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ORIGINAL RESEARCH

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# Pre-clinical evaluation of APrevent® VOIS for unilateral vocal fold paralysis medialization

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## Abstract

**Objective:** To evaluate the concept and efficacy of an adjustable implant (Prototype SH30: porcine implant and APrevent® VOIS: human concept) for treatment of unilateral vocal fold paralysis (UVFP) via in vivo mini-pig studies, human computed tomographic (CT) and magnetic resonance (MR) image analysis, ex-vivo aerodynamic and acoustic analysis.

**Methods:** Feasibility testing and prototype implantation were performed using in-vivo UVFP porcine model ($n = 8$), followed by a dimensional finding study using CT and MR scans of larynges ($n = 75$) for modification of the implant prototypes. Acoustic and aerodynamic measurements were recorded on excised canine ($n = 7$) larynges with simulated UVFP before and after medialization with VOIS-Implant.

**Results:** The prototype showed in the in-vivo UVFP porcine model an improved glottic closure from grade 6 incomplete closure to complete closure ($n = 5$), to grade 2 incomplete closure ($n = 2$) and grade 3 incomplete closure ($n = 1$). On human CT/MR scans the identification of the correct size was successful in 97.3% using the thyroid cartilage alar "distance S" as the only parameter, which is an important step towards procedure standardization and implant design. Results were confirmed with implantation in human laryngeal cadavers ($n = 44$). Measurements of the acoustic and aerodynamic effects after implantation showed a significant decreased phonation threshold pressure ($p = .0187$), phonation threshold flow ($p = .0001$) and phonation threshold power ($p = .0046$) on excised canine larynges with simulated UVFP. Percent jitter and percent shimmer decreased ($p = .2976$; $p = .1771$) but not significant.

**Conclusions:** Based on the preclinical results four sizes, differing in medial length, implant width and expansion direction of silicone cushions, seem to be enough to satisfy laryngeal size variations. This concept is significantly effective in medializing

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UVFP and improving the aerodynamic and acoustic qualities of phonation as reported in a preliminary clinical outcome study with long-term implantation.

**Level of Evidence:** N/A

**KEYWORDS**
adjustable implant, type I (medialization) thyroplasty, UVFP, vocal fold paralysis, VOIS

## 1 | INTRODUCTION

Unilateral vocal fold paralysis (UVFP) occurs after damage to the recurrent laryngeal nerve and may result in decreased laryngeal function and incomplete glottal closure, as the affected vocal fold no longer moves in sync with the contralateral vocal fold. Consequently, dysphonia or dysphagia may occur, severely impairing quality of life of those affected.[1]

Symptomatic unilateral paralysis has been treated effectively with a variety of surgical techniques. Type I thyroplasty, developed by Isshiki in 1974,[2] is a successful phonosurgical procedure for improving voice quality.[3,4] The procedure involves the insertion of an implant through a window on the ipsilateral thyroid cartilage ala, pushing the paralyzed vocal towards the midline. This leads to an improvement of the deficient glottal closure, thus to an improved voice quality and performance.

Due to its low cost and the possibility to perform individual adjustments intraoperatively, the silastic blocks are a commonly used implant material.[3] However, it is reported that the silicone is associated with steep learning-curve, which significantly increases the duration of surgery and its outcome. As a result, intraoperative edema is more intense, leading to suboptimal shaping of the medialized vocal fold.[4]

To overcome this shortage, alternative implants such as hydroxyapatite implants, polytetrafluoroethylene (Gore-Tex) stripes, or preformed implants like titanium vocal fold medializing implant (TVFMI) and Montgomery silicone blocks.[5–9] Crucial to the surgical outcome with these implants is proper positioning, selection of the best-fit size and fixation. Incorrect positioning, an improperly sized or inadequately fixated implant can lead to insufficient medialization, granuloma formation due to erosion of the overlying mucosa, implant extrusion and thus impair the improvement of voice quality, requiring revision surgeries.[4,10]

To address these issues, we have developed a high-precision implant that can be easily inserted, allowing intra- and postoperative adjustment to preserve long-term vocal functionality.

This article reports the initial preclinical results in the development of APrevent®'s Vocal Implant System (VOIS). The objective of these studies was to establish the concept, the development of a standardized surgical procedure, the evaluation of implant sizing based on computed tomography (CT), with final confirmation by fresh human laryngeal cadaver study and analysis of aerodynamic and acoustic characteristics of phonation after implantation of the VOIS system.

## 2 | IMPLANTS

The APrevent® Vocal Implant System is a novel solution introduced by APrevent® for type I or medialization thyroplasty and treatment of glottic insufficiency. The APrevent® VOIS consists of three components: a titanium housing with integrated port chamber and port membrane, a screw fixation plate and a silicone cushion, that can be inflated and deflated by injecting or removing filler material to/from the implant port. The preformed silicone cushion of VOIS can be adjusted intra- and post-operatively to optimally fit individual anatomic conditions of each patient. VOIS is available in four sizes from X-small (XS) to large (L). The implant has been CE certified since December 2019 and is now being launched to the market.

## 3 | MATERIALS AND METHODS

The initial implantation study and feasibility evaluation of VOIS was performed by implantation in in-vivo paralyzed porcine larynges with a specifically customized prototype, which can be filled with saline solution after implantation to adjust its dimensions and is placed as posterior as possible to approach the vocal process of the arytenoid cartilage. Subsequently, the implant prototypes were modified in their dimensions by analyzing CT scans of human larynges to fit different ethnic groups and genders, followed by an aerodynamic and acoustic analysis before and after implantation in excised canine larynges. These preclinical studies are described below.

### 3.1 | In vivo simulated unilateral vocal fold paralysis porcine model

An in vivo simulated UVFP animal model was used for verification and validation of the concept with intra- and postoperative adjustability (Figure 1). For the animal study, an adjustable implant with the dimensions customized for porcine larynges was designed and was approved by Institutional Animal Care and Use Committee (IACUC, No. PIG-106010). Mini-pig larynges were chosen as they most resemble those of humans. Eight healthy miniature Lanyu pigs (4 male and 4 female; $n = 8$) with a weight between 39.0 and 54.3 kg were used for this study, with the simulated UVFP condition serving as control for comparison with the post-implantation condition with the APrevent® Implant 30SH to evaluate efficacy. For this purpose, each pig was anesthetized by intramuscular injection of Azeperonum (40 mg/mL) and

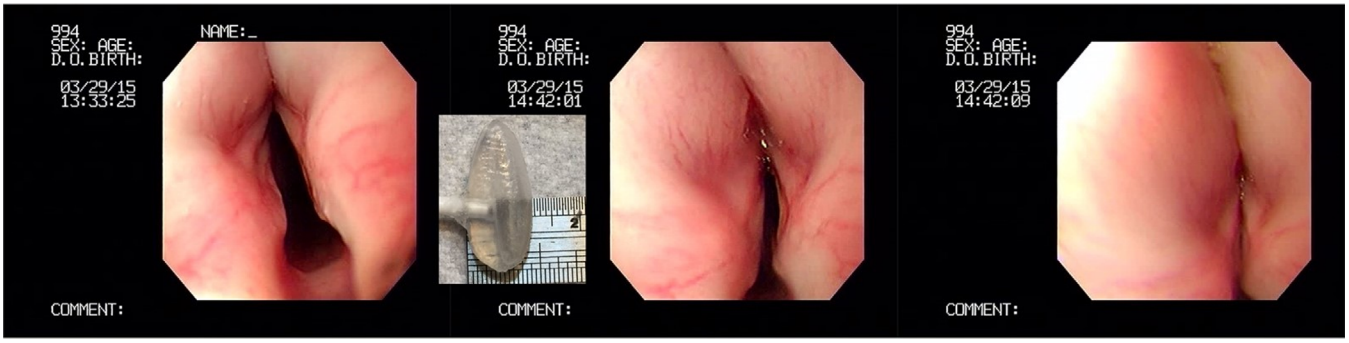


**FIGURE 1** Implantation of APrevent® Implant 30SH.

Atropine (0.5 mg/mL) IM, followed by intravenous injection of Zoletil 50 (125 mg tiletamine hydrochloride, 125 mg zolazepam hydrochloride). The animals were intubated endotracheally. To induce UVFP, a prelaryngeal longitudinal skin incision was made under sterile conditions to expose the thyroid-, cricoid cartilage and the first two to three tracheal rings. The recurrent laryngeal nerve was visualized and transected using an intraoperative neuromonitoring device (NIM-Response® 3.0, NIM TriVantage®-7.0 Tube, Medtronic). In a second step, the thyroid ala was created on the side of the UVFP, with dimensions (11 mm × 8 mm). The reason for standardizing the thyroplasty window position was the almost uniform size of the thyroid cartilage within the same strain. Movements of the vocal folds and closure of the glottis were assessed with Olympus video-assisted endoscopic system before and after unilateral resection of the recurrent laryngeal nerve, and after implantation of the prototype. Glottic closure was evaluated according to the classification of Södersten and Lindestad[11] which defines successful closure as superior closure by at least three degrees than preoperative. Fine adjustments to the implant were made by injecting physiologic saline solution through a subcutaneous port while medialization movements of vocal folds and closure of glottic gap were recorded.

## 3.2 | CT/MR-scan analysis of laryngeal dimensions for development and validation of APrevent® VOIS implantation procedure

After feasibility testing on animal models, the implant prototypes were modified in dimensions to fit human larynges. CT images of human larynges (Caucasians $n = 34$; Asians $n = 19$) were analyzed using OsiriX MD v9.0 (Pixmeo, Geneva, Switzerland) to obtain information about laryngeal dimensions and vocal fold length, and to evaluate the variations between larynges of a specific gender and different ethnical groups. Caucasian larynges were provided by the Institute of Anatomy at the Medical University of Vienna, according to regulations using material from voluntary body donors. Anonymized MR-scans ($n = 12$; male = 6/12, female = 6) were retrospectively analyzed by author Böttcher A., Universitätsklinikum Eppendorf, Hamburg, Germany. According to § 12 HmbKHG (Hamburg hospital law) formal consent was not required. Anonymized CT scans of Asian larynges from routine clinical examinations in the context of screening for head and neck diseases were analyzed retrospectively. Formal patient consent was not required due to anonymization.

As a reference for implant design, size and expansion patterns, morphometric landmarks were measured on axial cross-sectional CT scan images at the level of the vocal cord process. The most important parameters to be considered are the vocal process, the length of the thyroid cartilage lamina "Distance S", the thyroid cartilage width "Width" and thyroid cartilage "Angle". In addition, we used these landmarks to assess whether it is possible to determine the appropriate implant size by measuring the "Distance S" and if the proposed implant also meets the requirements of the previously defined "best-fit implant" (Figure 2). The implant length should extend as far posteriorly as possible but not to the cricoid cartilage. The length is sufficient if it extends over the entire vocal process. Sufficient medialization is defined as successful, if the distance "M" between the implant and the vocal process is within 3 mm without the implant exceeding the vocal process.

## 3.3 | Effect of VOIS implantation on the aerodynamic and acoustic properties of phonation

Aerodynamic and acoustic measurements were performed in seven excised canine larynges in a controlled, repeatable, and soundproof environment during complete normal closure, UVFP, and after medialization of the vocal folds using the adjustable VOIS implant. For this purpose, larynges with dimensions similar to those of humans were selected and excised according to the protocol described by Jiang and Titze.[12] For the examination of simulated UVFP condition, vocal fold is adducted on one side with a 3-Pronged micrometer. The adducted vocal fold level is adjusted before the trial by moving the micrometer superior and inferior until it is in the same plane as the unadducted vocal fold. The equipment for aerodynamic and acoustic measurements was provided by the Laryngeal Physiology Laboratory at the University of Wisconsin. The adjustable VOIS implant and surgical instruments were provided by APrevent®

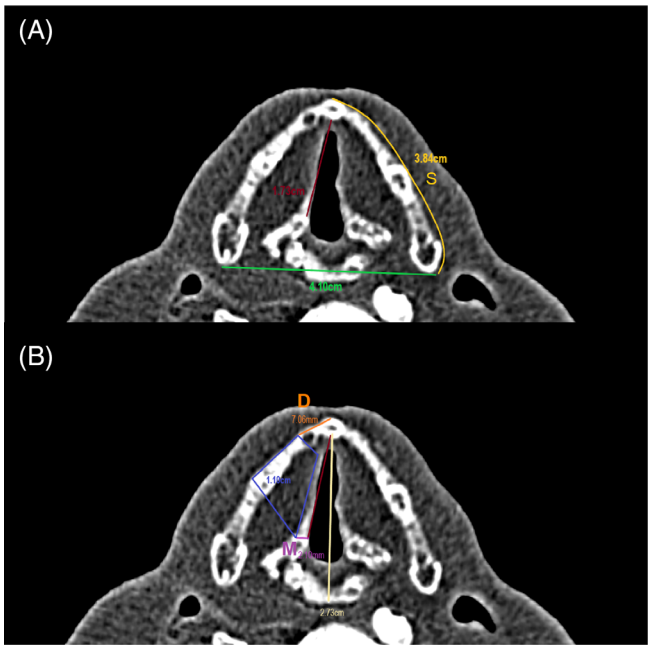


**FIGURE 2** Axial laryngeal CT-scan. (A) To determine the size of VOIS implant; (B) Select suggested implant size based on "Distance S" (Figure 2A) and Table 2 to check the fit of the implant.

Biotech GmbH, Austria. The VOIS implant was inserted into the paralaryngeal space through a thyroplasty window on the thyroid cartilage ipsilateral to the paralyzed vocal fold according to the protocol described by senior author Ho GM. After implantation of VOIS implant, the silicone cushion is slowly filled with saline using a digital syringe, in 0.03 mL steps, not exceeding the maximal filling volume, until the adjustable VOIS implant has reached the optimal medialization (=glottic midline).

The aerodynamic and acoustic trials were conducted as a sequence of 5-second periods of phonation, followed by 5-second periods of rest for all three conditions. During each trial, airflow passing through the larynx system was manually increased gradually and consistently until phonation commenced.

### 3.3.1 | Södersten and Lindestad classification

Medialized vocal fold was examined for the type of vocal fold closure.[11]

### 3.3.2 | Aerodynamic analysis

Phonation threshold flow (PTF), phonation threshold pressure (PTP), and phonation threshold power (PTW) were determined using a custom Lab VIEW 8.5, graphically displaying the spectrogram, airflow, and pressure signals as functions of time for each trial; airflow and pressure values corresponding to the onset of phonation were recorded as PTF and PTP, respectively. PTW was calculated as the product of these values. Vocal Efficiency ($V_E$) is equal to acoustic energy divided by aerodynamic energy.

### 3.3.3 | Acoustic analysis

Acoustic analysis was performed by measuring the signal-to-noise ratio (SNR) and the interference parameters percent jitter and percent shimmer. The voice signal was trimmed using GoldWave 5.1.2600.0 program Version 5.70, the analysis was done using Computerized Speech Lab (CSL™, Pentax) software.

## 3.4 | Statistical analysis

The results of the studies are presented as mean ± standard deviations (SDs). Statistical analysis was performed using the SPSS statistical program (v27 IBM SPSS Statistics, Chicago, IL). Paired t-tests were used to determine whether the implant insertion had a significant effect on the measured parameters. If data were not normal, a Mann–Whitney rank sum test was performed. A significance level of $\alpha = 0.05$ was used.

# 4 | RESULTS

## 4.1 | In vivo simulated unilateral vocal fold paralysis porcine model

After implantation all subjects with implanted test device resulted in an improvement from grade 6 incomplete closure to grade 1 complete closure ($n = 5$), grade 2 incomplete closure ($n = 2$), and grade 3 incomplete closure ($n = 1$). All animals implanted with the test device showed improved closure of >3°, when compared to the UVFP state (Table 1).

## 4.2 | CT- and MR-scan analysis—human

Thyroid lamina length measurements ranged from 29.8 to 48.0 mm and interlaminar distance from 26.5 to 49.4 mm. A comparison between female and male larynges of Caucasians and Asians, including the thyroid lamina length "Distance S", thyroid cartilage "Width" and thyroid cartilage "Angle", is given in Table 2. The proposed implant size and the best-fit implant size matched in 73 ($n = 73/75$) cases and differed in 2 of the 75 subjects ($n = 2/75$). Table 3 shows the average measures for "Distance S", "Width", "Angle", and implant size, grouped by female and male. Based on the data obtained from the measurements, prototypes with different expansion patterns were fabricated to guarantee the effectiveness of the glottal closure. From this verification we found out that prototypes with an adjustable medioposterior extension towards vocal process of the arytenoid cartilage by fluid delivery/removal might be the ideal concept for the final APrevent® VOIS implant to fit different laryngeal sizes and facilitation of optimal glottal closure (Figure 3).

### 4.3 | Acoustic and aerodynamic measurements

According to the classification of Södersten and Lindestad,[11] implantation with APrevent® VOIS implant showed complete closure in all cases ($n = 7$) validating the concept with an adjustable medioposterior extension of the silicone cushion. The results are given in Table 4 and graphically presented in Figure 3. The preoperative phonation threshold pressure of 23.51 cm $H_2O$ decreased significantly after VOIS implantation to 11.98 cm $H_2O$ ($p = .0187$). Phonation threshold flow also decreased significantly from 97.21 to 38.93 mL/s ($p < .001$) and phonation threshold power decreased significantly from 2388 to 508 mL/s cm $H_2O$ ($p = .0046$). Vocal efficiency increased significantly from 0.056 to 0.280 after implant insertion ($p = .0167$). For the fundamental frequency preoperative measurements were 81.90 Hz. Post-medialization with VOIS implant, they changed to 134.59 Hz. Differences were observed, but there were no statistically significant differences between the pre- and postoperative $F_0$ measurements ($p = .3567$). SNR increased from 1.069 to 3.471 after medialization ($p = .0906$). Mean jitter decreased from 4.89% to 3.77% and showed a reduction after medialization ($p = .2977$). The percent shimmer decreased from 39.04% to 28.44% after medialization ($p = .1771$).

## 5 | DISCUSSION

The aim of this study was to develop an efficient implant system with an easy to perform and standardized surgical procedure, that allows an uncomplicated and time-saving application, pre- and postoperative adaption to conform to individual structural variations and conditional changes, but most of all to yield good functional results.

Specifically, the functionality of the VOIS system, the surgical procedure for the most appropriate implant size and window locations were evaluated using the morphometric data of the thyroid cartilage for positioning the implantable components and using acoustic and aerodynamic analyses for quantitation of efficacy at preclinical stage.

One major cause for unsuccessful medialization thyroplasty and revision surgery is the lack of postoperative adjustment of implants for changes in vocal fold position.[10] The results of our in-vivo animal study show that using an adjustable silicone laryngeal implant to treat UVFP with glottic insufficiency is a safe, reasonable, and effective method. By using the pre-implantation condition as control, all subjects showed improvement in glottic closure after implantation of the prototype. The APrevent® prototype made of inert silicone (Nusil®, 30 Shore A) is specifically designed for use in the larynx of minipigs. It was also used as a prototype to examine potential irritation and toxic effects to ensure biocompatibility and safety for human use. No respiratory distress was observed during the follow-up period (13 and 26 weeks). Furthermore, no macroscopic infections or edema were observed after the subjects were euthanized. 63% of the prototype group showed complete closure of the cartilaginous portion ($n = 5/8$), while 25% showed incomplete closure of the cartilaginous part (IC 2; $n = 2/8$), and 12% showed triangular incomplete closure anterior to the vocal process (IC 3; $n = 1/8$). All subjects in the test device group showed complete closure of the anterior 2/3 of the folds. Incomplete closure could be caused by a too anterior placement of the implant, lack of implant fixation, as well as too less expansion to the posterior part of the APrevent® prototype. We concluded that implant adjustability (change in implant size and shape to fit into different laryngeal dimensions), ability of silicone cushion expansion towards the vocal process (closure of the posterior glottal gap), implant fixation (prevents dislocation and migration) and development of measuring instruments for the standardized procedure are essential and very critical for a successful surgery.[13–15]

Insufficient medialization in type I thyroplasty is also frequently caused by inadequately sized or misplaced implants, and implant migration. Medialization thyroplasty is highly dependent on using laryngeal morphometric data as landmarks during surgery. However,

**TABLE 2** Four different sizes (XS, S, M, L) and their dimensions and "Distance S" and implant-size specific "Distance D".

| Implant size | X-Small | Small | Medium | Large |
|---|---|---|---|---|
| Length | 9 mm | 11 mm | 15 mm | 18 mm |
| Width | 7 mm | 8 mm | 8 mm | 8 mm |
| Distance S | 28–33 mm | 33–38 mm | 38–42 mm | >42 mm |
| Distance D | 7 mm | 10 mm | 8 mm | >12 mm |

**TABLE 1** Analysis of glottic closure before and after implantation VOIS system in a porcine animal model.

| | Gender | Width (mm) | Glottis closure before implantation | Glottis closure after implantation |
|---|---|---|---|---|
| APrevent® prototype ($n = 8$) | Female | 44.0 | IC 6 | IC 3 |
| | Female | 44.5 | IC 6 | CC 1 |
| | Female | 48.5 | IC 6 | CC 1 |
| | Female | 44.0 | IC 6 | IC 2 |
| | Male | 49.0 | IC 6 | IC 2 |
| | Male | 54.3 | IC 6 | CC 1 |
| | Male | 49.5 | IC 6 | CC 1 |
| | Male | 45.5 | IC 6 | CC 1 |

Abbreviations: CC, complete closure as defined by Södersten and Lindestad classification; IC, incomplete closure as defined by Södersten and Lindestad classification.

morphometric studies have shown variations in thyroid cartilage dimensions due to individual anatomy, ethnical or sexual dimorphism.[16,17] These variations may lead to difficulties in implant placement with inadequate posterior medialization and procedure standardization with a static implant.[14] Therefore, the pre- and postoperative adjustability of the VOIS-Implant with individualized implant size, making standardization of the surgical procedure possible, can be helpful and beneficial to patients and health care providers. Besides, our analysis of the laryngeal dimensions provided positive evidence for gender specificity of implants. Due to wide dimensional variations during the studies, four implant sizes were designed and developed (X-small, small, medium, large) as given in Table 2. Identification of the correct implant size was successful in 97.3% using the thyroid cartilage lamina "Distance S" as the only parameter on CT scan images. Only two male subjects fit better into the medium-size group than into the small-size group, although, according to thyroid lamina length "Distance S" (36.3 mm/37.2 mm) the suggested implant size was "Small". However, after planning on the CT scan images, it became apparent that the implant size "Small" would not be the best fit in terms of implant length compared to the implant size "Medium" due to insufficient posterior extension and the larger "Distance M", that is, the horizontal distance between the implant and the vocal process of the arytenoid cartilage. The proposed ranges for "Distance S" for the "X-Small" and "Small" implants could be assigned 100% to the female group, while the proposed ranges for "Distance S" for the "Medium" and "Large" implants could be assigned 96% to the male group. Considering gender as an additional predictive factor, all female larynges received "X-Small" or "Small" implants and all male larynges received "Medium" or "Large" implants, demonstrating gender specificity in this study. Using "Distance S" as the primary predictive parameter and gender as an additional supportive predictive parameter, the proposed implant sizes could be matched to all laryngeal CT images.

**TABLE 3** Comparison of laryngeal dimensions and implant size between female/male Caucasians and Asians.

| | Caucasian | Asians | *p*-value |
|---|---|---|---|
| *Male larynx* | | | |
| Distance S (mm) | 41.80 ± 5.30 | 41.59.80 ± 3.09 | .7906 |
| Width (mm) | 40.00 ± 4.99 | 37.39 ± 4.93 | .2513 |
| Angle (degree) | 76.76 ± 8.77 | 67.04. ± 8.54 | .0555 |
| Implant size | M/L | M/L | |
| *Female larynx* | | | |
| Distance S (mm) | 32.58 ± 2.46 | 33.84 ± 1.45 | .7352 |
| Width (mm) | 35.12 ± 4.47 | 31.98 ± 1.48 | .1179 |
| Angle (degree) | 102.06 ± 8.60 | 98.26 ± 9.15 | .2980 |
| Implant size | XS/S | XS/S | |

*Note*: Measurement value shown as mean ± SD; *p*-value <.05, *statistically significant difference.

Under considerations of the facts originating from the animal studies, CT/MR image analyses, incl. large variation in laryngeal dimensions, importance of window location, expansion direction of silicone cushions, adjustability after device insertion and secure fixation of the implant, different prototypes for human larynges were fabricated to evaluate closure in fresh human larynges with the result indicating a better closure of the glottal gap, if the implant expansion can reach the vocal process in medioposterior direction (Figure 4). The final APrevent® VOIS implant resulted in complete closure of the glottis in our excised canine laryngeal study showing a significant improvement of aerodynamic and

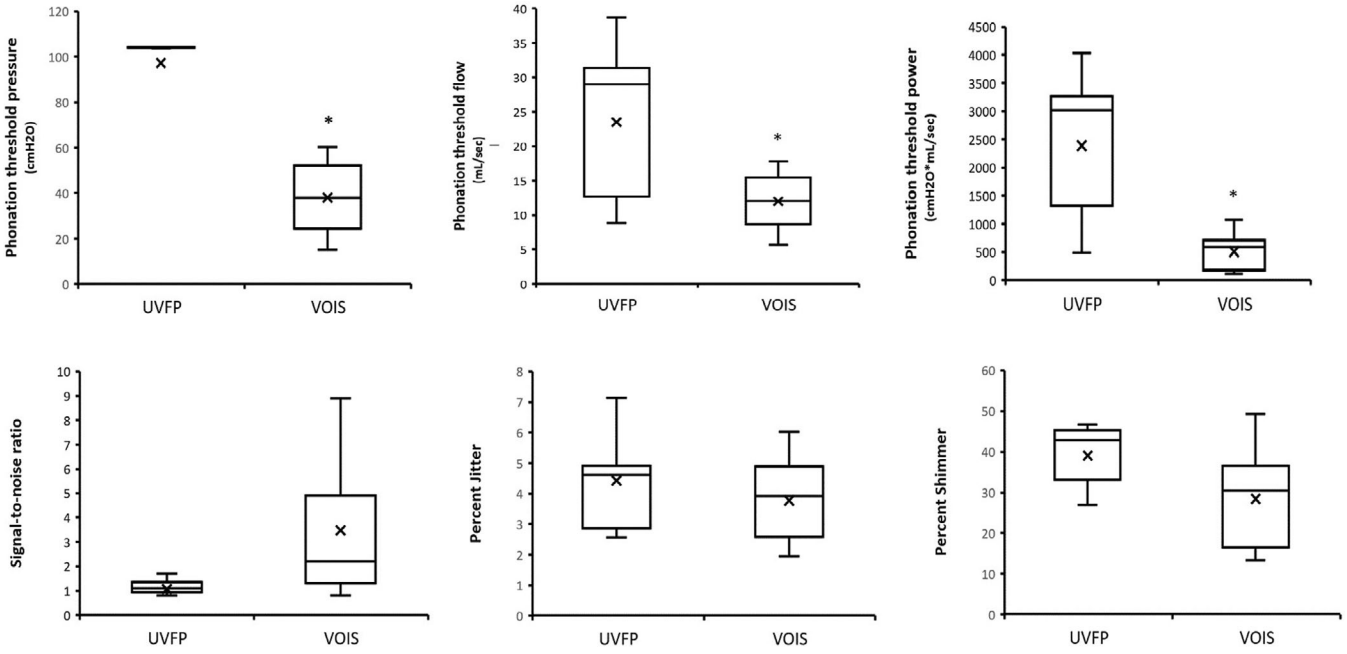


**FIGURE 3** Measurements of aerodynamic and acoustic analysis made before and after VOIS implantation.

acoustic properties of phonation after being fine-tuned. All measurements were performed in a controlled, repeatable, and soundproof environment.

**TABLE 4** Summary statistics before and after VOIS implant insertion.

| Parameter | UVFP | Post-VOIS | *p*-value |
|---|---|---|---|
| *Aerodynamic data* | | | |
| PTP (cm $H_2O$) | 23.51 ± 11.87 | 11.98 ± 4.490 | .0187[a] |
| PTF (mL/s) | 97.21 ± 18.54 | 38.03 ± 17.52 | .0001[a] |
| PTW (cm $H_2O$ mL/s) | 2388 ± 1333 | 508.3 ± 359.5 | .0046[a] |
| $V_E$ (mL) | 0.056 ± 0.049 | 0.280 ± 0.203 | .0167[a] |
| *Acoustic analysis* | | | |
| F0 (Hz) | 81.90 ± 43.59 | 134.6 ± 124.2 | .3567 |
| SNR (dB) | 01.07 ± 0.520 | 03.47 ± 02.95 | .0906 |
| Percent Jitter % | 04.42 ± 01.51 | 03.77 ± 1.410 | .2976 |
| Percent Shimmer % | 39.04 ± 07.87 | 28.44 ± 13.55 | .1771 |

*Note*: Measurement value shown as mean ± SD.
Abbreviations: F0, fundamental frequency; PTF, phonation threshold flow; PTP, phonation threshold pressure; PTW, phonation threshold power; SNR, signal-to-noise ratio; VE, vocal efficiency.
[a]*p*-value <.05; statistically significant difference.

Since sound quality is subjective, we used objective acoustic measures such as jitter, percent shimmer, and SNR to describe this perceptual unit. Aerodynamic performance was calculated from flow and phonation threshold pressure. The results are comparable to those of a previous study with TVFMI performed under the same conditions.[7] Decreased glottic gap correlated with improved vocal function as determined by acoustic, aerodynamic, and perceptual measurements. The reduced airflow required to initiate phonation also increased the acoustic quality of the vocal signal. The increased SNR was achieved by the reduced airflow as well as the increased acoustic power. In addition, a reduction in percent jitter and percent shimmer was noted due to the medialization of the vocal folds, which restored vocal folds' contact and periodicity of vibrations. An increase in F0 was also observed due to closure of the glottic gap.[18]

## 6 | CONCLUSION

The preclinical results of APrevent® VOIS demonstrate a simple and effective concept for type I thyroplasty to achieve expression medialization of the vocal fold. Our in-vivo animal study showed that our adjustable silicone laryngeal prototype is an effective treatment for

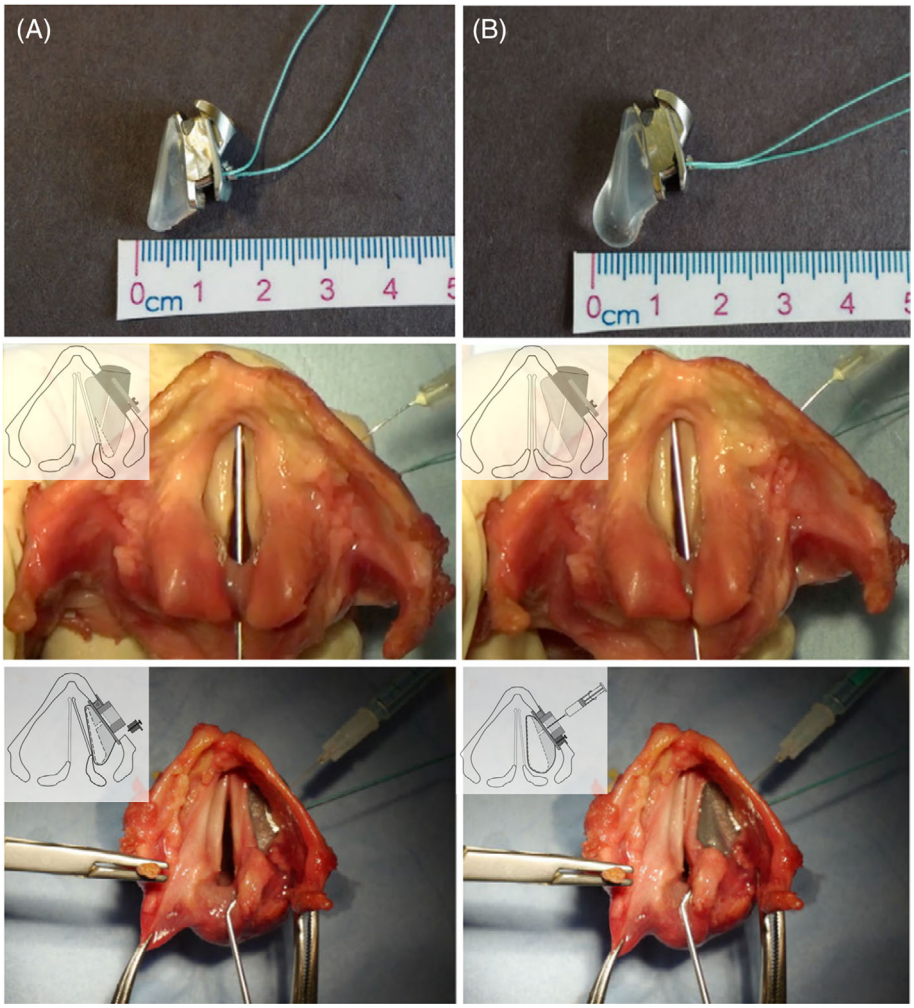


**FIGURE 4** Implantation of the prototype APrevent® VOIS implant. (A) Before expansion; (B) Implantation of prototype with extension of silicone cushion.

UFVP. Based on the CT/MR image analyses prototypes for human larynges were fabricated differing in medial length, implant width and expansion direction of silicone cushion. The final APrevent® VOIS implant showed complete closure of the glottis and improved aerodynamic and acoustic measurements in our excised canine laryngeal study. APrevent® VOIS can be easily inserted and allows individual result optimization by intra- and post-operative adjustments. Sufficient medioposterior expansion of the silicone cushion is a key point to close the posterior glottal gap. No revision surgery would be required for under- or over-corrections. As shown in our previously published preliminary clinical data[19,20] the APrevent® VOIS is a reasonable and efficient method to achieve sufficient vocal fold medialization with subsequent voice improvement, providing further supportive evidence in addition to the positive findings from the preclinical development and testing.

## ACKNOWLEDGMENTS

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## CONFLICT OF INTEREST STATEMENT

The first and also corresponding author declares to be the inventor of the VOIS-implant and standardized VOIS-implantation procedure. He became a paid employee of the company producing the implant after proof of concept and design freeze of the device. The other authors declare no conflicts of interest. The authors have no other funding, financial relationships, or conflicts of interest to disclose.

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