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Effect of changes in medial surface shape on voice production in excised human larynges

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Abstract: Clinical intervention of glottal insufficiency often focuses on correcting glottal gap as visualized from above. In contrast, changes in medial surface shape due to intervention have received less attention. This study investigated how changes in medial surface shape affect voice production in excised human larynges, by locally medializing the medial surface at different longitudinal and vertical locations. The results showed that localized medialization at a more inferior location yielded better improvement in glottal closure and higher-order harmonic excitation in the produced voice. This study shows that surgical intervention of glottal insufficiency should also aim at restoring desirable medial surface shape.

[DDO'S]
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1. Introduction

Glottal insufficiency, or the inability of the vocal folds to close the glottis adequately during phonation, due to either vocal fold paralysis, paresis, or atrophy, often leads to degraded voice production. An important goal of clinical treatment of glottal insufficiency is to restore proper glottal closure. Currently, surgical intervention procedures (medialization laryngoplasty, injection augmentation, etc.) often focus on the glottal gap as visualized from a superior view. In contrast, the medial surface shape along the vertical direction has received less attention, partially due to technical difficulties in direct visualization in a clinical setting.

The medial surface shape of the vocal folds, however, is known to play an important role in voice production. Previous studies (Titze and Talkin, 1979; Lucero, 1998; Alipour and Scherer, 2000; Zhang, 2008; Mau *et al.*, 2012) have demonstrated important effects of the medial surface shape on vocal efficiency and the phonation threshold pressure. More importantly, the vertical thickness of the medial surface has long been hypothesized to have an important role in regulating the glottal closure pattern of vocal fold vibration (van den Berg, 1968; Titze, 1994; Sundberg and Högset, 2001). Our recent computational simulations (Zhang, 2016a,b) showed that medialization alone does not always guarantee glottal closure during phonation. Vocal folds with very small medial surface thickness often vibrate without complete glottal closure despite that the two folds are fully medialized (Zhang, 2016b). Increasing the vertical thickness allows the vocal folds to better maintain adductory position and leads to increased duration of glottal closure during phonation (Zhang, 2016a,b). In comparison, the effects of changes in vocal fold stiffness and vocal fold medialization on the closed quotient (CQ) (the fraction of the cycle in which the glottis remains closed) are much smaller.

These recent studies thus suggest that voice research should pay more attention to medial surface shape and its control. Clinically, these findings indicate that in addition to medialization, clinical treatment of glottal insufficiency should also aim to restore optimal medial surface shape or vertical thickness in order to restore normal voice production. Due to technical difficulties, direct visualization and monitoring of medial surface shape along the vertical direction is currently not possible in the clinic. As a result, control of the medial surface shape during surgical intervention is often not targeted or monitored during surgical interventions of glottal insufficiency. Based on the findings of Zhang (2016b), the voice outcome can vary significantly depending on how differently surgical intervention shapes the medial surface contour, which may at least partially contribute to the reported large variability in voice outcomes (Anderson *et al.*, 2003).

The goal of the present study was to verify and demonstrate in excised human larynges the effect of changes in medial surface shape on voice production, particularly

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the effect on the glottal closure pattern as demonstrated in Zhang (2016b). Toward translation to clinical intervention of glottal insufficiency, we manipulated the medial surface shape through localized medialization of the vocal folds using a thin cotton-tipped wooden stick and observed its effect on vocal fold vibration. Compared with a full-size implant as often attempted in medialization laryngoplasty, the small dimension of the stick allowed us to minimize changes in vocal fold stiffness, more accurately target specific sites on the medial surface for localized medialization, and thus identify regions on medial surface shape that, when manipulated, would produce optimal improvement in voice outcome. Our hypothesis was that localized medialization at a more inferior location on the medial surface would increase the vertical thickness, and thus would yield better improvement on the glottal closure pattern. Conceptually, our experiment was similar to the intraoperative trial and error process in medialization laryngoplasty to identify the ideal implant shape and positioning, or the manual test described by Isshiki (1989) that is performed to predict the outcome of medialization laryngoplasty and identify the site for implant insertion to achieve the best outcome.

2. Method

Two adult human larynges, from a 73-yr-old male (M73) and a 77-yr-old female (F77), were harvested from autopsy less than 48 h postmortem and quick-frozen at −80 °C. One day before the experiment, the larynx was allowed to thaw overnight at −4 °C and soaked in isotonic saline the morning of the experiment until completely thawed. The epiglottis and false vocal folds were removed. A rectangular laryngoplasty window was then created on the right fold using an otologic drill. The inferior edge of the window was placed parallel to and about 2 mm from the inferior border of the thyroid cartilage. The superior edge was placed at the level of the true vocal folds, which were about half-way between the thyroid notch and the inferior border of the thyroid cartilage. The anterior edge was placed 5 mm posterolateral to the thyroid cartilage midline, and the posterior edge was 10 mm posterolateral to the anterior edge. The windows were approximately 10 mm × 5 mm. The cartilaginous glottis was closed by a suture placed through the two arytenoid cartilages.

The excised larynges were mounted onto an air supply pipe to simulate tracheal air pressure and flow, as described in previous experiments (Zhang *et al.*, 2015). Briefly, the setup consisted of a pressurized and regulated airflow supply, an expansion chamber that simulated the lungs (rectangular cross-section 42 cm × 42 cm × 48 cm), and a straight circular PVC tube to simulate the trachea (11 cm long cylinder with an inner diameter of 2.54 cm). The larynges were held motionless with a hose clamp over the trachea and non-penetrating circumferential pins.

Manipulation of medial surface shape was achieved similarly as in medialization laryngoplasty. Instead of a full-size implant, however, we used a wooden stick (7.6 mm long with a 2-mm diameter) laterally inserted into the laryngoplasty window to locally medialize the vocal folds. The small dimension of the stick allowed us to more accurately target specific sites on the medial surface for localized medialization, and evaluate the effect of different medialization locations on the produced voice. In this study, three locations along the vertical direction (superior, middle, inferior) and three locations along the longitudinal direction (anterior, middle, posterior) were investigated, resulting in a total of nine locations on the medial surface for each larynx. Targeting at different longitudinal and vertical locations was achieved by manually adjusting the horizontal and vertical orientation of the stick (Fig. 1). The placement of the three longitudinal locations was visually verified from a superior view from above. The superior view also facilitated the verification of the vertical placement of the target site because medialization at more inferior locations often led to a more divergent resting shape of the medial surface. The vertical distance between the three vertical sites was estimated to be about 5 mm, based on the orientation of the wooden stick and the insertion depth,

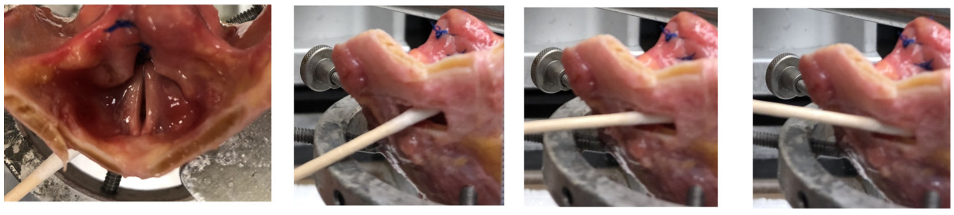

Fig. 1. (Color online) Localized medialization by inserting a wooden stick into the laryngoplasty window. Leftmost panel shows the experimental setup from a superior view. The three panels on the right show the orientation of the wooden stick aimed toward superior, middle, and inferior medialization, respectively.

which was comparable to the typical vertical dimension of human medial surface, confirming that the nine target sites were either on or near the medial surface.

For each larynx, the airflow was set at a constant value (320 ml/s for M73 and 340 ml/s for F77). Although no further flow adjustments were made during the experiment, manipulation of the medial surface shape did change the glottal resistance and led to small fluctuations in the mean subglottal pressure and flow, as described in Sec. 4 below. Acoustic and aerodynamic data as well as high-speed recordings of vocal fold vibration were collected for the baseline condition (without the wooden stick; condition 0) and the nine conditions of localized medialization (conditions 1–9). The mean subglottal pressure (measured at 2 cm from the entrance of the glottis using a Baratron 220 D pressure transducer, MKS Instruments, Inc., Andover, MA), mean flow rate (MKS 558 A mass-flow meter, MKS Instruments, Inc., Andover, MA), and outside acoustic pressure (20 cm downstream and 30° off axis using a B&K 2669 microphone) were measured. Vocal fold vibration was imaged using a high-speed camera (Phantomv711, Vision Research) from a superior view at 8000 frames per second. A MATLAB-based code extracted the glottal area waveform, from which the CQ, minimum and maximum glottal areas in pixels were calculated. To evaluate the effect of localized medialization on the produced voice, the voice spectra were calculated. The cepstral peak prominence (CPP), a measure of the relative differences between the harmonic and inharmonic energy in the voice spectrum (Hillenbrand *et al.*, 1994), was also calculated from the outside sound pressure.

3. Results

Figure 2 shows the CQ, minimum, and maximum glottal area in pixels, and CPP at different conditions of localized medialization. Both larynges had a considerable membranous glottal gap at the baseline condition, and thus barely vibrated at the set flow rate, as indicated by the small differences between the minimum and maximum glottal areas in Fig. 2. Localized medialization at all nine conditions reduced the glottal gap considerably, and led to sustained vocal fold vibration.

A noticeable effect of the vertical location of medialization can be observed. An example is shown in Fig. 3, which compares vocal fold vibration of larynx M73 at the baseline condition, and conditions with localized medialization at three different vertical sites. The minimum glottal areas were considerably smaller for the middle and inferior sites of medialization than conditions with superior medialization. Complete glottal closure during phonation was achieved for five of the six non-superior sites of medialization, as indicated by a non-zero CQ in Fig. 2 (top row). In the three conditions with inferior sites of medialization, the lower margin of the medial surface can be clearly seen (e.g., the third frame in the bottom row of Fig. 3) as the vocal fold medial surface alternated between a convergent and divergent shape. This contrasts with conditions with superior medialization in which the medial surface was hidden from the superior view during the entire cycle of vibration. This improved closure pattern in conditions with middle and inferior medialization led to a noticeably stronger excitation of higher-order harmonics in the output voice (Fig. 4), and the increased CPP values (Fig. 2, bottom).

In general, localized medialization led to smaller changes in larynx F77. However, similar trends were observed for larynx F77. For example, the minimum glottal area was significantly lower for conditions with middle and inferior medialization, although only one of the nine conditions exhibited complete glottal closure. As a result, the CPP values were improved in conditions of middle and inferior medialization, but the degree of improvement was smaller than that for larynx M73. Medialization at inferior locations in F77 also led to vibration with an alternatingly convergent and divergent medial surface shape, as compared to the medial surface hidden from the superior view for other medialization conditions.

4. Discussion and conclusion

The goal of this study was to verify previous findings that medial surface shape plays an important role in voice production, particularly in regulating the glottal closure pattern of vocal fold vibration (Zhang, 2016b). Changes in medial surface shape in this study were achieved through localized medialization. The results showed that the voice outcome, as quantified by CPP and the excitation of higher-order harmonics in output acoustics, was generally better when the medialization was performed at locations in the middle or inferior portion of the medial surface, which led to improved glottal closure during vibration.

It is unlikely that these observed changes were caused by changes in the subglottal pressure due to changes in the glottal resistance associated with different sites of medialization. While there was a noticeable increase in the mean subglottal pressure

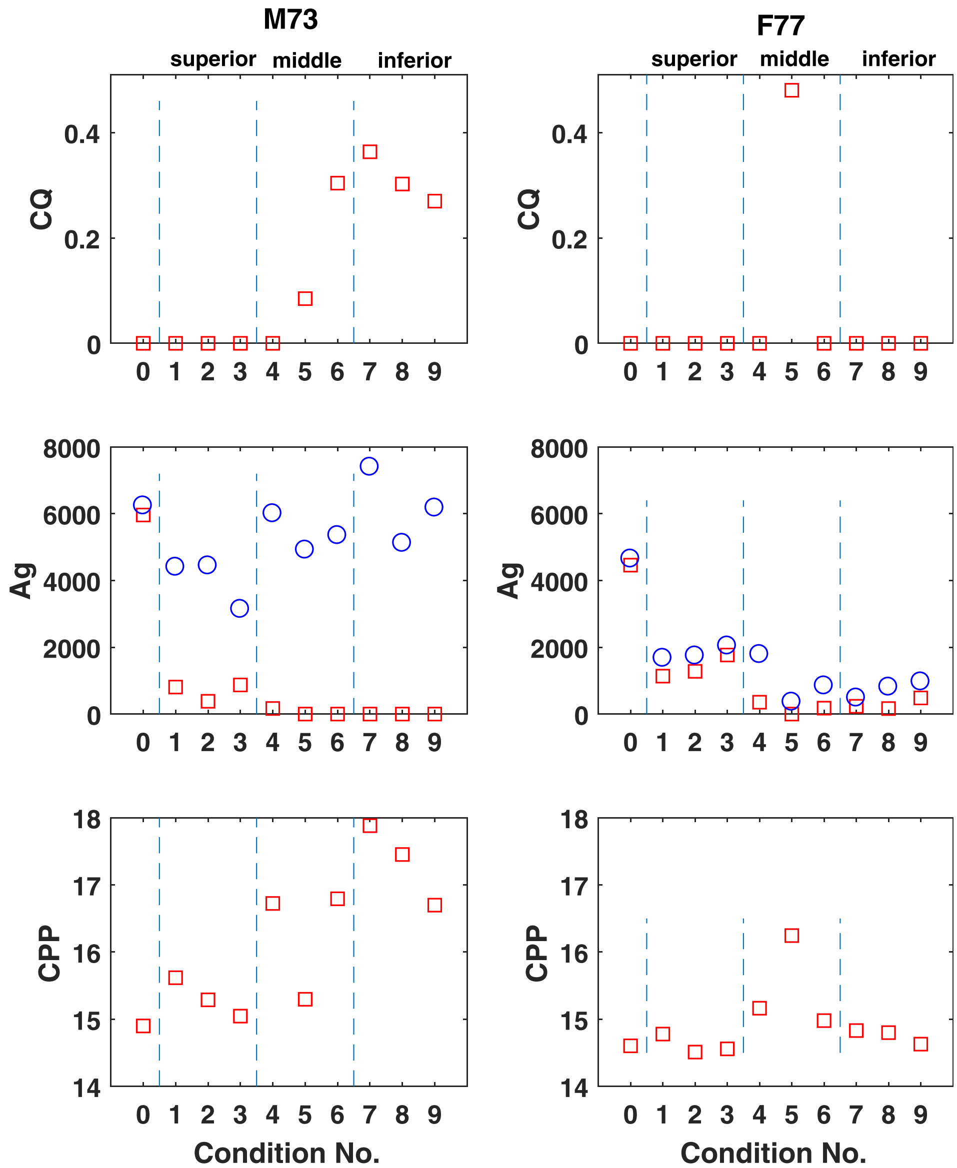

Fig. 2. (Color online) CQ (top row), minimum (squares) and maximum (circles) glottal areas in pixels (middle row), and CPP (bottom row) for the baseline condition 0 and the nine medialization conditions for the two larynges. In each panel, the vertical lines separate four regions that correspond from left to right the baseline condition, conditions with superior, middle, and inferior medialization. The medialization locations for the nine conditions are: (1) superior-anterior; (2) superior-middle; (3) superior-posterior; (4) middle-anterior; (5) middle-middle; (6) middle-posterior; (7) inferior-anterior; (8) inferior-middle; and (9) inferior-posterior.

from baseline to conditions of medialization (from 0.35 to 0.64 Pa for M73, and 0.73 to 1.32 kPa in F77), the mean subglottal pressure and flow rate remained generally the same across the nine medialization conditions. For M73, the subglottal pressure varied between 0.64 ± 0.07 kPa, and the mean flow varied between 320 ± 15 ml/s. For F77, the subglottal pressure and flow varied between 1.32 ± 0.17 kPa and 343 ± 27 ml/s, respectively. The small variations in both the subglottal pressure and airflow also indicated that the degree of medialization, or reduction in prephonatory glottal gap, was comparable across all nine conditions of medialization.

Thus, it is reasonable to conclude that the observed changes in the glottal closure pattern and acoustics were due to changes in medial surface shape. Although not directly visualized, considering the small dimension of the wooden stick, it is reasonable to assume that medialization at a superior location would decrease the vertical thickness of the medial surface, whereas medialization at an inferior location would increase the vertical thickness (Fig. 5). Thus, the results appeared to confirm the observation of Zhang (2016b) that increased vertical thickness improves glottal closure. The effect of this difference in the vertical thickness is twofold (Zhang, 2016b). First, increased thickness allows the vocal fold to maintain an adductory position against the airflow, thus improving glottal closure. Second, an increased thickness means that,

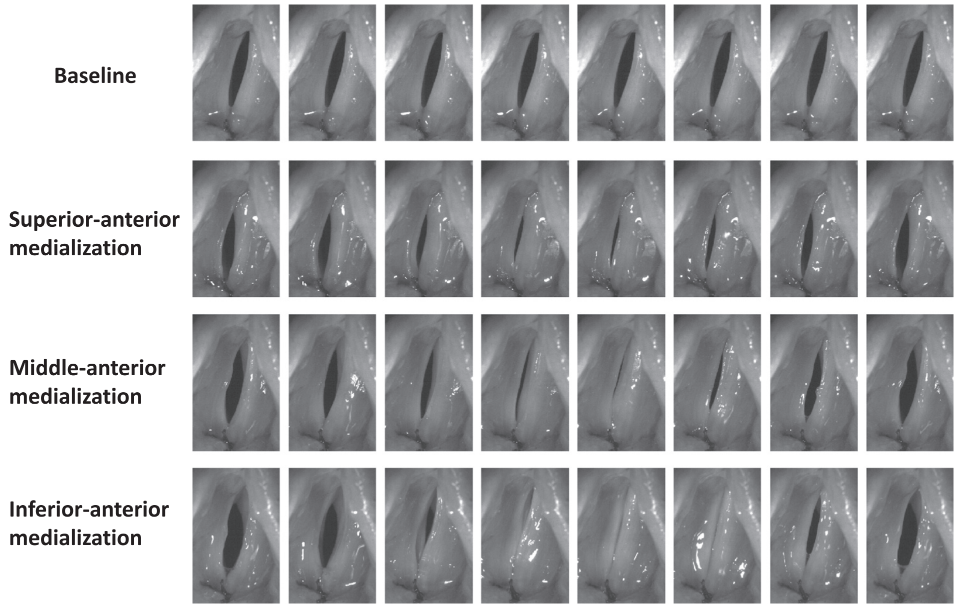

Fig. 3. Larynx M73. Superior view of vocal fold vibration at eight equal-spaced instants over one oscillation cycle for the baseline condition, and conditions with superior-anterior, middle-anterior, and inferior-anterior medialization.

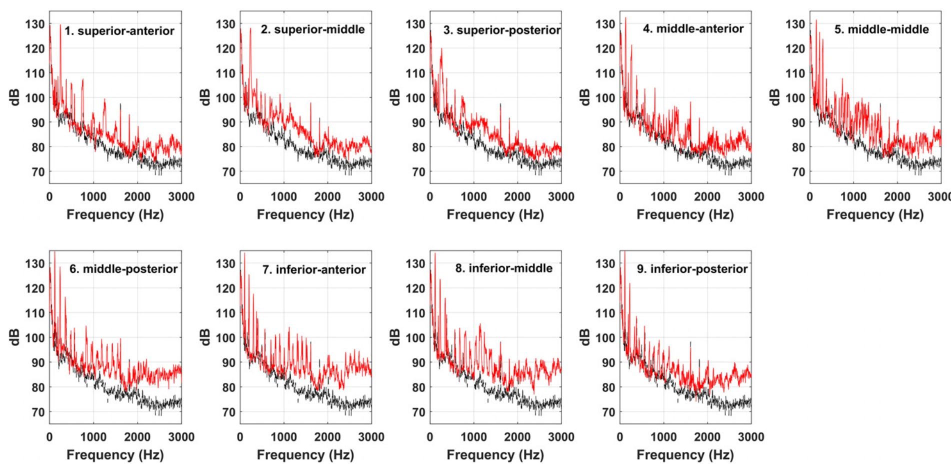

Fig. 4. (Color online) Spectra of outside sound pressure (solid red lines) for the nine medialization conditions in larynx M73. The dashed line in each panel is the spectrum from the baseline condition without medialization.

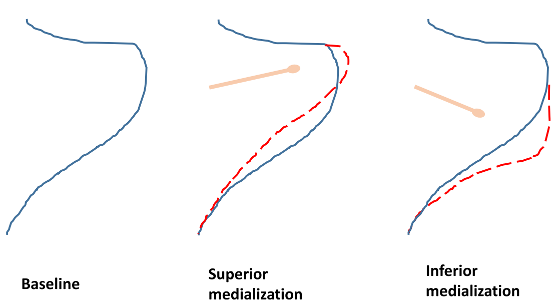

Fig. 5. (Color online) Hypothesized changes in medial surface shape due to different orientations of the wooden stick. Localized medialization at a superior location on the medial surface would decrease the medial surface vertical thickness, whereas medialization at an inferior location would increase the vertical thickness. Solid lines indicate medial surface contour at the baseline condition, and dashed lines indicate modified surface contour due to localized medialization.

when the lower margins of the medial surface start to open, the glottis would continue to remain closed until the upper margins start to open, thus prolonging the duration of glottal closure or the CQ. This phase difference between the opening of the upper and lower margins of the medial surface can be clearly observed in conditions of inferior medialization (Fig. 3 for M73).

Overall, the results of this study showed that in addition to medialization, surgical intervention of glottal insufficiency should also consider the impact of intervention on the medial surface shape. In fact, our results showed that if the medial surface shape is not properly controlled, the same degree of medialization can result in highly variable voice outcomes (Fig. 2).

It is interesting to note that an inferior localized medialization alone, instead of a full-size implant as often attempted in medialization laryngoplasty surgery, was able to cause M73 to vibrate with complete glottal closure for an extended duration, and this was achieved while the other fold was not medialized at all. This appears to imply that medialization location, rather than implant size, has a more important role in determining the voice outcome of medialization surgery.

One main limitation of this study is that the medial surface contour was not directly measured during the experiment. Also, the position and orientation of the wooden stick were manually controlled. It would be worthwhile to repeat the experiment with more precise control of the stick position and direct imaging of the medial surface contour in a hemi-larynx setup.

Acknowledgments

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