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Optimal thyroplasty implant shape and stiffness for treatment of acute unilateral vocal fold paralysis: Evidence from a canine *in vivo* phonation model

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Abstract

Medialization thyroplasty is a frequently used surgical treatment for insufficient glottal closure and involves placement of an implant to medialize the vocal fold. Prior studies have been unable to determine optimal implant shape and stiffness. In this study, various thyroplasty implant medial surface shapes (rectangular, convergent, or divergent) and stiffnesses (Silastic, Gore-Tex, soft silicone of varying stiffness, or hydrogel) were assessed for optimal voice quality in an *in vivo* canine model of unilateral vocal fold paralysis with graded contralateral neuromuscular stimulation to mimic expected compensation seen in patients with this laryngeal pathology. Across experiments, Silastic rectangular implants consistently result in an improved voice quality metric, indicating high-quality output phonation. These findings have clinical implications for the optimization of thyroplasty implant treatment for speakers with laryngeal pathologies causing glottic insufficiency.

Index Terms: vocal fold implant, glottic insufficiency, type I thyroplasty, Gore-Tex, Silastic, *in vivo* canine phonation

1. Introduction

Voice production is controlled largely by activities of laryngeal muscles, which regulate glottal shape and vocal fold stiffness [1]. Various laryngeal pathologies, such as paresis, paralysis, atrophy, and presbylarynx that lead to deviated states of glottal shape and vocal fold stiffness can cause incomplete glottal closure, also known as glottal insufficiency, and non-normal voice quality. One surgical treatment to improve glottic closure is type I medialization thyroplasty, in which an implant is inserted into the paraglottic space [2]. However, the effect of implant shape and stiffness on vocal fold medialization and ultimately voice quality are not well understood.

Optimization of implant features has been attempted since 1974 when type 1 thyroplasty was proposed [2]. The implant material, shape, and location are subjectively decided by the laryngologist(s), whose decision is based on perceived phonation quality at the time of surgery. During surgery, only a superior endoscopic view from above the larynx is available. Therefore, a direct visual examination of the implant effect on the vocal fold medial surface is often difficult. Furthermore, little is known about which implant shape and/or stiffness produce the best output with respect to metrics of voice quality.

Considering that the goal of phonosurgery is to restore physiologic function to vocal folds, implant shape and stiffness should typically mimic the shapes of the glottal channel that occur naturally during phonation. Some implants lack a fixed shape. For example, Gore-Tex, a fabric-like material made of expanded polytetrafluoroethylene, has no fixed geometric shape and is simply layered into paraglottic space to medialize the vocal fold. The previously reported effects of implant shape on vocal fold medialization are unclear. Orestes et al. found that divergent implants resulted in improvements in pressure/flow relationship and fundamental frequency (F0) range, which varied significantly depending on intrinsic laryngeal muscle actions and on the length of the implant in the anterior-posterior direction (i.e., depth of medialization) [3]. However, this study did not assess metrics of voice quality. The role of implant shape remains unclear, as Zhang et al. found that implant shape is less important than stiffness and depth of implant medialization [4].

Implants can be formed from a variety of stiffnesses, ranging from relatively soft (Gore-Tex) to much firmer (Silastic, titanium). It has been proposed that it is ideal to match the stiffness of the physiological vocal fold [4], but the stiffness of actively contracting muscles has not been measured and clinically voice can be improved with even very stiff implants. Previous *ex vivo* results suggest that softer implants are a better option than their stiff counterparts. Cameron et al. demonstrated that softer implants result in an improved voice quality (i.e., a spectral noise measure) at low airflow and stiffer implants at higher airflow [5]. Zhang et al. found that softer implants appear to be less affected by depth of medialization [4]. While the use of soft implants may seem appealing from a surgical perspective, additional experimentation proves that they can be more deformable and do not maintain the original shape [6].

Most prior investigations of optimal implant features lack *in vivo* neuromuscular stimulation and instead assess implants using *ex vivo* phonation without muscular activation [4, 5, 6]. Considering the role of neuromuscular stimulation in voice production, phonation produced without this may not accurately reflect the physiologic characteristics of pathologic voice examined clinically. Thus, the *in vivo* neuromuscular stimulation model allows for stronger comparison to clinical voice. Furthermore, this study utilizes unilateral neuromuscular stimulation to mimic expected contralateral compensation in unilateral medialization thyroplasty. The added neuromuscular stimulation closely mimics the physiologic actions of the laryngeal neuromuscular complex [7, 8, 9]. Thus, the contralateral neuromuscular stimulation model can inform compensatory changes commonly seen in patients who undergo unilateral medialization thyroplasty, allowing for a more realistic representation of clinical cases.

In this study, we aim to identify the optimal shape and stiffness of thyroplasty implants in an *in vivo* canine model of unilateral vocal fold paralysis and contralateral graded neuromuscular compensation. By assessing the effect of

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implant features on voice quality via a validated metric of voice quality (cepstral peak prominence, CPP) [10] and minimum contralateral neuromuscular stimulation needed for phonation, this study contributes to our understanding of the relation between the implant features and voice quality with the goal of improving voice clinically.

2. Methods

2.1. Implant creation

All implant stiffnesses and shapes tested are listed in Table 1. Silastic and Gore-Tex are materials most commonly used as thyroplasty implants. To assess the effect of implant stiffness, custom implants were created by mixing a three-component elastic silicone solution with varying mass ratios (Ecoflex 0030; Smooth On, Inc., Easton, PA). The ratio listed as x:y:z reflects the ratio of Part A:Part B:silicone thinner. Larger amounts of silicone thinner result in a softer implant as noted by the previously reported Young modulus values included in Table 1. kPa increases with stiffness, i.e., Z is stiffer than Y which is stiffer than X. The hydrogel material was custom made using temperature gradient crystallization techniques to create an anisotropic material that is stiffer in the transverse direction than the longitudinal direction. This property matches the physiological anisotropy condition of the vocal folds. Implants made of every material except Gore-Tex (no fixed shape) were created in three shapes: rectangular, divergent, and convergent.

Table 1: *Implant stiffnesses and shapes tested. Young moduli are listed per previous reports or own micro-indentation measurements.*

Stiffness, Young modulus in kPa	Shape
Silastic (S), 1386 [5]	Rectangular (R)
Gore-Tex (G), unknown	Divergent (D)
Silicone 1:1:2 (X), 9.3 [5]	Convergent (C)
Silicone 1:1:1 (Y), 21.6 [5]	Gore-Tex (G)
Silicone 1:1:0 (Z), 60.6	
Hydrogel (H), 134.5 and 96	

All implants were 6 mm thick as made using custom molds. Implants were carved into the appropriate shape after the thyroplasty window was created to ensure appropriate medialization of the vocal fold to midline regardless of anatomic variation.

2.2. *In vivo* canine phonation model

After obtaining Institutional Review Board and Institutional Animal Care and Use Committee approval, three canines were used for this study. Each canine underwent the same surgical procedure as previously described [7, 8, 9]. After the animal was anesthetized, the larynx and right recurrent laryngeal nerve (RLN) were exposed surgically. A type I medialization thyroplasty window (height 6 mm, width 10 mm) was created on the left side of the thyroid cartilage. Implants were then carved to fit within the window into the left paraglottic space.

To achieve phonation, humidified air was passed from the trachea through the larynx at a fixed rate. High-quality subglottal sound pressure was measured using a probe microphone placed flush with the inner wall of the tracheal tube providing airflow. Video recordings of the vibrating larynx were taken from a superior view using high-speed video.

2.3. Graded neuromuscular stimulation

Phonation with no implant (baseline) and with each implant was tested across 10 unique levels of contralateral RLN stimulation to mimic the wide range of laryngeal neuromuscular activation conditions observed during normal phonation. To achieve muscle activation and glottal closure, cuff electrodes were placed onto the right RLN. The RLN was stimulated with a frequency of 125 Hz and a pulse width of 1 ms. For any given implant, RLN levels were always tested in order from level 1 to level 10.

2.4. Experimental conditions

Table 2 demonstrates the implant shape and stiffness tested in each experiment. It also lists the RLN stimulation conditions for which stable phonation (about 1000 ms) was achieved across all implant conditions (see Subsection 2.5 for detail).

Table 2: *Implant features by experiment.*

	Phonatory RLN Levels	Implant Stiffness	Implant Shape
1	8-10	S,G,X,Y,Z,H	R,D,C,G
2	7-10	S,G,X,Y,Z,H	R,D,C,G
3	9-10	S,G,X,Y,H	R,D,G

Note that the stiffness Z and shape C were excluded for Experiment 3 as they performed the worst in Experiments 1-2.

Minimal flow rate that achieved stable phonation was used in each experiment. Due to physiologic anatomic variations between the larynges used in each experiment, flow rate varied across experiments (600 mL/s for Experiment 1 and 700 mL/s for Experiments 2-3) but was fixed within a given experiment.

Across experiments, order of implants tested was randomized, and baseline (no implant) was repeated at regular intervals (i.e., every 5 implants) throughout the experiment. A complete set of experimental conditions was repeated twice in each experiment. Samples with unstable or multiple phonation qualities caused by edema were excluded from analysis.

2.5. Acoustic measurements

First, we labeled RLN levels at which stable phonation occurred, through visual and auditory examination of samples. Only samples that were fully phonated were included in the analysis (1 second). Cepstral peak prominence (CPP) was taken from 5ms intervals spanning the period of stable phonation for each sample using VoiceSauce [11]. CPP is a validated voice quality metric that measures the relative amounts of harmonic versus inharmonic energy in voice [10]. The CPP of the baselines (no implant) before and after the condition were first averaged. Delta CPP was calculated as the difference between implant condition CPP and adjacent average baseline CPP. This normalization method allows for changes in baseline (i.e., due to increasing laryngeal edema over the course of the experiment) to be accounted for. Positive delta CPP value indicates increased CPP with implants compared to baselines, and negative indicates decreased CPP compared to baseline.

Onset of phonation was assessed using neuromuscular stimulation. Using the labeling of RLN levels at which stable phonation occurred, we determined the minimum contralateral RLN stimulation needed for phonation. Similar to assessment of CPP, minimum RLN level needed was normalized to nearby baseline (no implant) values. The minimum levels for the baselines before and after the implant condition were first averaged. Delta onset was calculated as the difference between minimum contralateral RLN stimulation for nearby baselines and for implant of interest. Negative delta onset value means more contralateral RLN stimulation was needed to initiate phonation, and positive indicates that less was needed.

2.6. Statistical analysis

The effect of implant type on phonation variables (delta CPP and delta onset) was analyzed using RStudio [11]. Note that the levels of the implant type factor varied by experiment as shown in the x-axis of figures below. CPP data from each experiment were analyzed with one-way ANOVA with Huber-White standard errors and post-hoc Dunnett's test comparing each of the top 3 implants to all others. Phonation onset data from each experiment were analyzed with Kruskal-Wallis one-way ANOVA test and post-hoc Dunn's test comparing each of the top 3 implants to all others. $p<0.05$ were considered significant.

3. Results

CPP results are presented in box and whisker plots and phonation onset results as bar plots. The upper and lower borders of the box reflect the 75th and 25th percentile of the data respectively. The upper and lower whiskers reflect 75th percentile + 1.5* (interquartile range) and 25th percentile – 1.5* (interquartile range) respectively. On these plots, the red line at 0 (baseline) indicates no change from baseline.

3.1. Experiment 1

All implants resulted in median delta CPP greater than 0, indicating improvement from baseline, as seen in Figure 1A.

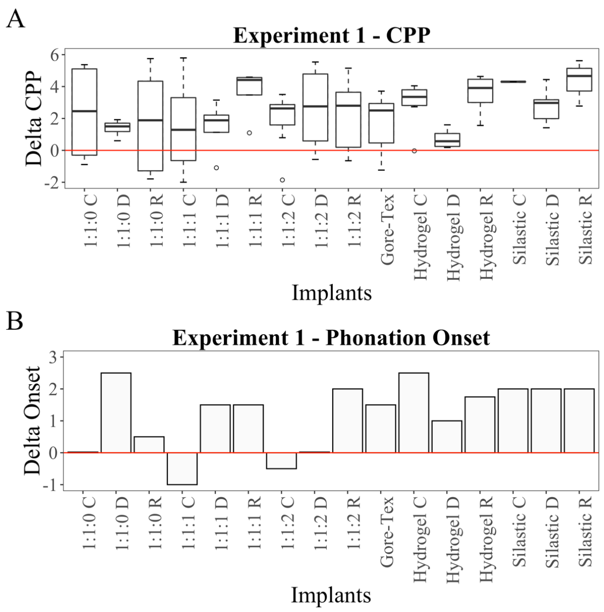

Figure 1: *Effect of implant type on A) delta CPP and B) delta onset for Experiment 1.*

Delta CPP was the highest for Silastic rectangular implants. Post-hoc testing revealed that delta CPP was higher for Silastic rectangular compared to 1:1:0 divergent, 1:1:0 rectangular, 1:1:1 convergent, 1:1:1 divergent, 1:1:2 convergent, and hydrogel divergent (all at $p<0.05$). Notably, delta CPP of Silastic rectangular was greater than that of Gore-Tex ($p<0.005$).

Phonation onset was assessed via minimal neuromuscular stimulation needed to achieve phonation. All implants except 1:1:0 convergent, 1:1:1 convergent, 1:1:2 convergent, and 1:1:2 divergent resulted in phonation with less neuromuscular stimulation than baseline (Fig. 1B). No implant was superior.

3.2. Experiment 2

Significant differences were found between delta CPP values of different implants ($p<0.001$). As seen in Fig. 2A, the highest value was from 1:1:0 rectangular, and this was not significantly greater than that of the next highest implants, 1:1:0 divergent and Silastic rectangular.

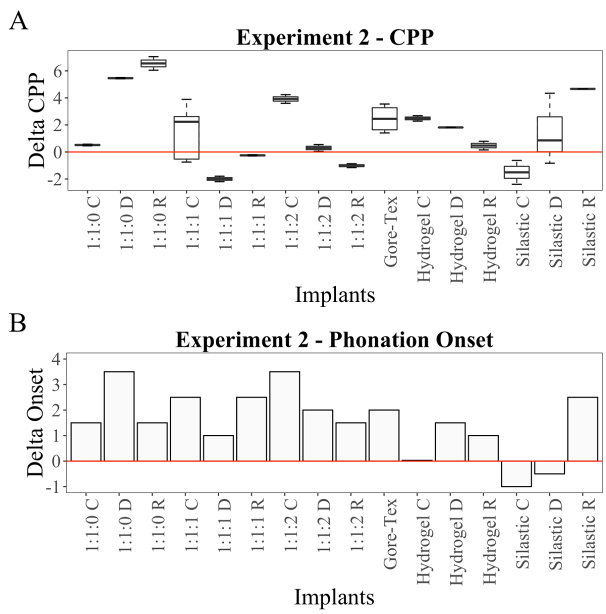

Figure 2: *Effect of implant type on A) delta CPP and B) delta onset for Experiment 2.*

Several implants resulted in negative median delta CPP values: 1:1:1 divergent, 1:1:1 rectangular, 1:1:2 rectangular, and Silastic convergent. The three implants with the highest delta CPP values all achieved significant difference compared to the implants that resulted in negative delta CPP (all at $p<0.05$). In this experiment, there was no significant difference between the delta CPP of Silastic rectangular and Gore-Tex.

Onset of phonation data followed a trend similar to Experiment 1 (Fig. 2B). Most implants resulted in improved onset of phonation, but hydrogel convergent resulted in no change from baseline and Silastic convergent and Silastic divergent in greater neuromuscular stimulation needed for phonation. No implant was found to be superior.

3.3. Experiment 3

As shown in Figure 3A, delta CPP was highest with Silastic rectangular implants and did not significantly differ from delta CPP of the next highest implant, Silastic divergent.

Delta CPP from both of these implants were significantly greater than all other implants tested ($p<0.05$). As in Experiment 1, delta CPP from Silastic rectangular implants was significantly greater than that of Gore-Tex ($p<0.001$). Unlike prior experiments, most implants (with the exception of Silastic divergent and Silastic rectangular) resulted in negative delta CPP, indicating worsened CPP compared to baseline.

Onset of phonation data showed patterns similar to Experiment 2 (Fig. 3B). Most implants resulted in improved onset of phonation, but 1:1:0 divergent and Silastic rectangular resulted in no difference from baseline and 1:1:1 divergent and hydrogel divergent in greater neuromuscular stimulation needed. The remaining implants resulted in decreased neuromuscular stimulation needed compared to baseline. There was no significant difference between implants.

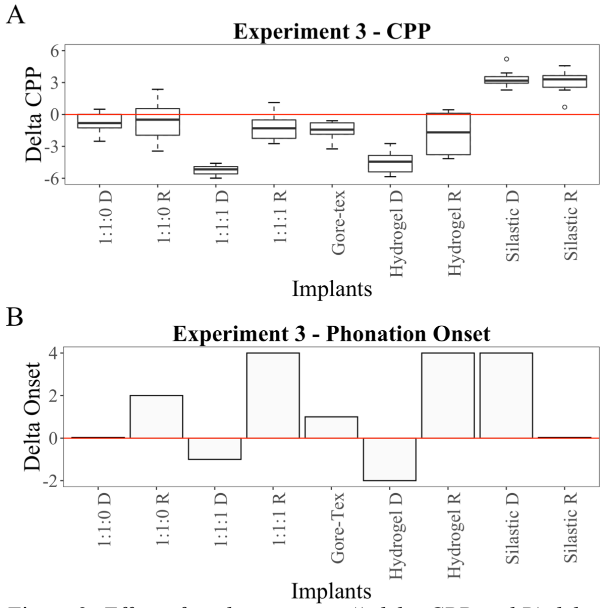

Figure 3: *Effect of implant type on A) delta CPP and B) delta onset for Experiment 3.*

4. Discussion

In this study, we identified implant stiffness and shape that are most effective at improving voice quality and neuromuscular compensation needed for phonation using three *in vivo* canine models of unilateral vocal fold paralysis with graded contralateral neuromuscular simulation.

Across experiments, Silastic rectangular implants were repeatedly amongst the three best implants with regards to voice quality and were superior to other implants. These findings are consistent with the findings of Cameron et al. that stiffer implants achieve higher CPP at airflows comparable to that used in this study [5]. This is inconsistent with Orestes et al. who proposed that divergent implants may be superior to rectangular implants, but these findings were based on aerodynamics data with no assessment of voice quality [3].

The consistent improvement in voice quality achieved with Silastic rectangular implants across larynges is informative clinically. Although the convenience of Gore-Tex (no intraoperative shaping needed) may be appealing clinically, our findings repeatedly show Silastic rectangular implants producing improved voice quality compared to Gore-Tex and consistently produced high improvement in voice quality compared to other implants. While there are no conclusive trends with regards to the Silastic stiffness or rectangular shape alone, there appears to be a strong synergy when Silastic stiffness and rectangular shape are present in one implant. Further investigation is needed to understand this relationship.

Overall, phonation quality improved with implants compared to baseline with no implant support. However, some implants from Experiments 2-3 resulted in negative delta CPP values, indicating worsened phonation quality compared to baseline without implant. This could be due to a number of factors including over-medialization of the vocal fold or unforeseen changes to glottal channel contour (i.e., medial surface shape changes). While these factors are beyond the scope of this preliminary study, further investigation is recommended. Given no systematic patterns observed regarding which particular implants result in negative delta CPP, this could reflect physiologic variation in individual larynges for certain implant features.

While most implants resulted in reducing neuromuscular compensation needed for onset of phonation than baseline, no implant was superior. We observed a few implants resulting in increased neuromuscular compensation needed. Cameron et al. [5], an *ex vivo* study that lacked neuromuscular stimulation, reported that subglottal pressure at phonation onset increased as implant stiffness increased. This would suggest that increased RLN stimulation would be needed with stiffer implants, but our current *in vivo* studies did not replicate this.

Some limitations in the study design come from the use of canine larynges. While canine larynges are not identical to human larynges, they exhibit remarkable similarities to human larynges and have been validated as an excellent model for the study of *in vivo* phonation [13, 14]. The small sample size (three animal models with limited number of repetitions) was unavoidable. The use of vertebrate *in vivo* models ethically necessitates using the minimum number possible. Additionally, laryngeal edema increases as experiments are prolonged, so all factors of interest (e.g., depth of medialization, a wider variety of implants, more repetitions) cannot be tested in one animal model. We highlight that a limited number of experiments does not draw away from the value of *in vivo* assessments of implants, as prior studies are largely *ex vivo* or computational. With neuromuscular stimulation, this *in vivo* study allows for stronger comparison to physiologic phonation with implants.

Finally, these findings allow us to pursue additional investigations of implant performance, particularly with regard to the relation between presented voice quality findings and laryngeal vibratory dynamics. As a part of this study, high-speed video recordings were taken of laryngeal vibration with the studied implants in place. In the future, we intend to analyze these videos to assess vibratory dynamics, including of the vocal fold medial surface, to better understand how variation in implant features affects phonation.

5. Conclusions

In conclusion, Silastic rectangular thyroplasty implants consistently result in an improved voice quality metric, indicating high-quality phonation. These findings have clinical implications, as they may suggest new ways to optimize treatment of glottic insufficiency.

6. Acknowledgements

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7. References

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