Influence of left-right asymmetries on voice quality in simulated paramedian vocal fold paralysis

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Abstract

Purpose: To determine the vocal fold structural and vibratory symmetries important to vocal function and voice quality in a simulated paramedian vocal fold paralysis.

Method: A computational kinematic speech production model was used to simulate an exemplar “voice” based on asymmetric settings of parameters controlling glottal configuration. These parameters were then altered individually to determine their effect on maximum flow declination rate, spectral slope, cepstral peak prominence, harmonics-to-noise ratio, and perceived voice quality.

Results: Asymmetry of each of the five vocal fold parameters influenced vocal function and voice quality, with measured change greatest for adduction and bulging. Increasing the symmetry of all parameters improved voice, and the best voice occurred with “overcorrection” of adduction, followed by bulging, nodal point ratio, starting phase, and amplitude of vibration.

Conclusions: While vocal process adduction and edge bulging asymmetries are most influential in voice quality for simulated vocal fold motion impairment, amplitude of vibration and starting phase asymmetries are also perceptually important. These findings are consistent with the current surgical approach to VFMI, where goals include medializing the vocal process and straightening concave edges. The results also explain many of the residual post-operative voice limitations.

Introduction

People with unilateral vocal fold motion impairment secondary to vocal fold paresis or paralysis (VFMI) frequently seek evaluation and management of weak, breathy voice. Surgical treatments improve voice quality by increasing closure of the glottal airspace during phonation, though some level of voice handicap or limitation often remains. A likely reason for continued dysphonia is residual asymmetries of vocal fold shape and muscle tone resulting in vibration asymmetries, a hypothesis examined in the current study.

Multiple structural and vibratory laryngeal asymmetries can occur with unilateral VFMI secondary to vocal fold paresis or paralysis. Reduced mobility of one arytenoid is the pathognomic feature of unilateral VFMI, with possible asymmetries of lateral-medial, superior-inferior, and anterior-posterior arytenoid position. Other asymmetries of structure and gross function include ipsilaterally enlarged ventricle, bowed (i.e., concave) edge, thinned immobile fold, vertical plane difference at rest or during phonation, and tilting towards the intact side (Isshiki & Ishikawa 1976; Yamada, Hirano, & Ohkubo, 1983; Yumoto, Nakano, & Oyamada, 2003). People with VFMI often present with constriction of the supraglottis in the form of anterior-posterior constriction and/or medial movement of the ventricular folds, particularly the contralateral ventricular fold (Pinho, Pontes, Gadelha, & Biasi, 1999; Bielamowicz, Kapoor, Schwartz, & Stager, 2004).

The left-right differences in structure, gross function, and muscle tone can lead to incomplete glottal closure, left-right (**L-R**) and anterior-posterior (**A-P**) vibratory asymmetry, aperiodic vibration, and altered amplitude of vibration and mucosal wave (Kokesh, Flint, Robinson, & Cummings, 1993; Hirano & Mori, 2000; Omori, Slavit, Kacker, Blaugrund, & Kojima, 2000; Eysholdt, Rosanowski, & Hoppe, 2003; Schwarz et al., 2006). Left-right vibratory

asymmetries (i.e., phase differences) and frequency differences between the vocal folds have been documented, sometimes shifting over time or increasing in magnitude and then resetting (von Leden & Moore, 1961; Wittenberg, Tigges, Mergell, & Eysholdt, 2000). Smaller vocal fold velocity and acceleration have also been reported for paralyzed folds than healthy folds (Lohscheller & Eysholdt, 2008).

The asymmetries might lead to slower opening and closing of the glottal airspace and a shorter time period where the airspace is maximally closed, observed as a more rounded glottal area waveform (A_g) with a longer open quotient (Q_o). A more rounded A_g will likely cause the glottal flow (U_g) to be closer to a sinusoid, though the anatomic and functional differences in supraglottal shape and vocal tract inertance will also influence U_g . A nearly sinusoidal U_g , with its associated gradual glottal flow shut-off, has been hypothesized to lead to higher amplitude of the fundamental frequency (f_o or **HI**) relative to other harmonics, energy loss causing increased first formant bandwidth, and rapid drop-off of harmonic amplitude across the source and acoustic spectra (Fischer- Jørgensen, 1967; Huffman, 1987; Hillenbrand, Cleveland, & Erickson, 1994). Complicating these expected spectral changes, turbulent DC flow will likely lead to noise in the region of F3 (Klatt & Klatt, 1990; Hillenbrand et al., 1994). As a group, these changes are consistent with breathy voice quality (Fischer- Jørgensen, 1967; Huffman, 1987; Klatt & Klatt, 1990; Hillenbrand et al., 1994), along with decreased loudness, roughness, diplophonia, asthenia, high pitch, and strain (Kiritani, Hirose, & Imagawa, 1993; Billante, Clary, Childs, & Netterville, 2002; Hartl, Hans, Vaissière, & Brasnu, 2003).

Injection laryngoplasty, medialization thyroplasty, and arytenoid adduction, three mainstays of treatment for unilateral VFMI, improve voice quality by altering the position and contour of the edge of the immobile vocal fold, increasing closure of the glottal airspace during

phonation. These procedures are generally effective in improving voice quality, though not always facilitating return to “normal” function. In one study, for example, 92% of 15 patients more than one year status post thyroplasty reported that the surgery improved their voice, yet only 13% were “extremely happy” with post-operative voice (Gray, Barkmeier, Jones, Titze, & Druker, 1992), citing continued challenges achieving adequate loudness, quality differences such as breathiness and hoarseness, altered sensations such as a need to clear the throat or throat tension, and functional limitations such as fatigue or needing to modify job responsibilities (Gray et al., 1992). Hogikyan, Wodchis, Terrell, Bradford, and Esclamado (2000) reported that the voice related quality of life (V-RQOL) scores were higher (better) for patients with vocal fold paralysis treated with type I thyroplasty than patients with untreated paralysis, yet not as high as for controls with normal voice. Leder and Sasaki (1994) reported that the number of breath groups during a standard reading passage was higher for patients status post thyroplasty than for normophonic controls.

Comparing patients with unilateral VFMI to a normative data set, Billante et al. (2002) found that 12 months post medialization thyroplasty with or without arytenoid adduction, voices were commonly rated as mildly breathy. Maximum phonation time, frequency range, jitter and shimmer remained abnormal, though intensity and mean airflow rate returned to the normal range (Billante et al., 2002). In another study, pre-to-post treatment improvement in postoperative voice quality, stroboscopic ratings, and voice handicap were reported for injection laryngoplasty using calcium hydroxylapatite or micronized acellular dermis, and for medialization thyroplasty with or without arytenoid adduction. Post-treatment values generally remained outside normal ranges (Lundy, Casiano, McClinton, & Xue, 2003). Thompson, Maragos, and Edwards (1995) reported improvements in glottal closure, amplitude of vibration,

and musosal wave after thyroplasty with or without arytenoid adduction, and six of the nine patients demonstrating preoperative asymmetric vibration continued to have asymmetric vibration postoperatively.

It is proposed that continued dysphonia is due to residual asymmetries of vocal fold shape and muscle tone with subsequent asymmetric vocal fold vibration. The effects of individual structural and vibratory vocal fold asymmetries when all other parameters were fully symmetric were described in Samlan, Story, Lotto, and Bunton (2014). When vocal process adduction, edge bulging, or nodal point ratio (an estimate of the pivot point of the rotational vibratory mode) was the only asymmetry present, the asymmetric parameter led to perceived voice quality changes. Isolated vibratory phase or amplitude asymmetries did not cause perceivable changes in voice quality (Samlan et al., 2014). Though it is important to understand the functional outcomes of individual parameter deviations from symmetry, it became clear during early work that the functional effects of any particular parameter manipulation were dependent upon the settings of the other parameters.

Continued subtle asymmetries of a group of vocal fold structural and vibratory parameters are hypothesized to explain some of the postoperative variability in vocal fold vibration and voice quality situations where glottal closure appears adequate yet patients continue to experience functional limitations of VFMI. The first aim of this study was to assess the vocal function effects of a constellation of slight asymmetries, none of which alone produced dramatic changes in vocal function or voice quality. Three asymmetries were programmed into a kinematic vocal fold model, creating an asymmetric exemplar. Model output was compared to the results generated using fully symmetric settings. It was expected that these minimal

asymmetries would cause measureable differences in vocal function in comparison to the fully symmetric case.

The second aim was to determine how systematically modifying symmetry of each of the five model parameters would alter the vocal function and voice quality of the asymmetric exemplar. It was hypothesized that, contrary to findings when the exemplar was fully symmetric (Samlan et al., 2014), all five parameters would affect vocal function and voice quality.

Speech Production Model

The speech production model consisted of a kinematic vocal fold model (Titze, 1984; Titze, 1989; Titze, 2006) aerodynamically and acoustically coupled to a wave reflection model of the trachea and vocal tract (Liljencrants, 1985; Story, 1995; Titze, 2002; Story, 2005) configured in the /a/ vowel shape described in Story (2008). The model is depicted in Figure 1. In this model, glottal flow is produced by the interaction of the glottal area with the acoustic pressures in the trachea and vocal tract. As detailed in previous publications, a noise component was added to the glottal flow when the Reynolds number (Re) within the glottis exceeded 1200 (Samlan & Story, 2011; Samlan, Story, & Bunton, 2013). All simulations were completed using a vocal tract consistent with an adult male and fundamental frequency of 100 Hz.

Five parameters specifying the left and right vocal fold surfaces were set independently. Brief descriptions of the parameters are provided in Table 1 and additional detail about each parameter can be found in Samlan et al. (2014). The parameters modified included: 1) adduction (ξ_{02}), 2) edge bulging (ξ_b), 3) nodal point (z_n), represented as the ratio of the nodal point to the thickness of the folds (z_n/T or R_{zn}), 4) amplitude of vibration (*Asym*), and 5) starting phase (φ).

Method

The purpose of Experiment I was to determine the effects of a combination of minimal asymmetries on voice production and vocal function. An asymmetric exemplar “speaker” was created using the kinematic speech production model described above. Parameter settings for the exemplar, or base, voice are listed in Table 2, and animations of their simulated vibration can be viewed in the online supplemental material. Three asymmetries were imposed to be consistent with a slight difference in left and right laryngeal muscle innervation (i.e., vocal fold paralysis): 1) the left edge bulging value, ξ_b , was 0 cm, so that the left edge was flat while the right edge was slightly convex at $\xi_b = 0.1$ cm, 2) the nodal point ratio was slightly lower for the left ($R_{zn} = 0.6$) than the right ($R_{zn} = 0.8$), and 3) an 80 degree starting phase difference was introduced (left $\phi = 1.4$ radians, right $\phi = 0$ radians). Vocal process position and amplitude of vibration were symmetric: left and right $\xi_{02} = 0.1$ cm, $Asym = 1.0$. The asymmetric base voice was compared to a fully symmetric base voice, whose settings for the left vocal fold surface were identical to those shown in Table 2 for the right fold. Comparison of the asymmetric and symmetric voices was completed through examination of glottal area (A_g), glottal flow (U_g), and output pressure (P_{out}) (analogous to the microphone signal) waveforms and spectra.

Five acoustic measures were computed from P_{out} . Maximum flow declination rate (**MFDR**) was measured from the derivative of U_g . The first and second harmonic amplitudes were measured using a peak-picking algorithm (Titze, Horii, & Scherer, 1987), corrected for the amplitude of the first formant (**F1**) as described by Hanson (1997), and their difference computed (**H1*-H2***). Mean RMS energy was calculated for three frequency bands of the P_{out} spectra: 59-398 Hz (**B0**), 395-2003 Hz (**B1**), and 2003-5001 Hz (**B2**). Two measures of spectral tilt were computed from these bands: B0-B1 and B0-B2 (deKrom, 1995; Hartl et al., 2003). The cepstral peak prominence (**CPP**) was measured from the cepstrum of P_{out} using VoiceSauce,

implemented in MATLAB (Shue, Keating, Vicenik, & Yu, 2011, downloaded from <http://www.phonetics.ucla.edu/voicesauce/>). VoiceSauce calculates CPP based on the method described by Hillenbrand et al. (1994). The harmonics-to-noise ratio (*HNR*) was calculated for a 250 ms steady state segment of P_{out} using a Praat script (Boersma & Weenink, 2010; Boersma, 1993).

The purpose of Experiment II was to determine the acoustic and perceptual effects of systematically modifying asymmetry of one parameter while others remained slightly asymmetric. The speech production model was programmed to produce 30 different steps of each of the five previously described parameters (ξ_{02} , ξ_b , R_{zn} , *Asym*, ϕ) while the remaining variables were maintained at their base settings (middle two columns of Table 2). The ranges through which the left surface was manipulated are found in the final column of Table 2. The 30 productions of each variable led to 150 unique /a/ vowels. The A_g , U_g and P_{out} for each simulation were simultaneously collected. The effects of the five kinematic model parameters on the six measures of vocal function were assessed qualitatively.

Perceptual rating: Twenty naïve listeners were recruited from the general population at the University of Arizona. All study procedures were approved by the University of Arizona Institutional Review Board. Every listener was at least 18 years of age and passed a 25 dB HL hearing screening at 0.5, 1, 2, and 4 KHz (ASHA, 1997).

The perceptual consequences of worsening or improving each model parameter individually were assessed using a visual sort-and-rate task (Granqvist, 2003; Esposito, 2010; Samlan & Kreiman, 2014). Each of the 20 listeners rated every sample. The listeners rated the samples through a series of six separate rating tasks presented in a randomized order. The stimuli for five of the rating tasks were 15 audio signals for a specific parameter, equally spaced across

the range listed in Table 2. Icons representing and linked to each of the 15 audio files were displayed on a monitor. Participants were instructed to arrange icons from worst voice to best voice, with the physical distance between the shapes representing the degree of difference. The parameter group and stimuli order were randomized for each listener and stimuli were represented by randomly selected icons (Figure 2). Responses were coded by distance from the left endpoint, with stacked stimuli assigned the same value.

In a sort-and-rate task, the distances among the stimuli relate only to those judged within the same task. Since it is not possible to compare stimuli across tasks (e.g., how the best voice achieved through improving symmetry of vibratory amplitude compares the best voice simulated using increased bulging), a sixth sort-and-rate task using three settings of each of the five parameters was created. The settings represent the most asymmetric, middle, and most “corrected” values.

Ratings were analyzed using PROXSCAL multidimensional scaling (MDS). Stepwise linear regressions were completed for each of the rating tasks to determine which of the acoustic measures explained the most variance in the MDS coordinates. Statistical analysis was completed using IBM SPSS[®] Statistics, Version 20.

Results

Experiment I: Comparison of asymmetric to fully symmetric exemplar

The mildly impaired exemplar used in the current study (“asymmetric”) was compared to the fully symmetric exemplar to determine the combined effects of the three small asymmetries. Figure 3a shows the schematic of the model at maximum contact for the symmetric (left column) and asymmetric (right column) cases. Left and right vocal processes are positioned 0.1 cm from midline for both cases. Observe that the edge contour (bulging) is symmetric in the image on the

left and the left surface is flat ($\xi_b = 0$ cm) in the image on the right. In the section above the surfaces, contact area is shown in red and A_g in blue, with the particular location in the vibratory series given by the end point in each trace; that is, maximum contact and minimum area.

Figure 3b shows four cycles of the glottal area, A_g , (symmetric on the left and asymmetric on the right) and 3c the time derivative of the glottal area (dA_g/dt , which will hereafter be referred to as dA_g for simplicity). Measures of these waveforms are compared in Table 3. Quotients were calculated using a baseline of 10% peak-to-peak amplitude. The maximum negative peak of dA_g is the maximum area declination rate (**MADR**). Note that the mild bulging, nodal point ratio, and starting phase asymmetries of the asymmetric exemplar increased maximum and minimum area, led to longer open phase, and decreased the closing velocity relative to the symmetric case.

The interaction of A_g with the vocal tract led to skewed U_g relative to A_g (Figure 3d). In comparison to the symmetric signal, increased minimum and maximum flow, more sinusoidal flow, and decreased MFDR were measured for the asymmetric exemplar (Table 3). Glottal flow spectral slope was steeper for the asymmetric exemplar, with noise replacing harmonic energy after approximately 500 Hz (Figure 3f).

The pressure signal radiated from the lips (P_{out} ; Figure 3g) results from interaction of the glottal flow with the pressures and shape of the vocal tract. Audio files of these signals can be found in the on-line supplementary materials. Compared to the P_{out} of the symmetric voice, the P_{out} for the asymmetric voice demonstrated reduced amplitude of the periodic component and smaller magnitude of the primary negative pressure pulse. The P_{out} spectrum (Figure 3h) of the asymmetric voice revealed steeper spectral slope and less prominent formants than for the symmetric exemplar. Acoustic measures reflected these changes: $H1^*-H2^*$ and $B0-B1$ increased,

and B0-B2, CPP, and HNR decreased (Table 3). Note that the B0-B2 grouped with CPP and HNR, as it likely represents increased noise energy in the B2 region.

In summary these minimal asymmetries of bulging, nodal point ratio and phase led to changes in all signals when compared to a fully symmetric exemplar. The A_g became more rounded, U_g more sinusoidal with a DC offset, and MFDR decreased. The spectral slope became steeper in the low frequencies and inharmonic replaced harmonic energy in the higher frequencies.

Experiment II: Symmetry modifications

In this experiment, the effects of increasing and eliminating individual asymmetries were determined by sweeping each of the five left-sided parameters through the range of values listed in the right-most column Table 2, one at a time, while all other parameters remained set as specified for the asymmetric exemplar (two middle columns of Table 2). The changes to vocal function measures are described below, followed by changes to perceived voice quality.

Relation of asymmetries to vocal function measures

The changes that occurred in each of the six vocal function measures as a particular model parameter was modified are shown in Figures 4 through 8. In each figure, the model parameter is on the x-axis, with the most asymmetric value at the left and most “corrected” value on the right side of the graph. Changing the parameter values from those at the left to those at the right edge of the graph, therefore, was always expected to improve vocal function. One vocal function measure is on the y-axis for each panel. Table 4 lists the “best” (maximum or minimum, as appropriate) value of every vocal function measure for the five parameters so that the changes occurring as the result of the individual parameter “corrections” can more easily be compared to the remaining parameters.

Adduction asymmetries (ξ_{02}): The influence of ξ_{02} on measures of vocal function was evident when left ξ_{02} was set to 0.4 cm, then decreased to symmetry ($\xi_{02} = 0.1$ cm) and continued past midline to $\xi_{02} = -0.1$ cm (Figure 4). MFDR increased 128,626 cm³/s² to a maximum value of 156,180 cm³/s² as ξ_{02} decreased from 0.4 (left border of the figure) to -0.07 cm. H1*-H2* decreased by 22.2 dB to a minimum of -2.9 dB as ξ_{02} decreased from 0.4 cm to -0.1 cm. The ratio B0-B1 increased 20.5 dB as ξ_{02} decreased from 0.4 to 0.09 cm (near the symmetric ξ_{02} value) reaching a maximum of 11.3 dB before it decreased 16.5 dB to a minimum of -4.8 dB at $\xi_{02} = -0.1$. Spectral slope measure B0-B2 increased by 33.1 dB to a maximum of 22.6 dB as ξ_{02} decreased from 0.4 cm to -0.07 cm, then decreased by 12.5 dB as left ξ_{02} continued to decrease. CPP increased by 20.3 dB to a maximum of 35.9 dB as ξ_{02} decreased from 0.4 cm to -0.1 cm. The sharpest rise in CPP occurred from approximately $\xi_{02} = 0.05$ to $\xi_{02} = -0.1$ cm. HNR increased by 42.8 dB to a maximum of 42.8 dB as ξ_{02} decreased from 0.4 cm to -0.1 cm. Most of that increase, 37.5 dB, occurred between the ξ_{02} settings of 0.05 and -0.1 cm.

In summary, as ξ_{02} for the asymmetric exemplar decreased from 0.4 cm to -0.1 cm, MFDR, CPP, HNR, and B0-B2 increased and H1*-H2* decreased. These findings are consistent with decreasing severity of dysphonia with decreasing vocal process separation. Most of the CPP and HNR increase occurred when the left adduction was set at or medial to the symmetric value.

Bulging asymmetries (ξ_b): In the asymmetric exemplar, the baseline setting for bulging was 0 cm. The effects of decreasing left ξ_b to -0.05 cm and increasing it to 0.15 cm are found in Figure 5. Decreasing left ξ_b to -0.05 cm decreased MFDR by 21,372 cm³/s², and increasing left ξ_b from -0.05 cm to 0.15 cm increased MFDR by 45,768 cm³/s² to a maximum MFDR of 154,606 cm³/s². Decreasing bulging from 0 cm to -0.05 cm increased H1*-H2* by 2.7 dB. H1*-H2* decreased by 8.5 dB to a minimum of 2.4 dB as ξ_b increased from -0.05 to 0.15 cm. B0-B1

decreased by 0.3 dB when ξ_b decreased from 0 cm to -0.05 cm and decreased by 8.6 dB to a minimum of 2.1 dB as ξ_b increased from -0.05 to 0.15 cm. B0-B2 decreased by 2.8 dB as ξ_b decreased from 0 cm to -0.05 cm and increased by 11.5 dB to a maximum of 20.5 as ξ_b increased from -0.05 to 0.05 cm. CPP decreased by 1.1 dB as left ξ_b decreased to -0.05 cm and increased by 7.5 dB as ξ_b increased from -0.05 cm to 0.15 cm. HNR decreased by 2.4 dB as left ξ_b decreased to -0.05 cm, and increased by 16.4 dB as ξ_b increased from -0.05 cm to 0.15 cm.

In summary, increasing the convexity of the vocal fold edge from $\xi_b = -0.05$ to 0.15 cm caused changes in MFDR and the spectrum consistent with decreasing severity of dysphonia. MFDR, B0-B2, CPP, and HNR increased, while H1*-H2* and B0-B1 decreased. Values did not reach those attained through decreasing ξ_{02} .

Nodal point ratio asymmetries (R_{zn}): The left R_{zn} was both decreased and increased from the base value of 0.6, while the right R_{zn} was maintained at 0.8. Results are shown in Figure 6. MFDR was lowest ($118,001 \text{ cm}^3/\text{s}^2$) at $R_{zn} = 0.43$ and increased from that mid-thickness location by $24,622 \text{ cm}^3/\text{s}^2$ as R_{zn} decreased to 0.1 and by $32,315 \text{ cm}^3/\text{s}^2$ to a maximum of $150,316 \text{ cm}^3/\text{s}^2$ as R_{zn} increased to 0.9. The highest H1*-H2* (17.3 dB) occurred at $R_{zn} = 0.21$. H1*-H2* decreased by 0.8 dB as R_{zn} decreased to 0.1 and by 11.6 dB as R_{zn} increased to 0.9, where it reached its lowest value of 5.7 dB. The highest B0-B1 was 11.6 dB, occurring when $R_{zn} = 0.51$. A 1.7 dB decrease occurred as R_{zn} decreased to 0.1 and a 5.2 dB decrease as R_{zn} increased to 0.9. The lowest B0-B2 was 8.8 dB at $R_{zn} = 0.16$, with B0-B2 increasing 0.4 dB as R_{zn} decreased to 0.9 and B0-B2 increasing 5.6 dB as R_{zn} increased to 0.9. The minimum CPP of 16.9 dB occurred at $R_{zn} = 0.38$. CPP increased by 1.4 dB as R_{zn} decreased to 0.1 and increased 5.2 dB to a maximum CPP of 22.4 dB as R_{zn} increased to 0.9. HNR increased by 6.9 dB to a maximum of

6.8 dB as R_{zn} increased from 0.1 to .90. Most of this increase occurred between R_{zn} settings of 0.6 and 0.9.

In summary, increasing left R_{zn} from the lowered setting of the asymmetric exemplar caused MFDR, CPP, B0-B2, and HNR to increase, and H1*-H2* and B0-B1 to decrease. Returning the left vocal fold to a higher R_{zn} improved vocal function even in the setting of persistent bulging and phase asymmetries.

Asymmetric amplitude of vibration (Asym): The Asym value for the asymmetric exemplar was 1.0, indicating no baseline amplitude asymmetry. For this group of simulations, the vibratory amplitude of the left surface was set to 0% of that of the right surface ($Asym = 0$), and then gradually increased until it was equal to the amplitude of the right surface ($Asym = 1$). With the return to symmetry, changes in acoustic measures were small and are shown in Figure 7. MFDR increased $50,348 \text{ cm}^3/\text{s}^2$ to a maximum of $124,777 \text{ cm}^3/\text{s}^2$. H1*-H2* decreased 3.1 dB to a minimum of 8.5. B0-B1 varied by 1.0 dB over the Asym range and B0-B2 increased 2.2 dB, CPP by 3.7 dB, and HNR by 1.4 dB.

In summary, decreasing left amplitude of vibration to zero in the context of the asymmetric base voice produced very small changes in vocal function that improved as vibratory amplitude was gradually increased. As left amplitude increased from 0 to 100% of that of the right, H1*-H2* decreased, and MFDR, B0-B2, CPP, and HNR increased.

Starting phase asymmetries (ϕ): The left and right folds were out of phase by 1.4 radians for the asymmetric base voice. As observed in Figure 8, the lowest MFDR occurred when the left ϕ was 2.4 radians and MFDR increased $63,310 \text{ cm}^3/\text{s}^2$ to a maximum of $140,353 \text{ cm}^3/\text{s}^2$ as left ϕ decreased to 0 (i.e., symmetric). Over the same range of ϕ values, H1*-H2* decreased 11.1 dB to a minimum of 5.4 dB, B0-B1 decreased by less than 1.0 dB, and B0-B2 increased by 3.5 dB to a

maximum of 12.5 dB. CPP increased 4.0 dB to 20.1 dB as ϕ returned to symmetry, and HNR increased 2.4 dB to its maximum value of 3.1 dB at 0.76 radians.

As with symmetry of vibratory amplitude, increasing the vibratory phase difference between the folds worsened vocal function. Even the 1.4 radian phase shift present in the asymmetric base voice influenced vocal function, as seen through improved measures with increased symmetry. As with amplitude asymmetry, the impact was much smaller than for the other three parameters.

Relation of individual asymmetries to perception

Comparative influence of individual parameters on perceived quality: The relative influence of each of the parameters on perceived overall voice quality was determined using MDS. A one-dimensional solution fit the data well for each model parameter. Dispersion Accounted For, *DAF*, was greater than or equal to 0.97, indicating the distances in the solution described at least 97% of the variance in the ratings. Though the direction of ratings is not maintained in the MDS solutions, mean ratings were higher for the most corrected (sample 15) than the most asymmetric (sample 1) sample for all five parameters rated. For ease of interpretation, MDS solutions are therefore displayed so that the samples rated lowest are on the left side of the figure and highest are on the right.

Adduction asymmetries (ξ_{02}): The MDS solution for voice quality of the adduction samples is shown in Figure 9a, with the most asymmetric sample (#1; $\xi_{02} = 0.4$ cm) anchoring the figure on the left and the most over-corrected adduction (#15; $\xi_{02} = -0.08$ cm) anchoring the figure on the right. In general, listeners perceived each 0.03 cm ξ_{02} increment as different, and each movement towards (or past) midline as successively better. Two measures explained significant variance in the MDS coefficients: H1*-H2* and B0-B2 (Adjusted $r^2=0.994$,

$F(1,12)=1157.6, p<.05$). Both measures correlated highly ($r > .9$) with one another and with MFDR.

Bulging asymmetries (ζ_b): Voice quality improved as bulging increased from -0.05 cm (#1) to 0.14 cm (#15; Figure 9b). With a few exceptions, each 0.01 cm increase in bulging led to improved voice quality. One measure explained significant variance in the MDS coefficients: B0-B2 (Adjusted $r^2=.966$, $F(1,13)=399.483, p<.05$). B0-B2 correlated highly ($r > .9$) with each of the five remaining measures.

Nodal point ratio asymmetries (R_{zn}): In general, voice quality was perceived as the worst when nodal point ratio was 0.21 to 0.38 (#3 through #6; Figure 9c) and best when nodal point ratio was 0.82 to 0.87 (#14 and #15). Nodal point ratios of 0.54-0.65 (#9 through #11) were perceived between the two extremes. B0-B2 best explained the MDS coefficients (Adjusted $r^2=.939$, $F(1,13)=215.754, p<.05$) and correlated highly ($r > .9$) with H1*-H2*, CPP, HNR.

Asymmetric amplitude of vibration (Asym): Listeners perceived differences in voice quality as left amplitude of vibration was altered (Figure 9d). Though voice quality did not improve in a monotonic manner as left amplitude increased to that of the right, the vowels rated as worst were simulated using the smallest left-sided amplitudes ($Asym \leq 0.14$), and vowels identified as best were simulated using higher vibratory amplitudes ($Asym \geq 0.76$). The measure MFDR explained the most variance for amplitude of vibration ratings (Adjusted $r^2=.907$, $F(1,13)=137.665, p<.05$). MFDR correlated highly ($r > .9$) with H1*-H2*, B0-B2, and CPP.

Starting phase asymmetries (ϕ): Although raters perceived differences in voice quality with incremental changes to left phase symmetry (Figure 9e), they did not perceive a monotonic improvement with increased symmetry. The most asymmetric starting phases (i.e., left starting phase of 2.4 to 2.1 radians) produced the worst voice quality. The voice perceived as “best” was

not simulated using symmetric starting phase, but when left ϕ was 0.41 radians. Vowels simulated with more symmetric starting phase settings ($\phi = 0.91$ to 0.08 radians) were rated as better than those less symmetric, and the largest changes between adjacent samples occurred for intermediate starting phase values ($\phi = 2.07$ to 0.91 radians). Together, H1*-H2* and B0-B2 explained significant variance in the MDS coordinates (Adjusted $r^2 = .982$, $F(1,13) = 389.859$, $p < .05$). H1*-H2* and B0-B2 correlated highly ($r > .9$) with one another and with MFDR, CPP, and HNR.

Relative influence of model parameters on perceptual rating: The relative influence of each of the model parameters on perceived overall voice quality was assessed through the sixth sort-and-rate task. Again, a one-dimensional solution adequately explained the variability in listener results (DAF = .97). As observed in Figure 10, adduction (rust-colored markers) had the most substantial influence on voice quality, with the highest rating occurring for the vowel simulated with the left process crossing midline ($\xi_{02} = -0.08$ cm, A3) and the lowest rating for the vowel where the left process was set farthest from midline ($\xi_{02} = 0.4$ cm, A1). High bulging (B3, green marker), high nodal point (N3, blue marker), medium bulging (B2), and increased phase symmetry (P3, purple marker) were rated as improving voice quality relative to the vowel whose configuration was closest to baseline Pete (V3, pink marker). Other modifications worsened voice quality relative to V3. Low or medium nodal point ratio (N1, N2), decreased bulging (B1), and medium reduction in left amplitude of vibration (V2) worsened quality to a smaller extent, while increasing the distance of the left vocal process from midline (A2), large left-right phase difference (P1), and elimination of left vibratory amplitude (V1) worsened quality to a larger degree. Audio and video samples from the highest and lowest values of each parameter modification can be found in the supplemental materials.

Stepwise linear regression showed adduction, bulging, and vibratory amplitude explained a significant amount of variance in MDS solution (Adjusted $r^2=.65$, $F(1,11)=9.839$, $p<.05$). Three vocal function measures (H1-H2, MFDR, and HNR) together explained significant variance in the MDS solution (Adjusted $r^2=.941$, $F(1,11)=75.353$, $p<.05$).

Discussion

A computational model was used to vary individual anatomic or kinematic features of the vocal folds, alone and in combination, and determine the effects of each feature on vocal function and voice quality. In Experiment I, we determined that small left-right asymmetries of edge bulging (ξ_b), nodal point ratio (R_{zn}), and starting phase (ϕ) negatively changed vocal function, even in the context of symmetric vocal process adduction. The changes that occurred in the A_g , U_g , and output pressure signals were similar to those described for breathy voice by Fischer- Jørgensen (1967), Huffman (1987), Hillenbrand et al. (1994), and Klatt & Klatt, (1990), and summarized in the introduction. The vocal fold surfaces closed the glottal airspace slightly less than in the symmetric exemplar, even though the vocal process adduction (ξ_{02}) values were identical for the two exemplars. To determine whether the incomplete closure was the primarily the result of decreased bulging, nodal point ratio, or starting phase, the minimum area of the asymmetric exemplar was compared the cases where only one of the three asymmetries was present. The minimum area for the exemplar (0.0209 cm^2) was higher than for any of the individual components (0.0113 cm^2 for ξ_b , 0.0040 for R_{zn} , and 0.0024 for ϕ), demonstrating that the glottal area changes were not the result of just a single component parameter.

The glottal area and glottal flow skewing quotients were lower for the asymmetric exemplar, reflecting slower decreases in area and flow than occurred for the symmetric exemplar. The glottal flow skewing that occurs secondary to interaction with pressures of the

sub- and supra-glottal vocal tract was weaker for the asymmetric exemplar, the consequences of which were illustrated in the asymmetric exemplar's steeper spectral slope. Taken together, these changes indicate that the combination of three small asymmetries (bulging, nodal point ratio, and starting phase) modified the voice signal in a manner consistent with breathy voice quality.

The asymmetric exemplar used in this first experiment became the basis for Experiment II, where individual model parameters were manipulated to determine how they worsened and improved the vocal function and voice quality of the asymmetric exemplar. While all five parameters influenced vocal function and voice quality, the largest and most consistent improvements occurred with “overcorrection” of adduction (i.e., moving ξ_{02} from the symmetric value of 0.1 cm to, and slightly past, midline). Overcorrection of bulging resulted in the next highest improvement, followed by increased symmetry of nodal point ratio, starting phase, and amplitude of vibration. Highly asymmetric adduction, decreased phase symmetry, and decreased left amplitude of vibration worsened voice quality. In spite of the finding that 0.1 cm overcorrection improved voice more than midline placement, cautious clinical interpretation is recommended, given that overcorrection might lead to patient sensations (e.g., fullness, need to clear throat, etc.) that would limit benefit.

Even though some changes in quality were likely larger than others, naïve listeners were able to distinguish differences in voice quality with manipulation of each parameter. The changes to voice quality with adduction, bulging, and amplitude of vibration were almost monotonic, in that almost every increment of parameter setting in the direction hypothesized to improve voice resulted in better voice quality. This was not the case for changes to nodal point ratio or starting phase, though there were patterns of better voice with higher nodal point ratio and more phase symmetry and worse voice with lower nodal point ratio and less phase symmetry. The finding

that each parameter negatively and positively influenced voice quality and vocal function augments the understanding of asymmetry gained from Samlan et al. (2014), demonstrating the importance of the context of a particular asymmetry. When other asymmetries are present, unilateral amplitude and starting phase asymmetries have more influence on voice quality than when amplitude of phase is the sole asymmetry.

The current study demonstrated one context in which amplitude and starting phase asymmetries are perceptually important. Even though setting the adduction and bulging values to cross midline overrode the effects of the other three asymmetries, nodal point ratio, amplitude and phase asymmetries affected voice quality when glottal closure was less complete. The findings are consistent with the current surgical approach to VFMI, where goals include medializing the vocal process and straightening concave edges. The results also explain many of the residual voice limitations post-operatively. The findings provide direction to clinicians, in that working towards improving the remaining asymmetries should further improve voice quality in patients with VFMI.

Clinical Application:

As discussed in the introduction, differences in left-right starting phase and amplitude of vibration might be expected as part of normal left-right asymmetries in human bodies and behavior, though asymmetry is also a hallmark of disordered vocal fold patterns. As part of a constellation of mild asymmetries in the current study, however, phase and amplitude asymmetries increased dysphonia and worsened measures of vocal function beyond what was achieved with any of the asymmetries alone. Improving phase and amplitude asymmetries improved voice quality, even in the context of other asymmetries. The discussion below

highlights how the five asymmetries investigated (adduction, bulging, nodal point ratio, phase, and amplitude) are likely mitigated using current treatments for VFMI.

Medical treatments that might improve laryngeal nerve regeneration in some cases of unilateral VFMI are under investigation (Mattsson, et al., 2005; Hydman, Remahl, Björck, Svensson, & Mattsson, 2007; Mori et al., 2007; Hydman, Björck, Persson, Zedenius, & Mattsson, 2009; Rosen et al., 2014; Sridharan, Rosen, Smith, Young, & Munin, 2015), though surgical treatment to improve voice quality remains the standard of care. Surgical approaches fall into the general categories of arytenoid adduction, medialization (e.g., injection or thyroplasty), and reinnervation. Each type of treatment might alter multiple vocal fold structure and kinematic properties, though through different mechanisms. Arytenoid adduction would primarily alter vocal process adduction (ξ_{02}), possibly resulting in a straight, as opposed to concave, bulging value (ξ_b), increased amplitude of vibration (Asym) and decreased L-R phase difference (ϕ) (Kokesh et al., 1993). The goal for medialization thyroplasty and injection laryngoplasty is typically improved ability of the vocal folds to close the glottal airspace through medial displacement of the membranous vocal fold, changing the contour of the medial edge (adduction (ξ_{02}) and bulging (ξ_b) parameters of the kinematic model). As with arytenoid adduction, improved ability to close the airspace might also improve Asym and ϕ . In addition, it is likely that the distribution of mass, shape of the edge thickness (e.g., convergent, divergent, or rectangular), muscle activation, and aerodynamic quantities influence the nodal point ratio (R_{zn}). Nerve regeneration, either through surgically-guided reinnervation or spontaneous post-injury regeneration, is the only method to restore neurologic input to the immobilized thyroarytenoid muscle. The resulting central input, corresponding with the intact neurologic signals to the contralateral vocal fold, may offer the greatest likelihood of correcting residual nodal point,

phase and amplitude asymmetries, which appear to be important in perception of poor voice quality in a minimally asymmetric model with adequate glottal closure.

Further investigation is necessary to better predict the effects of individual or combinations of asymmetries on voice when other asymmetries are more substantial. Future directions would also include investigation of how the vertical location of increased bulging affects vocal function.

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Table 1: Speech production model parameters

Symbol	Parameter name and description	Definition
ξ_{02}	Adduction, vocal process separation	Distance, in mm, of the superior aspect of the vocal process from midline during vibration. Larger values reflect vocal process positioning further from midline.
ξ_b	Bulging, edge contour	Curvature of the medial surface of the vocal fold in the vertical dimension. Likely reflects thyroarytenoid muscle contraction (Alipour & Scherer, 2000). Expected value in a healthy vocal fold $\approx 0.1 - 0.2$ mm (Titze, 2006). Decreased ξ_b means a less curved edge, negative ξ_b indicates a concave (i.e., bowed) edge.
$R_{zn}, z_n/T$	Nodal point ratio, pivot point ratio	Nodal point is the pivot point around which the rotational mode changes phase. Represented as the ratio of the nodal point to the thickness of the folds (z_n/T). The “normal” value is not known. A high nodal point indicates greater vibratory mass and larger amplitude of the lower portion of the folds (Titze & Story, 2002).
Asym	Asymmetry, left amplitude of vibration, amplitude asymmetry	The amplitude of vibration of the right vocal fold surface was determined by rule based on vocal fold length, lung pressure, and threshold pressure (Titze, 2006). Amplitude of left vocal fold surface was scaled as a percentage of the right. A value of “1” indicates equal amplitude.
ϕ	Starting phase	Difference in timing between lateral-medial movements of the two folds, in radians. Both surfaces set at $\Phi = 0$ radians indicates that the vocal fold surfaces move as mirror images so that they are at midline and maximum amplitude at the same time instants as one another.

Table 2: Parameter values for the baseline voice. The highlighted values were asymmetric.

	Right vocal fold surface	Left vocal fold surface	Range (L)
ξ_{02} (cm)	0.1	0.1	0.4 to -0.01
ξ_b (cm)	0.1	0	-0.05 to 0.15
R_{zn}	0.8	0.6	0.1 to 0.9
Asym	-	1.0	0 to 1
φ (radians)	0	1.4	2.4 to 0

Table 3: Vocal function measures for exemplar voices. A_g = glottal area; Q_o = open quotient; Q_s = speed quotient; MADR = maximum area declination rate; U_g = glottal flow;

	Symmetric	Asymmetric
Maximum A_g (cm²)	0.1	0.14
Minimum A_g (cm²)	≈ 0	0.02
$A_g Q_o$	0.46	0.60
$A_g Q_s$	1.2	0.99
MADR (cm²/s)	67	52.5
Maximum U_g (cm³/s)	265.4	317
Minimum U_g (cm³/s)	9.2	74
$U_g Q_o$	0.49	0.66
$U_g Q_s$	1.6	1.3
MFDR (cm³/s²)	194,279	124,777
H1*-H2* (dB)	1.5	8.5
CPP (dB)	25.2	18.7
B0-B1 (dB)	0.1	11.4
B0-B2 (dB)	19.3	10.9
HNR (dB)	15	2.4

Table 4: Comparison of best (maximum or minimum) vocal function measures across parameters. The best value for each measure is highlighted in bold font and the worst value in italic font.

Parameter	Maximum MFDR (cm ³ /s ²)	Minimum H1*-H2* (dB)	Minimum B0-B1 (dB)	Maximum B0-B2 (dB)	Maximum CPP (dB)	Maximum HNR (dB)
ξ_{02}	156,180	-2.9	-4.8	26.6	35.9	42.8
ξ_b	154,606	2.4	2.1	20.5	26.1	17
R_{zn}	150,316	5.7	6.4	14.4	22.4	6.8
Asym	<i>124,777</i>	<i>8.5</i>	<i>11.1</i>	<i>11.4</i>	<i>19.6</i>	<i>2.3</i>
φ	140,353	5.4	10.1	12.5	20.1	3.1

Figure Legends

Figure 1: Vocal fold model

Figure 2: Sort and Rate Task Each shape was linked to an audio file and the shapes dragged from the top half of the screen (where the blue rectangle and oval shapes are sitting) down to the horizontal line and arranged in order from the worst voice (left) to best voice (right), with the physical distance between the shapes representing the degree of difference.

Figure 3: Figures in the left column results of the symmetric exemplar and figures in the right column are results of the asymmetric exemplar. a) Model schematic at maximum glottal closure b) Glottal area (A_g) c) Derivative of the glottal area (dA_g) d) Glottal flow (U_g) e) Derivative of the glottal flow (dU_g) f) Spectrum of the glottal flow g) Output pressure (P_{out}) h) Spectrum of the output pressure

Figure 4: Changes in vocal function measures with decreasing left ξ_{02} (adduction): a) MFDR, b) $H1^*-H2^*$, c) B0-B1, d) B0-B2, e) CPP, and f) HNR.

Figure 5: Changes in vocal function measures with increasing left ξ_b (bulging): a) MFDR, b) $H1^*-H2^*$, c) B0-B1, d) B0-B2, e) CPP, and f) HNR.

Figure 6: Changes in vocal function measures with increasing left R_{zn} (nodal point ratio): a) MFDR, b) $H1^*-H2^*$, c) B0-B1, d) B0-B2, e) CPP, and f) HNR

Figure 7: Changes in vocal function measures with increasing left Amplitude of Vibration (increasing Asym) a) MFDR, b) $H1^*-H2^*$, c) B0-B1, d) B0-B2, e) CPP, and f) HNR.

Figure 8: Changes in vocal function measures with decreasing left starting phase: a) MFDR, b) $H1^*-H2^*$, c) B0-B1, d) B0-B2, e) CPP, and f) HNR.

Figure 9: Perceived voice quality with changes in model parameters: a) adduction (ξ_{02}), b) bulging (ξ_b), c) nodal point ratio (R_{zn}), d) asymmetry (Asym), and e) starting phase (Φ).

Figure 10: Perceived voice quality changes across model parameters: MDS solution where A = adduction, B = bulging, N = nodal point ratio, V = asymmetry (amplitude of vibration), P = phase. A letter followed by the number 1 is the most asymmetric of that parameter, 2 = midpoint value of that parameter, and 3 = most symmetric or overcorrected value of that parameter.

Number of trials remaining: 6

Next trial

Worst
voice

Best
voice

a

b

c

d

e

f

g

h

a) Adduction

b) Bulging

c) Nodal Point Ratio

d) Amplitude of Vibration

e) Starting Phase