tunnel through the superficial layer of the lamina propria has been created, the soft tissue flap is inserted into the tunnel with the distal end of the flap extended to the posterior end of the tunnel (figure 7).

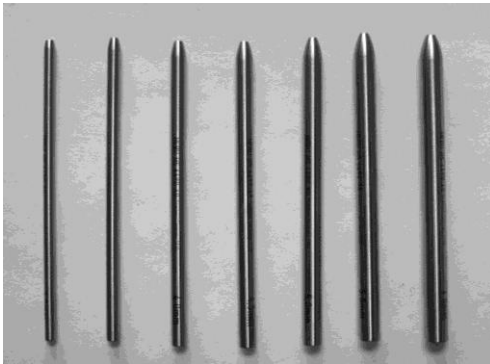


Figure 6. Dilators used for the insertion and fixation of the soft tissue flap in Reinke's space (Dailey).

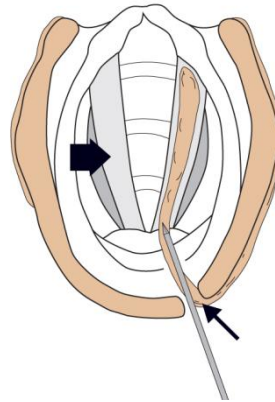


Figure 7. Insertion of the soft tissue flap (thin arrow) into the lamina propria (bold arrow) (Dailey).

CLIENT INFORMATION

The design project that we are challenged with this semester has been proposed by Dr. Seth Dailey, an otolaryngologist for the University of Wisconsin, Department of Surgery. Dr. Dailey specializes in voice, airway and swallowing disorders. He is also interested in designing and testing novel surgical strategies for reconstruction of the impaired or injured larynx.

PROBLEM STATEMENT

Dr. Seth Dailey has requested the development of a device to affix a soft tissue flap to the arytenoid cartilage during vocal fold reconstruction. The implanted fat tissue of the flap will match the viscoelasticity of the lamina propria and, therefore, allow enhanced oscillation of the scarred or damaged vocal fold. This fixation device should endure typical laryngeal movements that may otherwise dislodge the soft tissue flap, such as coughing, sneezing and swallowing.

COMPETITION

Pre-existing methods for the treatment of vocal fold scarring include implants and injections. One successful procedure for the correction of large glottic defects is a type I thyroplasty as modernized by Isshiki. In this procedure an implant is placed in the vocal folds intending to improve the medial displacement of the vocal fold. However, implants are usually exogenous, costly, can extrude, require an external incision, and do not automatically correct lamina propria alterations (Dailey).

Similarly, injections are used as an additional method for the treatment of vocal fold scarring. Injection agents such as collagen and Radiesse™ are widely available, effective, safe, and easily delivered into the paraglottic space. Drawbacks to the injection treatment include variable durabilities, rejection or migration of the injection and a difficulty in revising the injection (Dailey). The fact that pre-existing methods merely address the symptoms instead of the defects in the lamina propria provides a strong motivation for improved techniques for the treatment of scarred vocal folds. Furthermore, because autologous tissue implants have already been proven effective at treating vocal fold scarring in the short term, providing vasculature for these implants would provide a significant improvement, as proposed in the local vascularized flaps for augmentation of Reinke's space.

PREVIOUS DESIGNS

Several designs for attaching the tissue flap to the arytenoid have been tried before our team's involvement with this project. Many of the devices (figure 8) would use a screw or other device to provide an anchor in the arytenoid cartilage. Suture thread would be attached to this anchor and the distal end of the flap, allowing the flap to be pulled into the vocal fold canal. Because of the nature of the minithyrotomy procedure a length of suture would be inaccessible and remain in the vocal fold. Because of this a single device providing anchorage to the arytenoid cartilage and the flap's distal end would be preferred over a device which relies on sutures to attach the flap to the anchor.

The most recent design is a micro-corkscrew which has achieved moderate success (figure 9). The screw is approximately 1.5mm long and 0.5mm wide. To attach to flap to the arytenoid, first the screw is embedded in the adipose tissue at the distal end of the flap. Next the flap is placed in a cannula and inserted through the vocal fold until it reaches the arytenoid. The screw is twisted three times into the cartilage and the cannula removed. To avoid any torsion on the flap it is counter-rotated prior to insertion. Drawbacks of using this device include counter-rotation of the flap and difficulty fixing the screw in the desired location on the arytenoid cartilage. Furthermore devices that do not disrupt the arytenoid cartilage and instead attach the flap to surrounding soft tissues should also be pursued.

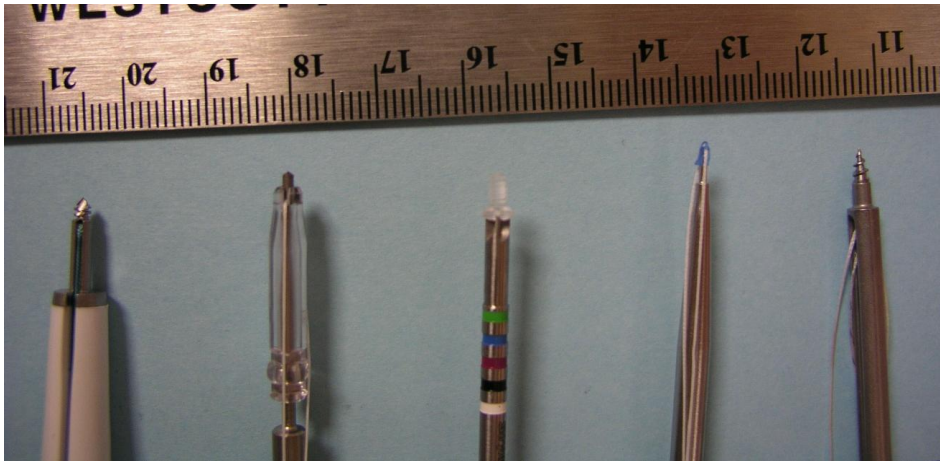


Figure 8 (left). Several previously designed devices.



Figure 9 (below). Micro corkscrew with delivery cannula.

DESIGN SPECIFICATIONS

The requirements specified by our client cover a range of topics, including size, ease of delivery, strength, biocompatibility, cost, and minimizing tissue damage. Our device must be simple, easy to manufacture, and cost-effective. It also must be biocompatible while still providing a strong anchor for the tissue flap inside of the lamina propria. On top of all that, it must be easy to use and easy to integrate into the surgical procedure. To achieve a device to satisfy these needs, we have proposed four possible designs.

DESIGN ALTERNATIVES

IMPROVED CORKSCREW

The corkscrew design has been proven to provide a strong anchor to the arytenoid and is the basis of the first design. For a corkscrew design to be successful modifications must be made to increase the ease of delivery into the cartilage and to avoid counter-rotation of the flap. A two part screw which allows the screw to rotate independently from the tissue attachment point was proposed. However this design was set aside because of the difficulty of producing complex parts on such a small scale. Next a design which combines a pin and a single twist corkscrew was proposed (figure 10). The pin would help accurately place the screw in the cartilage. This design would still need the flap to be pre-rotated once.

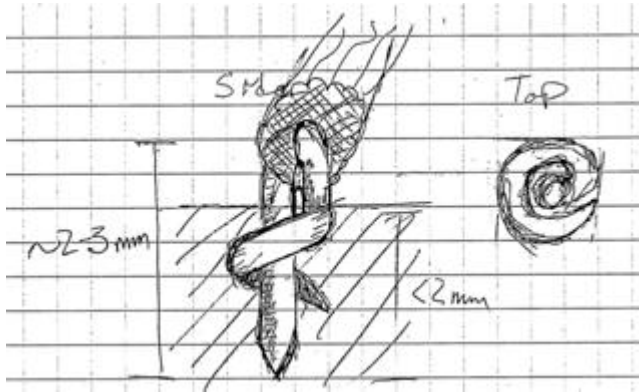


Figure 10. Sketch of improved corkscrew design with side and top view.

BARBED NAIL

A previous barbed design utilizing the suture anchor technique did not provide an adequate anchor into the arytenoid. This design failed because the barbs that deployed were inadequate and pulled out of the cartilage. However we feel that a modified device with redesigned barbs would have more success. A thin nail would be outfitted with barbs on one end and a cap on the other. The nail would be pinned through the tissue flap and inserted into the arytenoid. When tension is applied to the barbs pivot outwards and embed into the arytenoid cartilage, holding the anchor in place. This design simplifies the fixing process and does not require counter-rotation of the flap. In addition the nail has the possibility to be made from bioabsorbable materials. Drawbacks to this design include difficulties designing the barbs on a micro scale and disruption of the arytenoid.

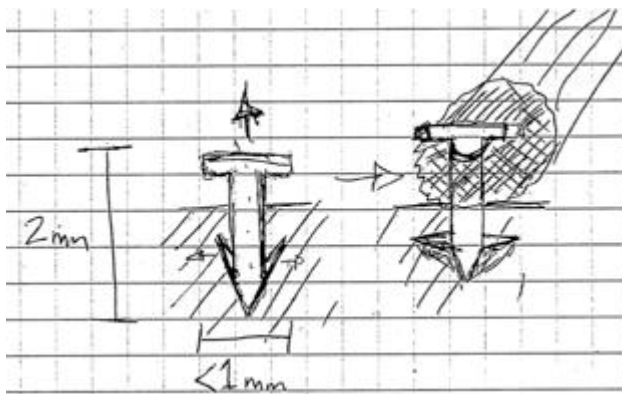


Figure 11. Sketch of barbed nail design. Pivoting barbs can be seen before and after the barbs are engaged in the arytenoid.

SOFT TISSUE GLUE

As an alternative to attaching the flap to the arytenoid the third design uses a tissue glue to attach the flap to the surrounding soft tissue in the vocal fold. Surgical glues are based on cyanoacrylate “Super” glues but modified for use in a biological environment. Modifications include addition of octyl cyanoacrylate plasticizers and creating longer alkyl chains (WPI). Nexaband is a commercially available tissue glue which we may use for testing.

GECKO TAPE

The final design uses a developing technology known as “Gecko” tissue tape to attach the flap to surrounding soft tissues. The tape is made of biodegradable polymers and adheres to wet tissues by mimicking the fibrous nano-architecture of the gecko footpad. This is accomplished by nano molding a PGSA polymer into the desired pillar shape. A thin layer of oxidized dextran is applied to the film which provides aldehyde functionalities to promote covalent cross-linking with tissue (Mahdavi). At this time gecko tissue tape is still under development at MIT and Northwestern laboratories.

DESIGN MATRIX

Our client asked us to continue with more than one design for the project since no design would be proven effective until it was used in a live surgical procedure. To fulfill the requirement we decided to weigh our proposed designs and continue with the best two. In order to help determine which final design was the best to pursue, the design matrix below was constructed.

	Weight	Nexaband Glue	Improved Corkscrew	Barbed Nail	Gecko Tape
Size	15	5	2	3	4
Ease of Delivery	25	3	2	4	2
Strength	15	3	5	3	3
Biocompatibility	20	2	3	3	4
Minimize Tissue Damage	20	4	2	3	4
Cost	5	2	4	4	0
Total	100	3.25	2.75	3.3	3.15

Table 1. Design Matrix

Our designs were evaluated based on the categories listed: size, ease of delivery, strength, biocompatibility, minimizing tissue damage, and cost. After weighing each category based on its importance to the overall product we rated each design. Ease of delivery was the most important category due to our client’s need to keep the surgical process simple and quick. Biocompatibility and minimizing tissue damage were the next most important aspects. The design must be biocompatible, not to lead to infection or unwanted swelling. The aforementioned could cause discomfort in the patient or prolonged healing time. Our device must also minimize the damage to the lamina propria, arytenoid cartilage, and surrounding tissues. Damaged tissue could lead to further scarring and possibly permanent damage in the vocal folds. For this reason we weighted the category with second-highest priority. The categories with the next highest priorities were size and strength. These are both important

categories, but are weighted less because they are not directly related to the healing of the tissue and strength may not be a significant issue considering the device will likely experience limited stress. The lowest ranked category was cost. Cost received the lowest weight since we were not given a specific budget.

FINAL DESIGNS

Following the design evaluations, we discovered that the barbed nail design and soft-tissue glue were the best options. Both designs are small and easy to deliver while providing a strong anchor for the tissue flap. While the other designs are still viable options in the future, we will focus mainly on the barbed nail and soft-tissue glue designs for the time-being and continue brainstorming to improve our current designs.

FUTURE WORK

The focus for the remainder of the semester will be on the soft tissue glue (NexaBand) method and the barbed nail design. In this section, the future development and testing of each design will be discussed.

BARBED NAIL

Development of the barbed nail design will require the selection of a suitable material. Possible materials include titanium, stainless steel, and biodegradable polymers. Both titanium (TiAl6V4) and stainless steel (AISI 316L) have been used extensively in orthopedic implants (Bombac). The physical properties of these materials are an ideal match for bone; however, they may not be suitable for cartilage fixation. Although a permanent implant of this nature will elicit some degree of a foreign body reaction or immune response, stainless steel and titanium are known to be highly biocompatible. This biocompatibility is established by a thin oxide film found on the surface of the material (Bombac). On the other hand, polymers such as poly(glycolic acid), poly(lactic acid) or a mixture (PLGA) will allow the biodegradation of the barbed device over time. By controlling the relative concentrations of glycolic and lactic acid in the PLGA polymer, the rate of polymer degradation can be specified. The high biocompatibility of PLGA is a result of its hydrolytic degradation into monomers which are found naturally in the body. A device composed of a biodegradable polymer will avoid potential biocompatibility issues. Fabrication of the design will depend upon the chosen material.

After material selection and fabrication, the device will be tested in prosected canine larynges to develop an ideal method of implantation. Once a method is determined, the device will be implanted into canines as a model to measure the effectiveness of the device's fixation. The duration and strength of attachment will be assessed one to two weeks postoperatively. Furthermore, the biocompatibility of the implant will be analyzed using histological methods. With measurable success, there exists a possibility of use in patients, whom have few treatment alternatives.

SOFT TISSUE GLUE

The first step in the design of a soft tissue glue fixation method is the acquisition of the glue. Based on our research and expert opinions, we have decided to use NexaBand. In order to successfully fix the tissue flap in place, we must develop a method of glue application. Possible methods to be tested include: 1) application to the tip of the tissue flap, 2) application to the inferior edge of the tissue flap in contact with the superficial lamina propria, and 3) if still more bonding strength is necessary, application to a larger portion of the tissue flap.

The duration and strength of the glue attachment will be tested in a manner similar to that of the barbed nail design. In addition to these tests, we must characterize the effects of the glue on vocal fold oscillation. Ideally, the glue will not adversely affect the viscoelasticity of the vocal folds and consequent sound generation; however, these changes are certainly possible if the volume of applied glue is sufficiently large.

CONCLUSIONS

The development of a soft tissue flap fixation device will complement the newly designed minithyrotomy procedure in the treatment of vocal fold damage. Not only will the device serve to securely attach the tissue flap in Reinke's space, but its method of delivery will be simple and efficient. The method of implantation will help limit the damage to the delicate vasculature of the tissue flap. By protecting the flap's blood supply, the tissue will remain healthy and intact for a greater duration postoperatively. With the vascularized tissue flap secured in place, vocal fold function will be improved and possibly restored.

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APPENDIX A. PROJECT DESIGN SPECIFICATIONS

#36- Fixation device for laryngeal soft tissue flap for vocal fold reconstruction

March 9, 2011

Team: Ross Comer, Bryan Jepson, Christa Wille, William Zuleger

Client: Seth Dailey, MD

Advisor: John Webster

Function:

The device will secure a perichondrial tissue flap into the lamina propria layer of the vocal folds. Insertion of this flap into the vocal fold will benefit individuals with scarred and damaged vocal folds. This fixation device should endure typical laryngeal movements that may otherwise dislodge the soft tissue flap.

Client Requirements:

- Surgical procedure should involve limited rotation of the tissue flap
- Fixation must be held for at least two weeks
- Device must be able to be inserted via minithyrotomy
- Insertion must not perforate the epithelial layer of vocal folds
- Insertion must maintain vasculature of the tissue flap
- Device must cause minimal damage to surrounding tissue

Design Requirements:

1) Physical and Operational Characteristics

a) Performance requirements

- i. Must effectively secure soft tissue flap and withstand typical laryngeal movements
- ii. Must remain sterile before implantation

b) Safety

- i. No negative biological effect
- ii. Sharp edges of design must remain within arytenoid cartilage

- c) *Accuracy and Reliability*
 - i. Must maintain position for minimum of two weeks
 - ii. Must accurately attach to desired location of arytenoid
 - d) *Life in Service*
 - i. Minimum of two weeks for attachment to ensure tissue regrowth
 - ii. Possibly a permanent implant
 - e) *Shelf Life*
 - i. Must remain viable for at least one year
 - f) *Operating Environment*
 - i. Within the superficial layer of the lamina propria of the vocal fold
 - g) *Ergonomics*
 - i. Must be easily inserted through metal dilator
 - ii. Insertion utensils should be easy to operate and maneuver
 - h) *Size*
 - i. 0.5 x 2 mm
 - i) *Weight*
 - i. Less than 10 grams
 - j) *Materials*
 - i. Must be biocompatible; permanent or biodegradable
 - ii. Possibly stainless steel, titanium, or poly(glycolic acid) and poly(lactic acid) copolymers
 - k) *Aesthetics*
 - i. N/A
- 2) Production Characteristics
- a) *Quantity*
 - i. One model, able to be mass produced
 - b) *Target Product Cost*
 - i. Less than \$100
- 3) Miscellaneous
- a) *Standards and Specifications*
 - i. FDA approval required for device implantation
 - ii. IRB approval required for human testing
 - b) *Customer*
 - i. Medical schools
 - ii. Hospitals
 - c) *Patient-related concerns*
 - i. Biocompatibility
 - ii. Immune response
 - d) *Competition*
 - i. Injections or implants
 - ii. Previous screw prototypes